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REVIEW

Copper in plant protection: current situation and prospects

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Summary. Copper has been used in agriculture to control oomycetes, fungi and bacteria for over a century. It plays important roles in integrated pest management, but is essential in organic farming, where disease management depends almost exclusively on its use. However, the use of this heavy metal may have log-term consequences due to its accumulation in the soil, which appears incompatible with organic farming's objectives. This awareness led the European Union to establish maximum limits on copper in organic farming since 2002 (Commission Regulation 473/2002), and further decisions on its use in crop protection are to be taken soon. At present, copper compounds are approved as plant protection products until 31 January 2019. This review examines the current state of copper use, the regulatory framework, and limits set for copper in organic farming. Strategies to reduce copper inputs are also considered, including: preventive phytosanitary measures, innovative formulations with reduced copper content, optimization of copper dosages, the use of forecasting models, the use of resistant varieties, optimization of agriculture management, and natural alternatives to copper-based products. This review also examines the main research projects exploring farming practices and appropriate alternatives to copper use for the control of plant pathogens. The review highlights that, while there is currently no replacement for this heavy metal having the same plant protection effectiveness, agronomic measures and management practices can be combined to reduce the amounts of copper used for this purpose.

Key words: copper ion, heavy metal, organic farming, integrated pest management, plant protection products.

Background

General information

Copper is an oligo-element essential for life, that participates in cellular physiological processes, such as energy production (Alaoui-Sossé, 2004), synthesis of phospholipids (Gallagher and Reeve, 1971) and haemoglobin (Elvehjem and Hart, 1929), iron absorption and transport (Alam and Raza, 2001), and ribonucleic acid production. It is present in almost all foods, with most human diets naturally including between 1 and 2 mg of copper per person per day (EFSA, 2018). Copper is present in the ecosystem, and agricultural soils contain the metal in varying degrees. The soil copper inputs from agrarian sources are essentially from manure, sewage sludge, fertilizers and pesticides (Mantovi, 2003). Copper use in agriculture began in the 1880s with Pierre-Marie-Alexis Millardet's discovery of a lime-copper mixture which is still known as "Bordeaux mixture" (McBride *et al*., 1981; Borkow and Gabbay, 2005). Since that time, copper has been used in agriculture as a fungicide and bactericide. The spectrum of activity of copper compounds involves many phytopathogenic microorganisms, making this metal one of the major components of fungicide and bactericide formulations throughout the world. While copper continues to play key roles in integrated pest management, it is essential for organic farming, since disease management in this system depends almost exclusively on its use.

Mechanism of action in plant protection

The active ingredient is the cupric ion (Cu^{++}); in the presence of rainwater and other environmental factors such as carbon dioxide in the air and dew, it

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acts against oomycetes, fungi and bacteria. Copper ions act non-specifically (multisite) at the cell membrane level, leading to the denaturation of structural and enzymatic proteins and altering membrane semipermeability. The copper ions dissolved in water layers on plant surface can enter the cell protoplasm of oomycetes, fungi and bacteria. Four classes of transporters have been implicated in copper transport: COPT, ZIP, YSL, and HMA (Williams *et al*., 2000; Burkhead *et al*., 2009; Aguirre and Pilon, 2016). Once inside the cells, copper ions interfere with numerous enzymatic reactions, blocking respiratory activity with consequent inhibition of spore germination. Copper is used as protectant, which means that copper ions must be present on plant surfaces before diseases occur.

Pathogen resistance to copper is unlikely to develop because of the multisite mode of action of copper ions. Oomycetes and fungi have shown no resistance to the various copper compounds, as reported by Fungicide Resistance Action Committee (FRAC, 2018). However, several bacterial pathogens have developed resistance to the metal. Bacterial resistance was observed in 1983 in *Xanthomonas campestris* pv. *vesicatoria* (Marco and Stall, 1983). In 1986, resistance was discovered in *Pseudomonas syringae* pv. *tomato* (Bender and Cooksey, 1986) and then in other pseudomonads (Sundin *et al*., 1989; Cooksey, 1990; Andersen *et al*., 1991; Goto *et al*., 1991). Copper tolerance has also been demonstrated in populations of *Erwinia amylovora* (Sholberg *et al*., 2001). The selection of copper-resistant strains is the major reason for disease control failures following management with copper bactericides (Behlau *et al*., 2012).

Copper resistance in bacteria is regulated by several genes (Cooksey, 1990) generally located in mobile genetic elements (plasmids, transposons) (Bondarczuk and Piotrowska-Seget, 2013). As reported by Yin *et al*. (2017), the main mechanisms regulating copper resistance in bacteria include: (1) the efflux ATPase pump encoded by copA can extrude copper ions from the cytoplasm into the periplasmic space (Rensing and Grass, 2003); (2) the cus system, where the cusA gene encodes a resistance nodulation cell protein with an antiport system (Outten *et al*., 2001); (3) the pco system, which encodes a multicopper oxidase protein responsible for the oxidation of copper (I) to copper (II) in the periplasmic space (Brown *et al*., 1997); (4) the cue system, which is the main mechanism responsible for copper resistance in *Escherichia coli*, where cueO encodes a periplasmic multicopper oxidase (Outten *et al*., 2001; Rensing and Grass, 2003); and (5) tcrB in *Enterococcus faecium* belongs to the CPX-type ATPase family of heavy metal transporters (Henrik and Frankm, 2002).

Effects on soil

Copper is applied as a contact protective foliar spray, so it remains deposited on leaf surfaces and is not absorbed into plant tissues. For this reason, the metal reaches the soil following application, through mechanical wind action or after being washed off by rain or irrigation. Since copper cannot be degraded, and its removal from the soil is negligible through leaching, run-off or plant uptake, this heavy metal can potentially remain as a contaminant in the environment for long periods and cause bioaccumulation and toxicity (Flores-Vélez *et al*., 1996; Eisler, 1998; Torres and Johnson, 2001; Xiong and Wang, 2005; Komárek *et al*., 2010; Mackie *et al*., 2012; Lamichhane *et al*., 2018). Since it is a metallic element, copper does not break down and continues to cycle in the environment after release (Eisler, 1998). Thus, repeated use of copper-based bactericides and fungicides to control plant diseases leads to copper accumulation in the soil. The metal interacts with soil constituents, rendering it insoluble and preventing percolation towards deep soil layers. Therefore, it tends to accumulate in surface soil layers with concentration decreasing with depth (Deluisa *et al*., 1996; Flores-Vélez *et al*., 1996; Leonardi *et al*., 2002; Ceccanti, 2004). Several surveys examining copper concentrations in soils show significant variations among and within countries (Komárek *et al*., 2010; Mackie *et al*., 2012). Table 1 presents concentrations of total copper recorded in topsoil of different vineyards in Europe, Australia and Brazil. Variations in copper concentration also depend on the production method. In fact, while conventional agriculture may use different types of pesticides (contact, cytotropic, translaminar or systemic pesticides), organic farming primarily uses cupric compounds for disease management, due to the lack of valid alternatives. Studies examining organic and conventional vineyards in Central Italy found greater concentrations of copper in organic vineyard soils compared with conventional vineyards (Beni and Rossi, 2009). Although limit values of copper in soil are set from 50 to 140 mg kg^{-1} of dry matter (Council Directive 86/278/EEC), it is difficult to establish the

Table 1. Total copper concentrations reported in vineyard topsoils (data from Komárek *et al*., 2010; Mackie *et al*., 2012).

Continent	Country	Total copper (mg kg^{-1})	Methods used	Reference
Europe	Czech Republic	2–168	$O_2 + O_3 + NOx$ at 400°C + $HNO_3 + HF$	Komárek *et al*., 2008
	France	323	HF	Flores-Vélez *et al*., 1996
		248–378	$HClO_4 + HF$	Besnard *et al*., 2001
		20–251	$HNO_3 + HCl$	Brun *et al*., 2001
		57–332	$LiBO_2$ at 550°C + HNO_3	Parat *et al*., 2002
		22–398	$HClO_4 + HF$	Chaignon *et al*., 2003
		17–34	$HClO_4 + HF$	Dousset *et al*., 2007
	Island	50–276	Digestion with aqua regia (ISO 11466, 1995)	Runjić and Čustović, 2017
	Italy	9–945	$HNO_3 + HCl$	Deluisa *et al*., 1996
		215–372	$HNO_3 + HCl$	Dell'Amico *et al*., 2008
	Portugal	58–130	-	Magalhães *et al*., 1985
	Slovenia	87–120	$HNO_3 + HCl$	Rusjan *et al*., 2007
	Spain	25–272	$HNO_3 + HCl + HF$	Fernández-Calviño *et al*., 2008
		55–112	$HNO_3 + HCl + HF$	Fernández-Calviño *et al*., 2009
Americas	Brazil	37–3216	$HNO_3 + HClO_4 + HF$	Mirlean *et al*., 2007
Oceania	Australia	9–249	15.5 M HNO_3	Pietrzak and McPhail, 2004
		6–223	$HNO_3 + HCl$	Wightwick *et al*., 2008

concentration of copper capable of causing toxicity to plants, as this does not depend on total copper content in the soil but on the proportion of available copper (forms of the metal that can be used by plants). Copper occurs in soils in different forms (ionic, complexed and precipitated) depending on soil characteristics such as texture, organic matter and pH. These factors vary in the environment, modulating copper availability and possible deficiency or toxicity (Flemming and Trevors, 1989). For example, Toselli *et al.* (2006) found a reduction in the growth of grapevines at copper concentrations above 400 mg kg^{-1} in sandy soils, while copper concentrations of 1,000 mg kg^{-1} in clay soils did not have this effect (Deluisa *et al*., 2007).

Copper is immobilised by various components (carbonates, iron oxides) or can be absorbed by colloids (clay minerals, organic fraction and humic substances) (Schiatti and Nutricato, 2006) that reduce available copper. The fate of organic substance-bound copper depends on the nature of the organic molecule to which it binds. The metal forms very stable complexes with the less soluble fractions of the organic molecules, while soluble organic molecules retain copper in solution (with favourable effects in copper shortage conditions and unfavourable effects in excess copper conditions) (Arias *et al*., 2006; Karlsson *et al*., 2006; Komárek *et al*., 2010). The complexes copper forms with humic and fulvic acids are probably the most important copper retention mechanisms in soils (Komárek *et al*., 2010).

In conclusion, if a soil is rich in organic substances with a good degree of humification, copper is less likely to remain in the soluble phase because it is attracted to the soil particles and is less available for plants, and the risk of phytotoxicity is low (Martin, 2009). Absorption, precipitation and complexation reactions are also influenced by pH (Janik *et al*., 2015); copper is immobilized as insoluble precipitates in alkaline soils, while the concentration of copper remaining in solution increases with decreases in pH, resulting in increased copper availability for plants (Mozaffari *et al.*, 1996; Martin, 2009).

Effects on micro and macroorganisms

Accumulation of copper is hazardous to micro and macroorganisms (McBride *et al.*, 1981; Mackie *et al.*, 2012). Microorganisms are generally more sensitive to copper than other organisms in soil biocoenosis (Giller *et al.*, 1998). Copper contamination can greatly modify both the size of microbial biomass and soil processes (Giller *et al.*, 1998; Kunito *et al.*, 2001). High copper concentrations can lead to reduced activity of some terrestrial microorganisms. These include bacteria (particularly *Azotobacter*, *Clostridium, Nitrosomonas* and *Nitrobacter*), particularly in acidic soils with low cationic exchange capacity (Fregoni and Bavaresco, 1984; Fregoni and Corallo, 2001), and fungi (Rühling *et al.*, 1984; Arnebrant *et al.*, 1987; El-Sharouny *et al.*, 1988; Gadd, 1993; Levinskaitë, 2001; Lugauskas *et al.*, 2005). Rajapaksha *et al.* (2004) demonstrated that fungal communities were more resistant to copper contamination than bacterial communities.

High copper concentrations can also reduce populations of earthworms and carabids (Paoletti *et al.*, 1988; Stefanelli, 1993; Donnarumma and La Torre, 2000; Klein, 2011). This can significantly disrupt the ecological balance, since earthworms play key roles in preserving healthy ecosystems (Maregalli, 2017). Several authors, reviewed by Beyer (1981), reported that earthworms can take up and accumulate heavy metals in their tissues. Chemicals from soil are taken up by earthworms, both dermally and orally (Vijver *et al*., 2003; Hobbelen *et al*., 2006). Body concentrations of copper may be attributed completely to the dermal uptake (Vijver *et al.*, 2003). Some authors have suggested that earthworms may avoid toxic copper levels by migrating to uncontaminated soil. They may also adapt to certain levels of contamination, although their reproductive capacity may be reduced (Langdon *et al*., 2001; Neaman *et al*., 2012; Bednarska *et al*., 2017). Earthworms are typical ecosystem engineers having major impacts on soil structure (Blouin *et al.*, 2013), with their activity affecting biotic and abiotic soil properties and plant growth (van Groenigen *et al.*, 2014). Studying the effects of copper amounts on soil organism communities, and specifically on earthworms in vineyards, Strumpf *et al*. (2015) suggest that adaptation effects of lumbricids cannot be excluded. Soil organisms may have developed mechanisms for on-demand copper uptake, purging or detoxification (e.g., via stress peptides - metallothioneines) through evolutionary adaptations.

Effects on aquatic organisms

Copper reaches aquatic systems from natural and anthropogenic sources (EPA, 2016). Since agriculture is one of the main anthropogenic sources, this heavy metal may reach and pollute groundwater through land drainage (Nóvoa-Muñoz *et al.*, 2007; Komárek *et al.*, 2010). Because it is moderately soluble in water and binds to sediments and organic matter, copper can interfere with aquatic organisms, such as sediment dwellers, algae, invertebrates and fish. The toxic effects on algae cause alterations in the entire food chain, because they are at its base. This creates cascade effects throughout aquatic ecosystems (Odum, 1971; Wright and Welbourn, 2002; Taub, 2004). Shellfish and fish are also exposed to this heavy metal via the food chain through gill extraction, which is unregulated transport of salts that are vital for the normal functioning of nervous and cardiovascular systems (Solomon, 2009). A study conducted in Trentino (Italy) in a small lowland stream polluted by copper at a concentration of 0.05 mg L^{-1} showed the state of physiological stress of the dipteran *Chironomus riparius.* Chironomidae have been extensively used as a model to test pollutant toxicity in sediments and fresh water environments (Lencioni *et al.*, 2016). Several studies evaluated the responses of copper exposure on coho salmon (*Oncorhynchus kisutch*) across biological scales, from the loss of functional responsiveness of receptor neurons in the olfactory epithelium (Baldwin *et al.*, 2003, 2011; Sandahl *et al.*, 2004, 2007; McIntyre et al., 2008), to the olfactory-mediated behaviour of individual animals (Sandahl *et al.*, 2007; McIntrye *et al.*, 2012), and decreased coho survival in predator–prey interactions after short-term exposure to 5–20 μg L^{-1} of dissolved copper (McIntrye *et al.*, 2012).

Effects on plants

In plants, excess copper adversely affects the metabolic activity of roots and the absorption of nutrients, through antagonist and synergistic effects (Fregoni and Bavaresco, 1984). Copper is normally present in the tissues of many plant species at concentrations ranging from 1 to 50 μg g^{-1} dry weight (Beni and Rossi, 2009). Copper deficiency is detected below

2–5 μg g^{-1} dry weight, while first symptoms of copper phytotoxicity have been recorded at concentrations of 15-20 μg g^{-1} dry weight (NAS, 1977; Yruela, 2005; Xiong and Wang, 2005). Plants growing in contaminated soils can accumulate high concentrations of copper in their tissues (Bargagli, 1998). Heavy metals tend to accumulate in hypogeous structures, with poor translocation to epigeous structures (Torres and Johnson, 2001). The main symptoms of copper excess are impaired root and shoot growth, resulting in less soil exploration by roots (Miotto *et al.*, 2014), nutrient deficiency, chlorosis, and, in severe cases, tissue necrosis and plant death (Marschner, 1995; Kopsell and Kopsell, 2007). Elevated cellular copper concentrations can cause oxidative stress by increasing the concentrations of reactive oxygen species (ROS), such as superoxide anion (O_2^-), singlet oxygen ($^1O_2$), hydrogen peroxide (H_2O_2) and hydroxyl radical (OH^-) (Apel and Hirt, 2004; Miotto *et al.*, 2014). However, there are heavy metal-tolerant plants that show no or very few signs of toxicity, despite growing in highly polluted environments and exhibiting high concentrations of copper in their tissues. These species belong to several families including Cruciferae, Caryophyllaceae, Gramineae, Leguminosae and Asteraceae (Xiong and Wang, 2005).

Effects on human and animal health

Heavy metals can be transferred easily to animals and humans through food chains, causing toxicity problems. For example, a relationship was found between the concentration of copper in *Shirpus robustus* seeds and in the livers of mice (Torres and Johnson, 2001). Studies examining the effects on animals have shown hepatic and gastrointestinal problems caused by copper accumulation, if ingested in large quantities and over long periods (Cohen, 1974; Spitalny *et al.*, 1984; Eife *et al.*, 1999). Sensitivity to copper toxicosis is species dependent. In general, poultry resist chronic copper toxicosis better than most mammals (NRC, 1977). Sheep are particularly sensitive to the toxic effects of copper, since their elimination mechanism is probably less efficient than other animals (Bremmer *et al.*, 1976; Linder and Hazegh-Azam, 1996; Oruc *et al.*, 2009). Oxidative stress is associated with copper toxicity because of redox reactivity, e.g. the ability of free copper or low molecular weight copper complexes to catalyse the reaction between the superoxide anion and H_2O_2, producing the hydroxyl radical (Halliwell, 1999). Copper can also bind to free thiols of cysteines, causing protein crosslinks and their impaired activity (Cecconi *et al.*, 2002). If ingested in large quantities through food or water, copper can also be harmful to humans. These include: gastrointestinal disorders (the symptom threshold is between 4 and 6 mg kg^{-1} of copper; liver damage (e.g. in rats exposed to dietary copper more than 100 times greater than nutritional requirement); immunity and neurological disorders (headache, vertigo, and drowsiness in factory workers exposed to 111–434 mg m^{-3} copper dust); and reproductive dysfunction (sexual impotence was reported in 16% of workers exposed to 111–434 mg m^{-3} copper dust) (Suciu *et al.*, 1981; ATSDR, 2004; Dorsey *et al.*, 2004; Roychoudhury *et al.*, 2016; Tóth *et al.*, 2016).

In their study of cumulative data on subjects exposed to copper or with presumed related dermatological hypersensitivity symptoms, Fage *et al.* (2014) indicated that a weighted average of 3.8% had positive patch test reactions to copper. The same study affirmed that this heavy metal is a very weak sensitizer compared to other metal compounds. However, copper can cause clinically relevant allergic dermatological reactions in some cases. Brewer (2012) considered the ingestion of inorganic copper through diet to be one of the environmental causative factors of Alzheimer's disease. Following inhalation of copper-containing fungicides, farmers have experienced serious acute and chronic respiratory problems, including lung cancer (Zuskin *et al.*, 1997; Santić *et al.*, 2005; Komárek *et al.*, 2010). Some studies have also highlighted that working with copper increases the risk of developing Parkinson's disease (Gorell *et al.*, 2004). Repeated long-term copper intakes greater than 30 mg d^{-1} have toxic effects, intakes of 10 to 30 mg d^{-1} have ill-effects, and intakes of up to 10 mg d^{-1} have no effect on the homeostatic metabolism (EFSA, 2018). However, it is difficult to assess the actual relationships between copper intake and human health because of uncertainties regarding copper concentrations in different foods and water (Bost *et al.*, 2016).

Regulatory frameworks and copper limits

Active substance copper compounds were approved as bactericides and fungicides by Commission Directive 2009/37/EC, but the approval period was limited to 7 years (to 30 November 2016) rather than the canonical 10 years, since the risk assessment revealed ecotoxicological problems. The variants of copper that were approved were copper hydroxide, copper oxychloride, Bordeaux mixture, tribasic copper sulphate and copper oxide, that exhibit different phytosanitary activities depending on their availability to release copper ions in solution (Richardson, 1997; La Torre *et al*., 2002; Muccinelli, 2006; Tomlin, 2009). In 2014, with Commission Implementing Regulation (EU) 85/2014, the expiry of the approval period was postponed to 31 January 2018, to provide notifiers time to complete the renewal process.

Following the examination of additional submitted data, the presence of some areas of concern led the European Commission to request the submission of monitoring programmes for vulnerable areas where copper contamination of the soil and water (including sediments) is, or may become, a concern (Commission Implementing Regulation (EU) 2015/232). This is to allow conclusions on the environmental risk assessments. The same Regulation established that the amounts of copper (application rates and number of applications) must be the minimum necessary to achieve the desired effects and must not cause any unacceptable effects on the environment, taking into account background levels of copper at each application site.

Restrictions on the maximum amounts of metallic copper usable as plant protection products raise the problem of the possibility of copper being applied at high doses as a leaf fertilizer to mask the use of copper-based plant protection products. Allowing the free use of copper as a fertilizer may lead to improper use of the metal, if it is used as a foliar fertilizer at high doses to mask antimicrobial activity that would otherwise require plant protection product authorisation. This illicit situation poses risks for the environment and human health, as well as unfair competition between operators, since fertilizers are not subject to the stringent authorization processes of plant protection products.

On January 2018, EFSA published the conclusions of the peer review of the pesticide risk assessment of active substance copper compounds (EFSA, 2018). Some information, identified as being required by the regulatory framework, was missing, and several concerns were identified. It was concluded that additional information should be requested from the applicants, and that EFSA should conduct expert consultation in the areas of mammalian toxicology, residues, environmental fate and behaviour, and ecotoxicology. The lack of these data prevents completion of the consumer risk assessment based on representative use.

On 19 January 2018, the European Commission approved extension of the approval period for copper compounds to 31 January 2019, because assessment of the substances was delayed for reasons beyond the applicants' control, and copper approvals would have expired before decision on their renewal (Commission Implementing Regulation (EU) 2018/84). In 2015, because copper fulfils two of the criteria (bio-accumulation and toxicity) for persistent, bio-accumulative and toxic (PBT) substances, Commission Implementing Regulation (EU) 2015/408 included copper compounds in the list of candidates for substitution, i.e. the list of active substances that have intrinsic hazard characteristics causing concern. Plant protection products containing candidates for substitution are subjected to a comparative assessment procedure, leading to their gradual replacement with products with safer toxicological and eco-toxicological profiles.

Discussion is currently (2018) underway regarding the possibility of reducing the contribution of copper to agriculture. This reduction must be compatible with actual effectiveness, and consider the use of copper in organic farming. The European Union had already set a maximum limit for the use of copper in organic farming in 2002, expressed in kilograms per hectare per year (Commission Regulation (EC) 473/2002).

The long-term environmental issues caused by copper due to its accumulation in the soil are incompatible with organic farming principles. The current accumulation rate limit is 6 kg ha^{-1} year^{-1}, although Member States may grant exemptions from this for perennial crops. The average quantity applied over 5 years, i.e. the year considered and the previous 4 years, must not exceed 6 kg ha^{-1} year^{-1}. This allows operators to apply more treatments during particularly rainy years, and fewer in drought years. Further limitations on copper use, or even its elimination from the list of authorized plant protection products in organic farming, is being debated in Europe.

The issue of copper use is viewed differently in different countries, because of differing pedoclimatic conditions. This has led to bans on the use of copper in some countries and to limit its use in others. Table 2 reports the restrictions and bans established for copper in some European countries. In Turkey the Organic Regulation is fully harmonized with EU Regulations on organic production, and there are the

Table 2. Restrictions and bans on copper use in some European countries.

Country	Organic farming	Integrated pest management[a]	Reference
Austria	Limit ranges from 2 to 4 kg Cu^{++}/ha/year depending on the crop; for vines, the limit is 3 kg Cu^{++}/ha/year		http://organicrules.org/custom/differences.php?id=2bbc
Czech Republic	Copper use is limited to 3 kg Cu^{++}/ha/year		http://organicrules.org/custom/differences.php?id=2bbc
Denmark	Copper is banned	Copper is banned	http://organicrules.org/custom/differences.php?id=2bbc
Finland	Copper is banned	Copper is banned	http://organicrules.org/custom/differences.php?id=2bbc
Germany	Copper use is limited to a maximum of 3 kg Cu^{++}/ha/year for all crops, with the exception of hops for which a limit of 4 kg Cu^{++}/ha/year was set		www.naturland.de
Netherland	Copper is banned	Copper is banned	http://organicrules.org/custom/differences.php?id=2bbc
Norway	Copper is banned	Copper is banned	http://organicrules.org/custom/differences.php?id=2bbc
Slovenia		Copper use is limited to 5 kg Cu^{++}/ha/year	Rusjan *et al.*, 2007
Sweden	Copper is banned It is allowed only as fertilizer at a maximum of 0.3 kg Cu^{++}/ha/year (higher doses of up to 1 kg/ha, are permitted only when a shortage of copper in the soil has been demonstrated)	Copper is banned It is allowed only as fertilizer at a maximum of 0.3 kg Cu^{++}/ha/year (higher doses of up to 1 kg/ha, are permitted only when a shortage of copper in the soil has been demonstrated)	KRAV, 2017
Switzerland	Copper use is limited to a maximum of 4 kg Cu++/ha/year for fruit-growing and horticulture and 6 kg Cu++/ha/year for viticulture (within 5 consecutive years maximum 20 kg copper metal per ha)		Federal Ordinance 910.181 on Organic Farming of the Federal Department of Economic Affairs, Education and Research of 22 September 1997 as amended

[a] Directive 2009/128/EC (article 14) imposed the obligation to apply the principles of integrated pest management by all professional users of plant protection products by 1 January 2014.

same limits set for copper compounds in the European Union (http://www.organicexport.info/turkey.html). Copper use can be avoided in Northern Europe because environmental conditions are unfavourable for disease development. In the Mediterranean basin, however, where the climate is conducive for occurrence and spread of several plant pathogens, complete elimination of this heavy metal in organic farming is not yet practicable. In Canada and the United States of America copper compounds are allowed, and there are no limits on their use. Only for organic farming it is suggested that copper-based materials are used to minimize accumulation of the metal in soil, as build-up of copper in soil may prohibit future use (Canadian General Standards Board, 2006; Departments and Agencies of the Federal Government of the United

States, 2018). Moreover, in Canada in organic farming no visible pesticide residues are allowed on harvested crops. Basic copper sulphate, copper oxide, copper sulphate and copper oxysulphate may be used to correct documented copper deficiencies. Copper ammonia base, copper ammonium carbonate, copper nitrate and cuprous chloride are prohibited as sources of copper for plant nutrients (Canadian General Standards Board, 2006). The International Federation of Organic Agriculture Movements (IFOAM) has limited total copper input in organic farms to a maximum of 6 kg ha^{-1} $year^{-1}$ (IFOAM, 2014). In biodynamic agriculture, copper is permitted up to a maximum of 3 kg ha^{-1} $year^{-1}$, based on a 5-year average, and using, preferably, a maximum of 500 g per treatment (www.demeter.it/wp-content/uploads/2015/08/STANDARD-PRODUZIONE-DEMETER-AGGIORNAMENTO-2016.pdf).

Strategies to reduce copper inputs

Innovative formulations

The need to reduce copper inputs has led to research on innovative formulation technologies with reduced copper contents, to provide comparable efficacy to that achieved with the use of traditional formulations, but with small copper amounts distributed per hectare. One strategy to maximize the effectiveness of the copper ion is to reduce the particle size of the active substance (micronization) to improve coverage of treated surfaces (Brunelli and Palla, 2005). Small particles with high surface/volume ratios ensure increased uniformity of coverage, distribution and adhesion, giving increased resistance to run-off (Flori *et al.*, 2006). Another strategy is to use copper microencapsulates (Weihrauch and Schwarz, 2014) to control the release of active ingredients and improve product adhesiveness and rainfastness. The amount of copper can also be reduced by combining with such as zeolites (Kim *et al.*, 2000; Demirci *et al.*, 2014; Rossainz-Castro *et al.*, 2016), clay-like bentonite (Tamm *et al.*, 2004; Caleca *et al.*, 2011), or homeopathic substances (Weihrauch and Schwarz, 2014) and terpenic alcohols (Gilardi *et al.*, 2015).

Zeolites have a high affinity for copper, and they adhere firmly to leaves, providing the metal different modes of action and release. The copper-zeolite combination makes a fraction of copper immediately available, while the other fraction, linked to the mineral phases, is released more slowly (Barbarick and Pirela, 1984; Reháková *et al.*, 2004; Ramesh et al., 2011). The copper-clay combination may also facilitate the release of copper ions in the presence of foliar wetting, holding the copper in a condition of low humidity. Moreover, by absorbing water, clay keeps the vegetation dry, reducing the risk of pathogen infections. Homeopathic substances may strengthen natural plant defences against pathogens or environmental stresses reducing copper requirements over long periods (Betti *et al.*, 2009; Dagostin *et al.*, 2011; Weihrauch and Schwarz, 2014; Jäger *et al.*, 2015). Combinations with terpene alcohols derived from coniferous oils is advantageous, as these alcohols can improve the coverage of treated vegetation, reduce drainage and increase copper efficiency (Borgo *et al.*, 2004; Bortolotti *et al.*, 2006; Dagostin *et al.*, 2011). These new formulations may allow distribution of copper at far below the large quantities used previously (Leonardi *et al.*, 2002; Gomez *et al.*, 2007; Mohr *et al.*, 2007, 2008; Kovačič *et al.*, 2013).

Dosage reduction

Copper input can also be limited by reducing doses in single treatments, while still ensuring good efficacy. Available formulations contain different proportions of copper and recommend different dose rates, depending on the type of copper compound. Recommended dosages have reduced significantly (Leonardi *et al.*, 2002; Weihrauch and Schwarz, 2014). Until recently, copper formulations required the distribution of high copper doses per hectare per single treatment (Brunelli, 2016). Currently, however, authorized plant protection products recommend average doses of approx. 1 kg Cu^{++} ha^{-1} per treatment (Cabús *et al.*, 2017). Although this rate is applied, for example, in areas where climatic conditions are conducive to development of grape downy mildew, with 12–14 treatments per year, the quantity of distributed copper metal is more than twice the limit set for copper by Commission Regulation (EC) no. 889/2008 in organic farming (Cabús *et al.*, 2017).

Several studies have been carried out to identify minimum effective copper doses. Dagostin *et al.* (2011) highlighted the possibility of effectively controlling grape downy mildew with 0.25 g L^{-1} of copper, obtaining greatest protection (99% efficiency) with 0.6 g L^{-1} of copper. Cabús *et al.* (2017) confirmed these results, and laboratory surveys have demonstrated effective downy mildew control with concentrations of 5 mg Cu^{++} m^{-2} of leaf area (equal to 0.2 g L^{-1} of copper). The concentration to be used in the field, corresponding to 5 mg Cu^{++} m^{-2} leaf area, has been calculated to be approx. 200 g Cu^{++} ha^{-1} (Cabús *et al.*, 2017). Therefore, copper doses from 200 to 400 g ha^{-1} $treatment^{-1}$ can provide good grape downy mildew control while respecting the copper limits imposed by European Community regulations for organic farming. Reduced amounts of copper have also been used to control *Pseudoperonospora humuli* on hop; copper compounds were found to be effective at 2–3 kg Cu^{++} ha^{-1}, compared to the maximum limit of 4 kg Cu^{++} ha^{-1} allowed in Germany for this crop (Weihrauch and Schwarz, 2014). Reduced amounts of copper have also been used to control late blight in organic potato. Six field trials were conducted in northern Germany to evaluate the efficacy of copper hydroxide at reduced rates compared to the common practise of the most important German organic farmer associations (3 kg copper ha^{-1}). There was clear tendency that reducing copper amounts did not impair tuber yields (Bangemann *et al.*, 2014).

Crop cover systems

Net crop covers can be used to reduce the use of agrochemicals in crop protection, and copper in particular. Crop cover systems protect plants from atmospheric precipitation (rain, hail, snow), and from frost. In addition, they offer anti-insect function, with subsequent reductions in virus infections, by preventing contact between plants and insect vectors (Scarascia-Mugnozza *et al.*, 2012). Nets are available in different textures and colours. The colour gives them photoselection properties, affecting intensity and spectrum of luminous flux, with different effects on photosynthesis and hence the quality and the quantity of production. Photoselective nets also influence the undercover temperature. Alaphilippe *et al.* (2016) reported an average increase in temperature (0.7°C) in Italian conditions, and decreases in photosynthetically active radiation (10 and 15%, respectively, in Southern France and Northern Italy) for fruit grown under row-by-row netting during summer, 2011 (Chouinard *et al.*, 2016). Nets can be especially useful in late spring, where increased temperatures may facilitate plant development. By influencing the microclimate under coverage, these systems can also be used for plant protection since they create unfavourable conditions for pathogen development, protecting plants from infection assisting rains and reducing moisture (Iglesias and Alegre, 2006). Decreased relative humidity (2.3%) was reported during summer 2011 in Italy (Chouinard *et al.*, 2016). Efficacy trials for these nets against grape downy mildew and apple scab showed a reduction of disease symptoms (Sévérac and Siegwart, 2013; Chouinard *et al.*, 2017). The disadvantages of net use are the installation cost and the high cost of labour required for net management (Chouinard *et al.*, 2016).

"Natural" alternative formulations to copper

Many studies have focused on identifying natural derivative molecules to replace copper or reduce its dosage, through their use alternately or in combination with copper. Good results have been achieved, although investigations need to be continued to permit the use in agricultural practice of the most promising substances (Ferrari *et al.*, 2000; Cao *et al.*, 2003; Dagostin *et al.*, 2008; La Torre *et al.*, 2012b, 2013, 2014a). Some substances that may represent an alternative to copper are also included in Annex II to Commission Regulation (EC) 889/2008, which lists the products permitted for plant protection in organic crop production. Copper alternatives include plant extracts, inorganic substances and clays, biocontrol agents, seaweed, or chitosan. Among plant extracts, that from *Equisetum arvense* was shown to control diseases caused by *Plasmopara viticola* (Dagostin *et al.*, 2011; Marchand, 2016), *Venturia inaequalis* (Kowalska *et al.*, 2011), *Phytophthora infestans* (Nechwatal and Zellner, 2015; Messgo-Moumene *et al.*, 2017) and *Alternaria solani* (Wszelaki and Miller, 2005); *Inula viscosa* extract controlled late blight in potato and tomato, downy mildew in cucumber, and downy mildew in grapevine (Cohen *et al.*, 2006; Dagostin *et al.*, 2011); extract of *Salvia officinalis* was reported to be active against downy mildew of grapevine (Dagostin *et al.*, 2010) and cucumber (Scherf *et al.*, 2010); nettle extract (*Urtica* spp.) was shown to control diseases caused by *Pl. viticola* (Robotic *et al.*, 2000; Bunea *et al.*, 2013), *Phytophthora capsici* (Lin *et al.*, 2005), *Alternaria alternata* (Feliziani *et al.*, 2013; Wojciechowska *et al.*, 2014), *A. solani* (Tapwal, 2011; Nabrdalik and Grata, 2015), *Botrytis cinerea* and *Monilinia laxa* (Feliziani *et al.*, 2013); *Yucca schidigera* extract was shown to control grapevine downy mildew (Gomez *et al.*, 2007; Dagostin *et al.*, 2011) and apple scab (Bengtsson *et al.*, 2009; Kunz and Hinze, 2014); tea tree (*Melaleuca alternifolia*) extracts were shown to be effective against grapevine downy mildew (Dagostin *et al*., 2011; La Torre *et al*., 2014a), and diseases caused by *Ph. infestans* (Reuveni *et al*., 2009) and *Xanthomonas vesicatoria* (Lucas *et al*., 2012); extracts from *Glycyrrhiza glabra* (licorice) were shown to control diseases caused by *Pseudoperonospora cubensis* (Scherf *et al*., 2010), *Ph. infestans* (Schuster *et al*., 2010; Treutwein *et al*., 2010; Nechwatal and Zellner, 2015), and *V. inaequalis* (Treutwein *et al*., 2010).

Inorganic substances are also copper alternatives for diseases control. Potassium hydrogen carbonate was shown to control *V. inaequalis* on apple (Schulze and Schönherr, 2003; Jamar *et al*., 2007, 2008; Kunz and Hinze, 2014; Wallhead *et al*., 2017), *Pl. viticola* (Sawant and Sawant, 2008; Dagostin *et al*., 2011), and *B. cinerea* and *Monilinia* spp. on stone fruits (Palmer *et al*., 1997; Amadei *et al*., 2014). Sodium hydrogen carbonate was shown to be effective against *Pl. viticola* (Lukas *et al*., 2016), *V. inaequalis* (Ilhan *et al*., 2006; Jamar *et al*., 2007; Kelderer *et al*., 2008) and *A. solani* (El-Mougy and Abdel-Kader, 2009). Calcium hydroxide can be used for *V. inaequalis* control (Schulze and Schönherr, 2003; Montag *et al*., 2006). Lime sulphur is indicated primarily for *V. inaequalis* control on apples (Jansonius *et al*., 2000), but also against pear scab caused by *Venturia pirina* (Jamar *et al*., 2017) and against *Pl. viticola* (Lukas *et al*., 2016). Sulphur can play a physiologically nutritional role reducing the appearance of *Alternaria* spp. and *V. inaequalis* symptoms on apple. Kunz and Hinze (2014) reported that sulphur products applied during the germination of *V. inaequalis* gave protective efficacy, although sulphur compounds are less effective than copper-based compounds for reducing apple scab (Holb and Kunz, 2016).

Potassium phosphonate has reduced diseases caused by *Pl. viticola*, *Pythium* or *Phytophthora* spp. (Speiser *et al*., 2000; Cook *et al*., 2009; Kelderer and Lardschneider, 2010). To reduce applications of copper-based fungicides, German authorities applied to the European Commission for the inclusion of potassium phosphonate in Annex II of Commission Regulation (EC) 889/2008 for organic viticulture, but the Expert Group for Technical Advice on Organic Production (EGTOP) rejected this request. The reasons for this refusal were that potassium phosphonate is synthetically manufactured, making it unsuitable for use on organically certified food crops, and because it leads to persistent phosphite residues in grapes and wine (EGTOP, 2014).

Clay preparations are used in crop protection to reduce or replace copper-based fungicides. They were reported to be active against grape downy mildew (Hofmann, 1996, 2002; Schmitt *et al*., 2002; Dagostin *et al*., 2011), late blight of potato (Michelante and Haine, 2004; Dorn *et al*., 2007), fire blight of apple (Plagge and Rommelt, 1997; Rommelt *et al*., 1999), and apple scab (Balaž *et al*., 2010). Clays control plant diseases through increasing aluminium at plant surfaces (Enkelmann and Wohlfarth, 1994). Aluminium ions were shown to inhibit spore germination of fungal pathogens (Andrivon, 1995; Van Zwieten *et al*., 2007).

Biocontrol agents may also be used to reduce copper use (Dagostin *et al*., 2011). Many of these have disease control capabilities, but only some are commercially available due to their variable effectiveness and to difficulties in registration processes. This is because these agents have inconsistent field performance, short shelf-lives, induce production of secondary metabolites of concern for human health and the environment, and/or incur high industrial production or formulation costs (Pertot *et al*., 2017). *Bacillus subtilis* was reported to reduce severity of downy mildew in cucumber plants (Mohamed *et al*., 2016), to control sugar beet Cercospora leaf spot (Collins and Jacobsen, 2003), and in combination with copper, reduce the number of copper treatments to effectively control citrus bacterial canker (Ibrahim *et al*., 2016) and early blight of tomato (Abbasi and Weselowski, 2014). The commercially available *B. subtilis* QST 713 was shown to be significantly or partially effective against *Ps. syringae* pv. *syringae* and *Xanthomonas* spp. on tomato under greenhouse conditions (Roberts *et al*., 2008; Gilardi *et al*., 2010). *Xenorhabdus bovienii* metabolites were reported to be active against *Ph. infestans* on potato plants (Ng and Webster, 1997). *Streptomyces violatus* was shown to control grape downy mildew (El-Sharkawy *et al*., 2018). Application of a commercial formulation containing *Pantoea agglomerans* strain C9-1 and *Pseudomonas fluorescens* strain A506 reduced severity of Xanthomonas leaf blight of onion, caused by *Xanthomonas axonopodis* pv. *allii.* New management strategies for Xanthomonas leaf blight are needed to reduce the amount of copper bactericides and delay or prevent the development of copper tolerance in populations of *X. axonopodis* pv. *allii* (Gent and Schwartz, 2005). *Lysobacter capsici* AZ78 was shown to control *Pl. viticola* (Puopolo *et al*., 2014a, 2014b) and *Ph. infestans* (Puopolo *et al*., 2014b). *Trichoderma harzianum* was reported to be effective against *Pl. viticola* (Palmieri *et* *al*., 2012; El-Sharkawy *et al*., 2018), and in combination with *Streptomyces viridosporus*, to control wheat leaf rust caused by *Puccinia triticina* (El-Sharkawy *et al*., 2015). *Trichoderma virens* DAR 74290 and *T. harzianum* T39 alone and in combination were reported to control pink rot of potato and root and stem rot of tomato caused by *Phytophthora erythroseptica* (Etebarian *et al*., 2000). *Trichoderma atroviride* was shown to control *Ph. infestans* (Al-Mughrabi, 2008). *Trichoderma asperellum* strain T34 was shown to control *Ph. capsici* in pepper (Segarra *et al*., 2013), *Ps. syringae* pv. *lachryimans* in cucumber (Segarra *et al*., 2007) and *Ps. syringae* pv. *tomato* in tomato (Segarra *et al*., 2009). Water extract of dry mycelium of *Penicillium chrysogenum* was reported to be active against *Pl. viticola* (Thuerig *et al*., 2006; Harm *et al*., 2011), *Ph. infestans* (Thuerig *et al*., 2006; Unger *et al*., 2006), *Peronospora destructor* (Thuerig *et al*., 2006) and *V. inaequalis* (Thuerig *et al*., 2006). *A. alternata* was shown to be effective in limiting *Pl. viticola* sporulation (Musetti *et al*., 2006). *Saccharomyces cerevisiae* combined with calcium chloride and chitosan was reported to reduce early and late blights caused by *A. solani* and *Ph. infestans* on tomato plants (El-Mougy *et al*., 2012). *Saccharomyces* extracts were shown to reduce grapevine downy mildew when applied either alone (Pujos *et al*., 2014) or in combination with laminarin (Romanazzi *et al*., 2016).

Seaweed extracts can be used in crop protection as alternatives to copper. The most known and used seaweeds are brown algae, with *Ascophyllum* and *Laminaria* as the main genera. Extracts of *Ascophyllum nodosum* were shown to control *Pl. viticola* (Lizzi *et al*., 1998; Dagostin *et al*., 2011). Laminarin extracted from *Laminaria digitata* can be used to control *B. cinerea* (Aziz *et al*., 2003), *V. inaequalis* (Mery and Joubert, 2012), and *Pl. viticola* (Aziz *et al*., 2003; Trouvelot *et al*., 2008; Chalal *et al*., 2015; Garde-Cerdán *et al*., 2017). Laminarin is not directly bactericidal or fungicidal, but the activity is related to enhancing plant resistance to pathogens.

Chitosan is a natural biodegradable polymer obtained from chitin. It was reported to be active against a variety of microorganisms (Rabea *et al*., 2003). Though chitosan has no direct action on pathogens, it can help reduce the need for copper by stimulating plant defence mechanisms. Chitosan has been shown to control *A. solani* (Abd-El-Kareem and Haggag, 2014), *Ph. infestans* (Atia *et al*., 2005; Nechwatal and Zellner, 2015), *Pl. viticola* (Aziz *et al*., 2006; Maia *et al*., 2012; Romanazzi *et al*., 2016; Garde-Cerdán *et al*., 2017), and *B. cinerea* (Ait Barka *et al*., 2004; Trotel-Aziz *et al*., 2006).

Disease forecasting models

Forecasting models can be used to reduce the amounts of copper applied, through increased efficiency of treatment timing. Study of the relationships between weather conditions and disease development can simulate the course of infections and identify optimal intervention periods. This knowledge allows reductions in the number of treatments, while maintaining efficient disease control with consequent benefits for crop production, the environment and human health. Disease forecasting models use information about the environment, crop, and pathogen to predict future occurrence of a disease. In this way, farmers and technicians are alerted at times of high disease risk, allowing them to perform timely disease control treatments. Many forecasting models have been developed to control fungal pathogens, oomycetes and pests. Some of the models useful for reducing copper inputs are reported in Table 3.

Disease resistant cultivars

The need to reduce agrochemical inputs has led researchers to develop disease resistant crop cultivars. In the case of grapevine, the use of downy mildew-resistant varieties can limit the use of copper (Pedneault and Provost, 2016), which is why these varieties are recommended as the most valid choice for organic viticulture (Pavloušek, 2010; Sivčev *et al*., 2010; Becker, 2013). Resistant plant varieties are selected from one or more generations of interspecific crosses where resistance features are transmitted by American and Asian species with low organoleptic characteristics to precious *Vitis vinifera* cultivars, which are highly susceptible to fungi and oomycetes (Wiedemann-Merdinoglu and Hoffmann, 2010; Zini *et al*., 2015). When vinified, the first hybrids obtained from crosses between European and American species, defined as first-generation hybrids, produced poor quality products and were therefore unsuccessful with winegrowers. These were followed by second, third and fourth generations, in which the portions of the genomes from American and Asian species were gradually reduced in favour of the European genomes. In this way, the quality characteristics of *V. vinifera* and a small portion of the genome from Asian

Table 3. Main plant disease forecasting models used to reduce copper inputs.

Host/Pathogen	Model	Parameters considered	Reference
Apple and pear tree / *Erwinia amylovora*	COUGARBLIGHT 2010	Hourly temperature Hourly or daily rainfall	Smith and Pusey, 2011
	MARYBLYT™	Daily minimum and maximum temperature Daily rainfall Daily leaf wetness	Lightner and Steiner, 1992
Apple tree / *Venturia inaequalis*	A-SCAB (Apple-SCAB)	Hourly temperature Hourly relative humidity Hourly rainfall Hourly leaf wetness	Rossi *et al.*, 2007
	MILLS A-3	Daily average temperature Leaf wetness	Mills, 1944 MacHardy and Gadoury, 1989
	RIMpro[a] (Relative Infection Measure PROgram)	Temperature Humidity Rainfall Leaf wetness Wind speed and direction Solar radiance Barometric pressure Phenological stage of plants	Trapman and Polfliet, 1997
Grapevine / *Plasmopara viticola*	USCS - DOWGRAPRI (DOWny mildew GRApe PRimary Infection)	Hourly temperature Hourly relative humidity Hourly rainfall Hourly leaf wetness	Rossi *et al.*, 2005 Caffi *et al.*, 2006 Rossi *et al.*, 2006 Rossi *et al.*, 2008
	EPI-Plasmopara (État Potentiel d'Infection - Plasmopara)	Temperature Rainfall Relative humidity	Strizyk, 1983 Brunelli *et al.*, 1990 Franchi *et al.*, 2010 Sanna *et al.*, 2014
	PLASMO (PLAsmopara Simulation MOdel)	Hourly temperature Hourly relative humidity Hourly rainfall Hourly leaf wetness (0=dry, 1=wet)	Orlandini *et al.*, 1993a Orlandini *et al.*, 1993b Orlandini *et al.*, 1993c Rosa *et al.*, 1993 Rosa *et al.*, 1997 Orlandini and Rosa, 1997 Rosa and Orlandini, 1997
	-	Temperature Rainfall Forecasted rainfall	Pellegrini *et al.*, 2010
	Vinemild	Temperature Rainfall Relative humidity	Blaise and Gessler, 1992 Blaise *et al.*, 1999a Blaise *et al.*, 1999b
	PRO (Plasmopara Risk Oppenheim)	Temperature Relative humidity Leaf wetness	Hill, 1990
	SIMPO (SIMulation of *P. viticola* Oospore-maturation)	Daily average temperature Relative humidity Rainfall	Hill, 2000

(Continued)

Table 3. (Continued).

Host/Pathogen	Model	Parameters considered	Reference
Grapevine/ *Plasmopara viticola*	DMCAST (Downy Mildew foreCAST)	Hourly temperature Hourly relative humidity Hourly leaf wetness	Park *et al.*, 1997
	POM (Prediction of Oospore Maturity)	Rainfall	Tran Manh Sung *et al.*, 1990
	MILVIT	Temperature Relative humidity	Magnien *et al.*, 1991
Kiwifruit/ *Pseudomonas syringae* pv. *actinidiae*	-	Hourly temperature Hourly rainfall Hourly relative humidity	Beresford *et al.*, 2017
Lettuce/*Bremia lactucae*	BREMCAST (BREMia foreCAST)	Temperature during the night Leaf wetness duration Relative humidity	Kushalappa, 2001
Onion/*Peronospora destructor*	ONIMIL (ONIon downy MILdew)	Hourly temperature Hourly or daily rainfall Hourly relative humidity	Battilani *et al.*, 1996a Battilani *et al.*, 1996b Battilani *et al.*, 1998a Battilani *et al.*, 1998b
Peach tree/*Taphrina deformans*	-	Temperature Daily rainfall Phenological stage of plants	Giosuè *et al.*, 2000 Thomidis *et al.*, 2010
Pear tree/ *Stemphylium vesicarium*	BSP-Cast (Brown Spot Pear Cast)	Hourly leaf wetness Average temperature during wetness period	Montesinos *et al.*, 1995 Llorente *et al.*, 2000
Sugar beet/ *Cercospora beticola*	CERCOPRI (CERCOspora PRimary Infection)	Hourly temperature Rainfall Relative humidity Varietal resistance index (From susceptible to resistant) Day of appearance of disease symptoms	Battilani and Rossi, 1986
	CERCODEP (CERCOspora Development of EPidemics)	Hourly temperature Rainfall Relative humidity	Rossi, 1995
Tomato and Potato/ *Phytophthora infestans*	IPI (Infection Potential Index)	Crop emergence or transplant date Minimum, average and maximum daily temperature Daily average relative humidity Total daily rainfall	Bugiani *et al.*, 1993
	MISP (Main Infections and Sporulation Period)	Hourly temperature Hourly relative humidity Hourly rainfall	Ruckstuhl and Forrer, 1998
	Öko-SIMPHYT	Temperature Rainfall	Tschöpe *et al.*, 2010 Tebbe *et al.*, 2014 Bruns *et al.*, 2017

(Continued)

Table 3. (Continued).

Host/Pathogen	Model	Parameters considered	Reference
Tomato and Potato/ *Phytophthora infestans*	Bio-PhytoPRE	Daily temperature Daily rainfall Daily relative humidity	Musa-Steenblock and Forrer, 2005a Musa-Steenblock and Forrer, 2005b
	BLITECAST	Maximum and minimum daily temperature Hourly rainfall Relative humidity Leaf wetness	Krause *et al.*, 1975 MacKenzie, 1981 MacKenzie, 1984
Winter wheat/ *Puccinia triticina* (syn. *P. recondita* f. sp. *tritici)*	RUSTPRI (RUST PRimary Infection)	Hourly temperature Hourly rainfall Hourly relative humidity Hourly leaf wetness	Rossi *et al.*, 1996
	RUSTDEP (RUST Development of Epidemics)	Hourly temperature Hourly rainfall Hourly relative humidity Hourly leaf wetness	Rossi *et al.*, 1997
Winter wheat/ *Puccinia striiformis* f. sp. *tritici*	-	Hourly temperature Hourly relative humidity Hourly rainfall	El Jarroudi *et al.*, 2017

[a] RIMpro provides also risk estimates for other diseases controlled by copper (pear scab, fire blight, sooty blotch, apple canker and Marssonina blotch).

or American species, bearers of disease resistance, led to good quality wines (Van der Meer and Lévite, 2010; Pedneault *et al.*, 2012; Rousseau *et al.*, 2013; Zini *et al.*, 2015). After more than a century from the first genetic improvement projects, new impetus to obtaining resistant varieties is being derived from modern breeding techniques, based particularly on the use of recombinant DNA, cisgenesis and genome editing. The genetic knowledge being acquired of complex characters that determine the quality of production, together with the possibility of identifying the best allelic variants within the *Vitis* genus, represent important innovation to obtain new varieties (Grando, 2007). To date, European breeding programmes have produced more than a hundred varieties and selections that have not retained the negative oenological characteristics of wild vines. For this reason, the European Union has allowed the cultivation of some of these in Union Member States (Zini *et al.*, 2015).

In the case of apple, the use of varieties that are resistant to scab caused by *V. inaequalis* or fireblight caused by *E. amylovora* can contribute to reduced copper inputs. A breeding programme to produce apple cultivars resistant to scab was initiated early in the 20th Century at the University of Illinois. This was based on a modified backcross programme to combine genes for resistance to apple scab from the crab apple *Malus floribunda* 821, and other species with commercially-acceptable traits (Hough, 1944). Resistance was conferred by a single qualitative dominant gene named *Vf* (*Venturia* resistance from *floribunda*) (Williams *et al.*, 1966). Subsequent hybridization and selection produced scab-resistant eating apples (Afunian *et al.*, 2004; Gessler and Pertot, 2012). Very few apple cultivars carry other sources of scab resistance. The widespread use of *Vf* may increase the risk of selecting for pathogen genotypes that are able to overcome this resistance (Lespinasse, 1989). In 1988, scab lesions were found on 'Prima,' a *Vf* selection, in an orchard in Germany (Parisi *et al.*, 1993). Only high diversity of resistance, as present in natural conditions (MacHardy *et al.*, 2001), can sustainably reduce *V. inaequalis* populations.

The use of fireblight resistant apple and pear cultivars is another approach to limit copper inputs, and resistant cultivars should be considered when establishing new orchards. As fire blight is known to infect rootstocks as well as scions, fire blight resistance breeding is relevant for both tissue types (Peil *et al.*, 2009). Selection for resistance to fireblight was initiated in the 19th Century in the USA, and at present it is conducted in other countries, particularly within Europe, using classical breeding or genetic engineering methods (Toth *et al.*, 2006; Peil *et al.*, 2008; Kellerhals *et al.*, 2011; Ozrenk *et al.*, 2012); However, most resistant cultivars do not meet fruit quality standards required by consumers.

The use of resistant varieties for late blight control in potatoes and tomatoes is also a promising strategy to reduce or replace the need for applications of copper-based products. Assuming that resistant varieties require 0 to 33% of the copper fungicides used to protect currently grown susceptible varieties, a reduction of 16.5 to 50% of copper fungicides could be achieved by growing more resistant potato varieties, and this result is very important in organic farming (Speiser *et al.*, 2006). Resistant genes were first described in potato (Wastie, 1991), but have also been reported (as *Ph* genes) in tomato (Gallegly and Marvel, 1955). Potato resistant genes (R-genes) were discovered in the closely related species *Solanum demissum* (Malcolmson and Black, 1966; Wastie, 1991). The tomato resistance genes have been identified in tomato wild species *Solanum pimpinellifolium* (Foolad *et al.*, 2008; Moreau *et al.*, 1998). Varieties with race specific (based on R-genes) are usually highly effective, but resistance is often not durable, as new and more aggressive *Ph. infestans* strains appear that overcome the resistance (Brouwer *et al.*, 2004; Pacilly *et al.*, 2016). Currently the number of resistant cultivars available is limited and there is a need to continue to search for new and more durable resistant genes (Pacilly *et al.*, 2016).

In the case of wheat, breeders have been selecting for resistance to rust diseases. Stem rust (*Puccinia graminis* f. sp. *tritici*), leaf rust (*P. triticina*) and stripe or yellow rust (*Puccinia striiformis* f. sp. *tritici*) can cause significant and severe losses to crops (Roelfs *et al.*, 1992). Using resistant varieties to prevent or avoid rust diseases is an important strategy to reduce copper inputs while reducing environmental impacts and increasing long-term agricultural sustainability. More than 187 rust resistance genes (80 for leaf rust, 58 for stem rust and 49 for stripe rust) have been derived from diverse wheat or durum wheat cultivars and related wild species, using different molecular methods (Aktar-Uz-Zaman *et al.*, 2017). The problem has been that other rust races have appeared in various parts of the world, reducing the efficacy of the newly identified sources of resistance (Figueroa *et al.*, 2018). Consequently, there is a constant need to develop new sources of resistance for controlling rust diseases (Kolmer, 2013).

In conclusion, reducing the use of copper through the use of resistant cultivars or varieties can reduce both crop production costs and the environmental impacts resulting from this important crop protection metal.

Research on copper-related issues

Farmers, advisors, industry, policymakers and researchers are all interested in solving the problems of copper use in plant protection. EU organic farmers are seeking help from the research community, since the use of this heavy metal can undermine the image of organic production, whose strong points are production safety and quality. In addition, some retail chains have recently begun demanding copper-free products with zero copper residues on food, and this affects the behavior of farmer producers. Several research projects have been initiated to find new strategies and appropriate alternative solutions (Table 4). The main features of these studies are summarized in Table 5. The projects have examined several strategies, outlined below.

Agronomic strategies

Measures to pre-empt onset of diseases. Studies have demonstrated the effectiveness of early crop establishment (for reducing potato late blight), the importance of the removal and destruction of crop residues, crop rotation and low plant population density. Adequate fertilization and balanced irrigation also play key roles. The Blight-MOP project showed that alternating rows of resistant and susceptible potato varieties in a field, or combining different varieties within rows, is an effective strategy. However, it was found that this system could cause problems for harvesting operations, and it has been evaluated on a small scale and is effective only when disease pressure is low (http://orgprints.org/10650/12/leifert-wilcockson-2005-blight_mop-report-Annexes.pdf). For grapevine protection, canopy management could be essential, reducing leaf populations and increasing fruit exposure to create microclimates that

Table 4. List of the main research projects on copper-related issues.

Project	Aim	Starting date	Ending date
After-Cu (Anti-infective environmentally friendly molecules against plant pathogenetic bacteria for reducing Cu) http://www.lifeaftercu.com/	Demonstration of the anti-infective properties of innovative peptide molecules against plant pathogenic bacteria, in order to reduce copper compounds and develop environmentally friendly and sustainable strategies for the control of plant bacterial diseases	1st January 2014	31st December 2015
ALT.RAMEinBIO (Reduction strategies and possible alternatives to the use of copper in organic farming) http://www.sinab.it/ricerca/altrameinbio-strategie-la-riduzione-e-possibili-alternative-all%E2%80%99utilizzo-del-rame	Identification of strategies and products able to replace or reduce the use of copper in organic viticulture, fruit growing and horticulture	15th January 2015	31st March 2018
Bio Bug Bang (Bioformulations with antimicrobial activity)	Identification and characterization of natural products or active substances and development of new formulations for the control of pathogenic bacteria of tomato and kiwifruit to reduce copper use in organic farming	11th November 2010	31st May 2012
BioImpuls (Organic potato breeding program) www.louisbolk.nl	Identification of a strategy to protect organic potatoes against late blight disease	2008	2019
Blight-MOP (Development of a systems approach for late Blight Management in EU Organic Production systems) http://research.ncl.ac.uk/nefg/blightmop/page.php?page=2	Reduction or replacement of copper for potato late blight control	1st March 2001	31st December 2005
CO-FREE (Innovative strategies for copper-free low input and organic farming systems) http://www.co-free.eu/	Development of plant protection products of natural origin including optimization of field application, characterization of the mode of action and identification of the spectrum of activity to improve “copper-free” production strategies without altering yield or quality of the cultures while reducing the environmental impact	1st January 2012	30th June 2016
EVERGREEN (Environmentally friendly biomolecules from agricultural waste as substitutes of pesticides for plant diseases control) http://life-evergreen.com/it/il-progetto/	Demonstration of the *in vitro* and *in vivo* efficacy and reliability of polyphenolic-based biomolecules extracted from agricultural non-food biomass and waste against phytopathogenic bacteria and nematodes, to replace current pesticides and application of copper compounds in both traditional and organic agriculture	1st October 2014	30th September 2016
PRADA (Setting-up a system to assess grapevine downy mildew infection on a territorial scale) http://www.ita-slo.eu/projects/projects_2000_2006/	Setting up an agro-meteorological system to assess the evolution of grapevine downy mildew on a regional scale	November 2004	March 2008

(Continued)

Table 4. (Continued).

Project	Aim	Starting date	Ending date
ProLarix (Development of a botanical plant protection product from Larix by-products) www.prolarix.eu	Optimization of extraction and up-scale the production of standardised technical grade Larix extract; Validation of the efficacy and integrate Larix extracts in state-of-the-art grapevine production systems; Development of a roadmap for registration and market introduction at EU and member state level	1st November 2013	31st October 2015
PRO.VI.SE.BIO (Vine and seed protection in organic farming)	Identification of strategies to reduce or replace the use of copper for grape downy mildew	18th February 2009	30th December 2011
PURE (Pesticide Use-and-risk Reduction in European farming systems with Integrated Pest Management) http://www.pure-ipm.eu/	Devolompment of practical Integrated Pest Management (IPM) solutions to reduce the dependence on pesticides in major farming systems in Europe, thereby contributing to the reduction of pesticide use while ensuring good pest control	1st March 2011	28th February 2015
RepCo (Replacement of Copper Fungicides in Organic Production of Grapevine and Apple in Europe) http://cordis.europa.eu/publication/rcn/11903_en.html	Identification of ways to reduce or replace copper fungicides in organic agriculture	1st November 2003	31st October 2006
STU.LI.RA. (Studies to comply with the limitations on copper quantities through the use of low-dose formulations or alternative means)	Assessment of alternative technical means (microbial antagonists, plant extracts, inorganic substances) and new copper formulations with low copper dosage to protect grapevines, fruit trees and vegetable crops in organic farming	1st January 2005	31st December 2009
VineMan.org. (Integration of plant resistance, cropping practices, and biocontrol agents for enhancing disease management, yield efficiency, and biodiversity in organic European vineyards) http://www.vineman-org.eu/	Development of innovative crop systems for more efficient control of key grape diseases (downy mildew, powdery mildew and grey mould), given the need to reduce the amount of copper in organic farming.	1st March 2010	31st August 2013

are unfavourable to pathogen development. The ALT.RAME*in*BIO project demonstrated the possibility of controlling grapevine downy mildew and apple scab by covering the crops with anti-rain protection (Keep in Touch® system). However, this strategy would lead to increased grapevine powdery mildew and increase the number of phytoseiid mites on apples (http://www.sinab.it/ricerca/altramein-bio-strategie-la-riduzione-e-possibili-alternative-all%E2%80%99utilizzo-del-rame).

Selection of resistant cultivars

The Blight-MOP project highlighted the usefulness of varieties resistant to potato late blight, such as Eden, Naturella, Escort, Sarpo Axona, Sarpo Mira and Sarpo Tomina (Speiser *et al*., 2006). The BioImpuls project has begun a long-term genetic improvement programme, to seek late blight resistant parental lines suitable for markets. To date, five parental lines have been developed: *Solanum bulbocastanum*, *S. edinense*, R8, R9 and Sarpo Mira (Lammerts van Bueren *et al*.,

Table 5. The principal features of projects on copper carried out in recent years.

Host/Pathogen	Project Acronym[a]	More effective products or strategies	Reference
Apple tree/ *Alternaria mali*	ALT.RAME*in*BIO	Calcium polysulfide; lime sulphur; acid clays; sulphur-based products	http://www.sinab.it/ricerca/altrameinbio-strategie-la-riduzione-e-possibili-alternative-all%E2%80%99utilizzo-del-rame
Apple tree/ *Marssonina coronaria*	ALT.RAME*in*BIO	Calcium polysulfide; lime sulphur; acid clays	http://www.sinab.it/ricerca/altrameinbio-strategie-la-riduzione-e-possibili-alternative-all%E2%80%99utilizzo-del-rame
Apple tree/ *Venturia inaequalis*	ALT.RAME*in*BIO	Low-dose copper formulations; lime sulphur; liquorice extract; sulphur-based products; cover crop system Keep In Touch®	http://www.sinab.it/ricerca/altrameinbio-strategie-la-riduzione-e-possibili-alternative-all%E2%80%99utilizzo-del-rame
	CO-FREE	*Cladosporium cladosporioides* H39	Köhl *et al.*, 2015; Schmitt *et al.*, 2017
	PURE	*Cladosporium cladosporioides* H39	Heijne *et al.*, 2015; http://www.pure-ipm.eu
	RepCo	*Yucca schidigera* extract; potassium hydrogen carbonate; coconut extract; rapeseed oil; *Cladosporium cladosporioides* R406; *Cladosporium cladosporioides* H39	Bengtsson *et al.*, 2006; De Jong and Heijne, 2006; Heijne *et al.*, 2006, 2007; Köhl, 2007; Köhl *et al.*, 2008; Dagostin *et al.*, 2011; http://cordis.europa.eu/publication/rcn/11903_en.html
	STU.LI.RA	Lime sulphur; carbonate + sulphur	Kelderer *et al.*, 2008, 2010
Grapevine/ *Botrytis cinerea*	VineMan.org	Epidemiological models; *Aureobasidium pullulans*; low copper dosages + sulphur; *Bacillus subtilis* QST713 + sulphur; agricultural practice (early leaf removal)	Legler *et al.*, 2013; Galbignani *et al.*, 2014; http://www.vineman-org.eu/nqcontent.cfm?a_id=11235&tt=t_law_market_www
Grapevine/ *Plasmopara viticola*	ALT.RAME*in*BIO	Reduced copper dosages; liquorice leaf extract; laminarin from brown seaweed (*Laminaria digitata*); cell walls of *Saccharomyces cerevisiae*; *Yucca schidigera* extract; potassium hydrogen carbonate; lime sulphur; acid clay; cover crop system Keep In Touch®	http://www.sinab.it/ricerca/altrameinbio-strategie-la-riduzione-e-possibili-alternative-all%E2%80%99utilizzo-del-rame
	CO-FREE	Preventive measures; low dose copper; potassium hydrogen carbonate; lime sulphur; *Lysobacter capsici* AZ78; RIMpro model	Puopolo *et al.*, 2014a, 2014b; Lukas *et al.*, 2016; Schmitt *et al.*, 2017; http://www.biofruitadvies.nl/rimpro/rimpr o_e.htm
	PRADA	Forecasting models	Cicogna *et al.*, 2005; Dietrich *et al.*, 2007
	ProLaris	Extract from *Larix decidua*	James *et al.* 2016; www.prolarix.eu; https://cordis.europa.eu/result/rcn/186831_en.html
	PRO.VI.SE.BIO	Forecasting model; low dose copper formulations	La Torre *et al.*, 2010, 2011, 2012a, 2014b; Lo Scalzo *et al.*, 2012; Menesatti *et al.*, 2013

(Continued)

Table 5. (Continued).

Host/Pathogen	Project Acronym[a]	More effective products or strategies	Reference
Grapevine/ *Plasmopara viticola*	RepCo	*Camellia oleifera* seeds + *Chenopodium quinoa*; *Chenopodium oleifera* seeds + *Quillaja saponaria*; *Yucca schidigera* extract; low dose copper formulations; potassium phosphonates; chitosan; fatty acids and potassium salts; tea tree oil; *Abies sibirica* extract; aluminium silicate	Dagostin *et al*., 2006, 2011; Gomez *et al*., 2007; Köhl, 2007; Mohr *et al*., 2007; Parveaud *et al*., 2010; http://cordis.europa.eu/publication/rcn/11903_en.html
	STU.LI.RA	Low copper-based formulations; *Salvia officinalis* extract	La Torre *et al*., 2007, 2008; Spera *et al*., 2007; Dagostin *et al*., 2010
	VineMan.org	FR-010 (substance not properly specified); epidemiological models; agronomic practices (canopy density, fruit exposure, leaf removal)	Legler *et al*., 2013; http://www.vineman-org.eu/nqcontent.cfm?a_id=11235&tt=t_law_market_www
Kiwifruit/ *Pseudomonas syringae* pv. *actinidiae*	After-Cu	Innovative peptide molecules (AP17, Li27, PSA21)	Mota and Cornelis, 2005; Cerboneschi *et al*., 2015; Tegli *et al*., 2015; http://www.lifeaftercu.com/
	Bio Bug Bang	Plant extracts (*Ficus carica* and *Punica granatum*)	Quattrucci and Balestra, 2011; Quattrucci *et al*., 2011
Lemon and orange tree/ *Pseudomonas syringae* pv. *syringae*	After-Cu	Innovative peptide molecules (AP17, Li27, PSA21)	Mota and Cornelis, 2005; http://www.lifeaftercu.com/
Oleander/ *Pseudomonas savastanoi* pv. *nerii* strain Psn 23	After-Cu	Innovative peptide molecules (AP17, Li27, PSA21)	Mota and Cornelis, 2005; Cerboneschi *et al*., 2015; Tegli *et al*., 2015; http://www.lifeaftercu.com/
	EVERGREEN	Polyphenolic extracts from vegetable residues	Biancalani *et al*., 2016
Olive tree/ *Pseudomonas savastanoi*	After-Cu	Innovative peptide molecules (AP1, Li27, PSA21)	Mota and Cornelis, 2005; Cerboneschi *et al*., 2015; Tegli *et al*., 2015; http://www.lifeaftercu.com/
Potato/ *Phytophthora infestans*	BioImpuls	Resistant varieties (partecipatory plant breeding)	Lammerts van Bueren *et al*., 2008, 2009; Lammerts van Bueren, 2010; Almekinders et al., 2014; www.louisbolk.nl
	Blight-MOP	Agronomic techniques (early sowing, removal and destruction of infected leaves, fertilization and crop rotation, removal of crop residues and low plant density); Bio-PhytoPRE forecasting model; resistant varieties; *Xenorhabdus bovienii*; *Pseudomonas putida*; low-dose copper formulations	Phillips *et al*., 2002; Musa-Steenblock and Forrer, 2005a; Speiser *et al*., 2006; http://orgprints.org/10650/12/leifert-wilcockson-2005-blight_mop-report-Annexes.pdf http://research.ncl.ac.uk/nefg/blightmop/page.php?page=2.
	CO-FREE	Öko-SIMPHYT (decision support system) *Lysobacter capsici* AZ78	Puopolo *et al*., 2014a, 2014b http://www.zepp.info/ackerbau/75-kartoff el/61-oeko-simphyt

(Continued)

Table 5. (Continued).

Host/Pathogen	Project Acronym[a]	More effective products or strategies	Reference
Tobacco/ *Pseudomonas savastanoi* pv. *nerii* strain Psn 23	EVERGREEN	Polyphenolic extracts from vegetable residues	Biancalani *et al.*, 2016
Tobacco/ *Pseudomonas syringae* pv. *tabaci*	After-Cu	Innovative peptide molecules (AP17, Li27, PSA21)	Mota and Cornelis, 2005; Cerboneschi *et al.*, 2015; Tegli *et al.*, 2015; http://www.lifeaftercu.com/
Tomato/ *Phytophthora infestans*	ALT.RAME*in*BIO	Low dose copper formulations; liquorice leaf extract; potassium hydrogen carbonate *Bacillus subtilis* strain QST 713; *Yucca schidigera*; *Abies sibirica* extract; chitosan hydrochloride	http://www.sinab.it/ricerca/altrameinbio-strategie-la-riduzione-e-possibili-alternative-all%E2%80%99utilizzo-del-rame
Tomato/ *Pseudomonas syringae* pv. *tomato*	ALT.RAME*in*BIO	Natural substances of plant origin (carvacrol, thymol, eugenol, gallic acid and coumarin)	Giovanale *et al.*, 2017; http://www.sinab.it/ricerca/altrameinbio-strategie-la-riduzione-e-possibili-alternative-all%E2%80%99utilizzo-del-rame
	Bio Bug Bang	Microencapsulated based on extracts from *Punica granatum* containing gallic acid and ellagic acid; essential oils (*Lavandula hybrida* and *Mentha* × *piperita*)	Quattrucci and Balestra, 2011; Quattrucci *et al.*, 2011
Tomato/ *Xanthomonas axonopodis* pv. *vesicatoria*	ALT.RAMEinBIO	Natural substances of plant origin (carvacrol, thymol, eugenol, gallic acid and coumarin)	http://www.sinab.it/ricerca/altrameinbio-strategie-la-riduzione-e-possibili-alternative-all%E2%80%99utilizzo-del-rame

[a] Project Acronyms and titles: After-Cu: Anti-infective environmentally friendly molecules against plant pathogenetic bacteria for reducing Cu; ALT.RAMEinBIO: Reduction strategies and possible alternatives to the use of copper in organic farming; Bio Bug Bang: Bioformulations with antimicrobial activity; BioImpuls: Organic potato breeding program; Blight-MOP: Development of a systems approach for late Blight Management in EU Organic Production systems; CO-FREE: Innovative strategies for copper-free low input and organic farming systems; EVERGREEN: Environmentally friendly biomolecules from agricultural waste as substitutes of pesticides for plant diseases control; PRADA: Setting up a system to assess grapevine downy mildew infection on a territorial scale; ProLarix: Development of a botanical plant protection product from Larix by-products; PRO.VI.SE.BIO: Vine and seed protection in organic farming; PURE: Pesticide Use-and-risk Reduction in European farming systems with Integrated Pest Management; RepCo: Replacement of Copper Fungicides in Organic Production of Grapevine and Apple in Europe; STU.LI.RA: Studies to comply with the limitations on copper quantities through the use of low-dose formulations or alternative means; VineMan.org: Integration of plant resistance, cropping practices, and biocontrol agents for enhancing disease management, yield efficiency, and biodiversity in organic European vineyards.

2008, 2009; Lammerts van Bueren, 2010; Almekinders *et al.*, 2014). Expanding the cultivation of resistant cultivars may become particularly important in the future.

Use of copper alternatives

The RepCo, PURE, ALT.RAME*in*BIO, Blight-MOP, Bio Bug Bang, ProLarix and After-Cu projects focussed on research and development for copper alternatives for control of plant diseases such as *Pl. viticola*, *V. inaequalis*, *Ph. infestans*, *Pseudomonas savastanoi*, *Ps. syringae* pv. *actinidia*, *Ps. syringae* pv. *syringae*, *Ps. syringae* pv. *tomato*, *X. axonopodis* pv. *vesicatoria*. The best results were obtained using plant extracts, biocontrol agents and inorganic products (Mota and Cornelis, 2005; Quattrucci and Balestra, 2011; Quattrucci *et al.*, 2011; Cerboneschi *et al.*, 2015; Heijine *et al.*, 2015; Tegli *et al.*, 2015; James *et al.*, 2016; Giovanale *et al.*, 2017).

Effective substances from different origins have been identified for *Pl. viticola* control. The formulation based on extracts of *Chenopodium quinoa* and of *Camellia oleifera* seeds (Teawet TQ Liquid), and the formulation based on extracts of *Quillaja saponaria* and *C. oleifera* seeds (Quiponin BS Liquid) have shown good potential, although the formulations need to be improved due to run-off problems (Dagostin *et al*., 2011). Extract from *Abies sibirica* gave very good control of downy mildew symptoms on grape bunches, with activity only 10% less than that of copper. Studies conducted in northern Italy, under the STU.LI.RA. project, showed efficacy of *Salvia officinalis* extract in greenhouse and field tests, although the formulation needs to be improved, as it presented run-off problems. The Larixine product, based on *Larix decidua* bark extract, that has been developed in the ProLarix project, showed good efficacy under field conditions (James *et al*., 2016). The chitosan-based product Chitoplant gave good control of grapevine downy mildew on leaves and bunches. Among inorganic products, formulations such as Tecnobiol (based on fatty acids and potassium salts) and Mycosin (based on aluminium silicate), and potassium phosphonates gave good results on leaves and clusters (Dagostin *et al*., 2006). The ALT.RAME*in*BIO project highlighted the good activity of liquorice leaf extract, laminarin and a formulation based on cell walls of *S. cerevisiae* against grapevine downy mildew. Potassium hydrogen carbonate and lime sulphur have been shown to be effective if used within a few hours of an infection period initiated when rainfall begins. Acid clay Ulmasud was also effective when used in particularly dry years and on robust and non-phytotoxicity sensitive varieties.

For control of *Ph. Infestans* (causing late blight of potato and tomato) the bacteria *X. bovienii* and *Ps. putida* gave good results in greenhouse tests on artificially inoculated potato plants. Laboratory and greenhouse tests demonstrated the efficacy of liquorice leaf extract, potassium hydrogen carbonate, *B. subtilis* strain QST 713, *Yucca schidigera* and *Abies sibirica* extract, and chitosan hydrochloride.

Against *V. inaequalis* causing apple scab, *Yucca schidigera* extract initiated leaf and fruit defences (De Jong and Heijne, 2006). Coconut extract, rapeseed oil and potassium hydrogen carbonate also showed the same control level as copper formulations against apple scab, during the primary infection period. Studies conducted in Italy under the STU.LI.RA. project showed best control of primary infection from lime sulphur, followed by carbonates combined with sulphur. Lime sulphur was also the most efficacious for preventing disease and for controlling secondary infections, second only to the copper-based formulations (Kelderer *et al.*, 2008, 2010).

Potassium hydrogen carbonate, investigated in the RepCo project, showed good efficacy, and these results contributed to the registration of this product in Europe (Heijne *et al*., 2007).

In the PURE project, the biocontrol agent *Cladosporium cladosporioides* H39 controlled apple scab in field trials, with efficacy comparable to copper hydroxide (Heijne *et al*., 2015). The RepCo project showed that *C. cladosporioides* R406 reduced ascospore production by *V. inaequalis* from treatments on overwintering leaves in autumn. When applied in summer, *C. cladosporioides* H39 reduced sporulation of the pathogen (Köhl *et al*., 2015). The ALT.RAME*in*BIO project confirmed efficacy of lime sulphur.

For control of phytopathogenic bacteria, the After-Cu project demonstrated the anti-infective properties of peptide molecules such as AP17, Li27 and PSA21 against pathogenic bacteria such as *Ps. savastanoi*, *Ps. syringae* pv. *actinidiae*, *Ps. syringae* pv. *syringae* and *Ps. syringae* pv. *tabaci*, with efficacy comparable to that of copper sulphate (Mota and Cornelis, 2005; Cerboneschi *et al*., 2015; Tegli *et al*., 2015). The EVERGREEN project demonstrated good efficacy of phenolic extract from agricultural waste against *Ps. savastanoi* pv. *nerii* strain Psn23 (Biancalani *et al*., 2016). The Bio Bug Bang project showed good antibacterial activity of gallic acid and ellagic acid (extracts from *Punica granatum*) against *Ps. syringae* pv. *tomato* and *Ps. syringae* pv. *actinidia* (Quattrucci and Balestra, 2011; Quattrucci *et al*., 2011). The ALT.RAME*in*BIO project demonstrated the inhibitory activity of essential oil constituents (carvacrol, thymol and eugenol), gallic acid and coumarin against *Ps. syringae* pv. *tomato* and *X. axonopodis* pv. *vesicatoria*, the causal agents, respectively, of tomato bacterial speck and bacterial spot (Giovanale *et al*., 2017).

Use of products with low copper contents

The RepCo, STU.LI.RA and PRO.VI.SE.BIO projects demonstrated ability to adequately control grapevine downy mildew using formulations with low amounts of copper, such as Labicuper, Naturam 5 and Glutex Cu 90 (Spera *et al*., 2007; La Torre *et al*., 2007, 2008, 2010, 2011, 2012a, 2014b).

Use of reduced copper dosages

The ALTRAME*in*BIO project verified the effectiveness of copper doses against grapevine downy mildew at rates of 200 and 400 g ha^{-1} per treatment, much less than average dosages recommended for commercially available copper compounds (http://www.sinab.it/ricerca/altrameinbio-strategie-la-riduzione-e-possibili-alternative-all%E2%80%99utilizzo-del-rame)

Disease forecasting models

The use of forecasting models can play a key role for optimizing treatments. The PRADA project demonstrated prediction of the course of grapevine downy mildew on a territorial scale, by combining data collected from meteorological stations with that from meteorological radar (Cicogna *et al*., 2005; Dietrich *et al*., 2007). Operators were accurately informed of disease development in their territories allowing them to provide adequate control measures. The RIMpro forecasting model, developed under the CO-FREE project for grapevine downy mildew control, showed good correlation between disease simulation and development. The Bio-PhytoPRE model, developed under the Blight-MOP project, enabled potato late blight control in field tests using copper-based formulations, applied with reduced doses, with no significant yield losses (Musa-Steenblock and Forrer, 2005a).

Conclusions

This review has examined aspects of the use of copper in plant disease management, and problems due to its environmental animal and plant toxicity. EFSA's conclusions on copper risk assessments have identified critical concerns for three organism groups (birds and mammals, aquatic organisms including sediment dwellers, and soil macro-organisms) (EFSA, 2018). Although different approaches have been studied, copper is still necessary at present, especially in organic farming, to contain plant diseases that are widespread among numerous crop species grown in the Mediterranean regions (grapes, olives, stone fruits, pome fruits) (Heibertshausen *et al*., 2007; Dagostin *et al*., 2011; Cabús *et al*., 2017; Kühne *et al*., 2017). Although no substances have yet been identified to replace copper in plant protection, and research efforts in this direction must continue, meaningful reductions in the quantities of copper used can be achieved with no concomitant economic losses, using this metal with care and only when strictly necessary. It is important to adopt appropriate measures and promote the adoption of an agro-ecological model that can increase agroecosystem resilience and prevent the occurrence of diseases. Location of the area and pedological characteristics must be evaluated when vineyards or orchards are planted, and crop varieties appropriate for the climate and the growing environment should be used. Where available, varieties resistant to major crop pathogens should be used. All measures to prevent pathogen occurrence must be taken (e.g. pruning for improved ventilation and light, under-sowing to prevent waterlogging, appropriate and balanced irrigation and fertilization, removal of crop residues, low plant population density, and cultural practices aimed at inoculum reduction). It is essential to understand pathogen biological pathways, and the phenological phases where infection risk is greatest. Phytosanitary status should be continuously monitored to modulate disease management treatments based on actual infection risks. It may also be useful to use copper in a combined strategy with other products, to reduce copper inputs, and to use products that increase plant resistance to pathogens (Hofmann, 2002). Appropriate and efficient equipment must be used for treatments, and disease forecasting models must be adopted, if available, to identify the optimal pesticide application times. At present, pathogens can be adequately controlled with reduced copper application rates (Heibertshausen *et al*., 2007; Cabús *et al*., 2017). Thus, the integration of different strategies can minimize concerns about persistence and toxicity of this important disease management metal.

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Literature cited

Abbasi P.A. and B. Weselowski, 2014. Influence of foliar sprays of *Bacillus subtilis* QST 713 on development of early blight disease and yield of field tomatoes in Ontario. *Canadian Journal of Plant Pathology* 36, 170–178. DOI:10.1080/07060661.2014.924027.

Abd-El-Kareem F. and W.M. Haggag, 2014. Chitosan and citral alone or in combination for controlling early blight disease of potato plants under field conditions. *Research Journal of Pharmaceutical, Biological and Chemical Sciences* 5, 941–945.

Afunian M.R., P.H. Goodwin and D.M. Hunter, 2004. Linkage of Vfa4 in *Malus* × *domestica* and *Malus floribunda* with *Vf* resistance to the apple scab pathogen *Venturia inaequalis*. *Plant Pathology* 53, 461–467.

Aguirre G. and M. Pilon, 2016. Copper Delivery to Chloroplast Proteins and Its Regulation. *Frontiers in Plant Science* 6, 1250. DOI:10.3389/fpls.2015.01250.

Ait Barka E., P. Eullaffroy, C. Clément and G. Vernet, 2004. Chitosan improves development, and protects *Vitis vinifera* L. against *Botrytis cinerea*. *Plant Cell Reports* 22, 608–614.

Aktar-Uz-Zaman M., M. Tuhina-Khatun, M.M. Hanafi and M. Sahebi, 2017. Genetic analysis of rust resistance genes in global wheat cultivars: an overview. *Biotechnology & Biotechnological Equipment* 31(3), 431–445. DOI: 10.1080/13102818.2017.1304180.

Alam S.M. and S. Raza, 2001. Micronutrient Fertilizers. *Pakistan Journal of Biological Sciences* 4, 1446–1450.

Alaoui-Sossé B., P. Genet, F. Vinit-Dunand, M.L. Toussaint, D. Epron and P.M. Badot, 2004. Effect of copper on growth in cucumber plants (*Cucumis sativus*) and its relationships with carbohydrate accumulation and changes in ion contents. *Plant Science* 166, 1213–1218.

Alaphilippe A., Y. Capowiez, G. Severac, S. Simon, M. Saudreau, S. Caruso and S. Vergnani, 2016. Codling moth exclusion netting: an overview of French and Italian experiences. *IOBC-WPRS Bulletin* 112, 31–35.

Almekinders C.J.M., L. Mertens, J.P. van Loon and E.T. Lammerts van Bueren, 2014. Potato breeding in the Netherlands: a successful participatory model with collaboration between farmers and commercial breeders. *Food security* 6, 515–524.

Al-Mughrabi K.I, 2008. Biological control of *Phytophthora infestans* of potatoes using *Trichoderma atroviride*. *Pest Technology* 2(2), 104–108.

Amadei M., M. Dimartino, A. Arbizzani and A. Allegri, 2014. Efficacy evaluation of two new formulations of potassium bicarbonate (Armicarb® 85 and Karma® 85) to control apple scab and *Monilinia* spp. on peach. In: *Atti Giornate Fitopatologiche* 2, 75–84.

Andersen G.L., O. Menkissoglou and S.E. Lindow, 1991. Occurrence and properties of copper tolerant strains of *Pseudomonas syringae* isolated from fruit trees in California. *Phytopathology* 81, 648–656.

Andrivon D., 1995. Inhibition by aluminium of mycelial growth and sporangial production and germination in *Phytophthora infestans*. *European Journal of Plant Pathology* 101, 527–533.

Apel K. and H. Hirt, 2004. Reactive oxygen species: metabolism, oxidative stress and signal transduction. *Annual Review of Plant Biology* 55, 373–399. DOI: 10.1146/annurev.arplant.55.031903.141701

Arias M., M. Paradelo, E. López and J. Simal-Gándara, 2006. Influence of pH and soil copper on adsorption of metalaxyl and penconazole by the surface layer of vineyard soils. *Journal of agricultural and food chemistry* 54, 8155–8162.

Arnebrant K., E. Bååth and A. Nordgren, 1987. Copper tolerance of microfungi isolated from polluted and unpolluted forest soil. *Mycologia* 79, 890–895.

Atia M.M.M., H. Buchenauer, A.Z. Aly and M.I. Abou-Zaid, 2005. Antifungal activity of chitosan against *Phytophthora infestans* and activation of defence mechanisms in tomato to late blight. *Biological Agriculture and Horticulture* 23(2),175–197.

ATSDR (United States Agency for Toxic Substances and Disease Registry), 2004. Toxicological Profile for Copper. U.S. Department of Health and Human Services, 272 pp.

Aziz A., B. Poinssot, X. Daire, M. Adrian, A. Bézier, B. Lambert, J.M. Joubert and A. Pugin, 2003. Laminarin elicits defense responses in grapevine and induces protection against *Botrytis cinerea* and *Plasmopara viticola*. *Molecular Plant-Microbe Interactions* 16, 1118–1128.

Aziz A., P. Trotel-Aziz, L. Dhuicq, P. Jeandet, M. Couderchet and G. Vernet, 2006. Chitosan oligomers and copper sulfate induce grapevine defense reactions and resistance to gray mold and downy mildew. *Phytopathology* 96, 1188–1194.

Balaž J., S. Aćimović, G. Aleksić, M. Bodroža and B. Cvetković, 2010. Evaluation of possibilities of *Venturia inaequalis* control by ecologically acceptable products. *Pesticidi i fitomedicina* 25, 335–342. DOI:10.2298/PIF1004335B.

Baldwin D.H., J.F. Sandahl, J.S. Labenia and N.L. Scholz, 2003. Sublethal effects of copper on coho salmon: Impacts on nonoverlapping receptor pathways in the peripheral olfactory nervous system. *Environmental Toxicology and Chemistry* 22, 2266–2274.

Baldwin D.H., C.P. Tatara and N.L. Scholz, 2011. Copper-induced olfactory toxicity in salmon and steelhead: Extrapolation across species and rearing environments. Aquatic Toxicology 101, 295–297.

Bangemann L.W., A. Westphal., P. Zwerger, K. Sieling and H. Kage, 2014. Copper reducing strategies for late blight (*Phytophthora infestans*) control in organic potato (*Solanum tuberosum*) production. *Journal of Plant Diseases and Protection* 121(3), 105–116.

Barbarick K.A. and H.J. Pirela, 1984. Agronomic and horticultural uses of zeolite. In: *Zeo-agriculture: Use of Natural Zeolites in Agriculture and Aquaculture* (W.G. Pond, F.A. Mumpton, eds.), Westview Press, Boulder, CO, USA, 93-103.

Bargagli R., 1998. *Trace elements in terrestrial plants: an ecophysiological approach to biomonitoring and biorecovery*. Springer, Berlin Heidelberg New York, 324 pp.

Battilani P. and V. Rossi, 1986. Modellamento dello sviluppo epidemiologico di *Cercospora beticola* Sacc. in funzione del clima. In: *Atti Giornate Fitopatologiche* 2, 283–294.

Battilani P., V. Rossi, P. Racca and S. Giosuè, 1996a. ONIMIL, a forecaster for primary infection of downy mildew of onion. *EPPO Bulletin* 26, 567–576.

Battilani P., P. Racca, V. Rossi, S. Giosuè, R. Roberti and P. Flori, 1996b. Validation of ONIMIL, a forecaster for primary infection of downy mildew on onion. *In: Proceedings, Workshop on Decision Systems in Crop Protection,* November 4-November 8, 1996, Munster, Germany.

Battilani P., V. Rossi, P. Racca and S. Giosuè, 1998a. A warning system for downy mildew infection on onion. In: *Atti, 7th International Congress of Plant Pathology*, Edimburgh, UK, No 3.1.24 (abstract).

Battilani P., R. Bottazzi, P. Racca V. and Rossi, 1998b. Ruolo dello stadio fenologico della cipolla nella previsione delle infezioni primarie di *Peronospora destructor*. In: *Atti Giornate Fitopatologiche*, 637–642.

Becker A., 2013. Piwis in der Praxis. *Schweizer Zeitschrift für Obst- und Weinbau* 3, 4–7.

Bednarska A.J., M. Choczyński, R. Laskowski and M. Walczak, 2017. Combined effects of chlorpyriphos, copper and temperature on acetylcholinesterase activity and toxicokinetics of the chemicals in the earthworm *Eisenia fetida*. *Environmental Pollution* 220, Vol. A, 567–576.

Behlau F., B.I. Canteros, J.B. Jones and J.H. Graham, 2012. Copper resistance genes from different xanthomonads and citrus epiphytic bacteria confer resistance to *Xanthomonas citri* subsp. *citri*. *European Journal of Plant Pathology* 133(4), 949–963.

Bender C.L. and D.A. Cooksey, 1986. Indigenous plasmids in *Pseudomonas syringae* pv. *tomato*: conjugative transfer and role in copper resistance. *Journal of Bacteriology* 165, 534–541.

Bengtsson M., H.J.L. Jørgensen, E. Wulff and J. Hockenhull, 2006. Prospecting for organic fungicides and resistance inducers to control scab (*Venturia inaequalis*) in organic apple production. In: *Joint Organic Congress*, May 30–May 31, 2006, Odense, Denmark.

Bengtsson M., E. Wulff, H.L., Jørgensen, A. Pham, M. Lübeck and J. Hockenhull, 2009. Comparative studies on the effects of a yucca extract and acibenzolar-S-methyl (ASM) on inhibition of *Venturia inaequalis* in apple leaves. *European Journal of Plant Pathology* 124, 187–198.

Beni C. and G. Rossi, 2009. Conventional and organic farming: estimation of some effects on soil, copper accumulation and wine in a Central Italy vineyard. *Agrochimica* 53, 145–159.

Beresford R.M., J.L. Tyson and W.R. Henshall, 2017. Development and validation of an infection risk model for bacterial canker of kiwifruit, using a multiplication and dispersal concept for forecasting. *Bacterial Diseases Phytopathology* 107(2), 184–191. DOI: 10.1094/PHYTO-04-16-0166-R.

Besnard E., C. Chenu and M. Robert, 2001. Influence of organic amendments on copper distibution among particle-size and density fractions in Champagne vineyard soils. *Environmental Pollution* 112, 329–337.

Betti L., G. Trebbi, V. Majewsky, C. Scherr, D., Shah-Rossi, T. Jäger and S. Baumgartner, 2009. Use of homeopathic preparations in phytopathological models and in field trials: a critical review. *Homeopathy* 98(4), 244–266. DOI: 10.1016/j.homp.2009.09.008.

Beyer W.N., 1981. Metal and terrestrial earthworms (*Annelida*: *Oligochaeta*). In: *Workshop on the role of earthworms in the stabilization of organic residues*, Vol. I, Beach Leaf Press, Kalamazoo, MI, 137–150.

Biancalani C., M. Cerboneschi, F. Tadini-Buoninsegni, M. Campo, A. Scardigli, A. Romani and S. Tegli, 2016. Global analysis of Type Three Secretion System and Quorum Sensing inhibition of *Pseudomonas savastanoi* by Polyphenols Extracts from vegetable residues. *PloS one* 11, e0163357.

Blaise P.H. and C. Gessler, 1992. Vinemild: toward a management tool for grape downy mildew. *Acta Horticulturae* 313, 257–262. DOI: 10.17660/ActaHortic.1992.313.32.

Blaise P.H., R. Dietrich and C. Gessler, 1999a. Vinemild: an application-oriented model of *Plasmopara viticola* epidemics on *Vitis vinifera*. *Acta Horticulturae* 499, 187–192. DOI: 10.17660/ActaHortic.1999.499.21.

Blaise P.H., R. Dietrich and M. Jermini, 1999b. A new demand function for grapevine fruits in Vinemild. *Acta Horticulturae* 499, 253–260. DOI: 10.17660/ActaHortic.1999.499.29.

Blouin M., M.E. Hodson, E.A. Delgado, G. Baker, L. Brussard, K.R. Butt, J. Dai, L. Dendooven, G. Peres, J.E. Tondoh, D. Cluzeau and J.-J. Brun, 2013. A review of earthworm impact on soil function and ecosystem services. *European Journal of Soil Science*, 161–182.

Bondarczuk K. and Z. Piotrowska-Seget, 2013. Molecular basis of active copper resistance mechanisms in Gram-negative bacteria. *Cell Biology and Toxicology* 29, 397–405.

Borgo M., A. Zanzotto and D. Bellotto, 2004. Use of different fungicides in control strategies against grapevine downy mildew in the province of Treviso. In: *Atti Giornate Fitopatologiche* 2, 163–170.

Borkow G. and J. Gabbay, 2005. Copper as a Biocidal Tool. *Current Medicinal Chemistry* 12, 2163–2175.

Bortolotti P.P., R. Nannini, M. Scannavini, L. Antoniacci and R. Bugiani, 2006. Evaluation of different copper compounds at low rates for the protection of grapevine from downy mildew in province of Modena. In: *Atti Giornate Fitopatologiche* II, 173–178.

Bost M., S. Houdart, M. Oberli, E. Kalonji, J.F. Huneau and I. Margaritis, 2016. Dietary copper and human health: current evidence and unresolved issues. *Journal of Trace Elements in Medicine and Biology* 35, 107–115

Bremner I., B.W. Young and C.F. Mills, 1976. Protective effect of zinc supplementation against copper toxicosis in sheep. *British Journal of Nutrition* 36, 551–561.

Brewer G.J., 2012. Copper toxicity in Alzheimer's disease: Cognitive loss from ingestion of inorganic copper. *Journal of Trace Elements in Medicine and Biology* 26, 89–92.

Brouwer D.J., E.S. Jones and D.A. St. Clair, 2004. QTL analysis of quantitative resistance to *Phytophthora infestans* (late blight) in tomato and comparisons with potato. *Genome* 47, 475–492.

Brown D.R., K. Qin, J.W. Herms, A. Madlung, J. Manson, R. Strome, P.E. Fraser, T. Kruck, A. von Bohlen, W. Schulz-Schaeffer, A. Giese, D. Westaway and H. Kretzschmar, 1997. The cellular prion protein binds copper *in vivo*. *Nature* 390, 684–687.

Brun L.A., J. Maillet, P. Hinsinger and M. Pépin, 2001. Evaluation of copper availability to plants in copper-contaminated vineyard soils. *Environmental Pollution* 111, 293–302.

Brunelli A., L. Draghetti, I. Gherardi, A. Vercesi and P. Cortesi, 1990. Verifica del modello EPI-Plasmopara in Emilia-Romagna. *Notiziario sulle malattie delle piante* 111 (III Serie n° 38), 247–265.

Brunelli A. and O. Palla, 2005. Evoluzione dei fungicidi rameici e aspetti fitoiatrici. *Phytomagazine* 12, 9–13.

Brunelli A., 2016. L'evoluzione dei fungicidi rameici e aspetti fitoiatrici. *Terra e vita* 14, 2–3.

Bruns C., H. Schulz, C. Tebbe, P. Racca, D. Werren, M.R. Finckh and B. Kleinhenz, 2017. Erweiterung des Entscheidungshilfesystems Öko-SIMPHYT zur Reduktion der Kupferapplikationen gegen *Phytophthora infestans* im ökologischen

Kartoffelanbau. In: *14. Wissenschaftstagung Ökologischer Landbau*, March 7–March 10, 2017, Campus Weihenstephan, Freising-Weihenstephan, Germany.

Bugiani R., P. Cavanni and I. Ponti, 1993. An advisory service for the occurrence of *P. infestans* on tomato in Emilia-Romagna region. *EPPO Bulletin* 23, 607–613.

Bunea C.I., D. Popescu, A. Bunea and M. Ardelean, 2013. Variation of attack degree of downy mildew (*Plasmopara viticola*) in five wine grape varieties, under conventional and organic control treatments. *Journal of Food, Agriculture & Environment* 11(3-4), 1166–1170.

Burkhead J.L., K.A. Reynolds, S.E. Abdel-Ghany, C.M. Cohu, and M. Pilon, 2009. Copper homeostasis. *New Phytologist*, 182, 799–816. DOI: 10.1111/j.1469-8137.2009.02846.x.

Cabús A., M. Pellini, R. Zanzotti, L. Devigili, R. Maines, O. Giovannini, L. Matteidi and E. Mescalchin, 2017. Efficacy of reduced copper dosages against *Plasmopara viticola* in organic agriculture. *Crop Protection* 96, 103–108.

Caffi T., V. Rossi, R. Bugiani, F. Spanna, L. Flamini, A. Cossu and C. Nigro, 2006. Validation of a simulation model for *Plasmopara viticola* primary infections in different vine-growing areas across Italy. In: *Proceeding, 5th International Workshop on Grapevine Downy and Powdery Mildew* (I. Pertot, C. Gessler, D. Gadoury, W. Gubler, H.H. Kasemeyer, P. Magarey, ed.), June 18–June 23, 2006, San Michele all'Adige, Italy, 112–114.

Caleca V., G. Lo Verde, V. Lo Verde, M. Palumbo Piccionello and R. Rizzo, 2011. Control of *Bactrocera oleae* and *Ceratitis capitata* in organic orchards: Use of clays and copper products. *Acta Horticulturae* 873, 227–234.

Canadian General Standards Board, 2006. *Organic Production Systems Permitted Substances Lists*. Government of Canda, CAN/CGSB-32.311-2006.

Cao K., S.T. Wang, P. Kessler, P.M. Fried and H.R. Forrer, 2003. Krautfäulebekämpfung im Bio-Kartoffelanbau ohne Kupfer? *AGRARForschung* 10(5), 182–187.

Ceccanti B., 2004. Accumulo e comportamento del rame nei vigneti biologici. *L'Informatore agrario* 60, 123–128.

Cecconi I., A. Scaloni, G. Rastelli, M. Moroni, P.G. Vilardo, L. Costantino, M. Cappiello, D. Garland, D. Carper, J.M. Petrash, A. Del Corso and U. Mura, 2002. Oxidative Modification of Aldose Reductase Induced by Copper Ion. Definition of the metal-protein interaction mechanism. *Journal of Biological chemistry* 277(44), 42017–42027. DOI: 10.1074/jbc.M206945200.

Cerboneschi M., C. Biancalani, M.V. Ortenzi, S. Macconi, P. Bogani, S. Biricolti, S. Smeazzetto, F. Tadini-Buoninsegni, M.R. Moncelli and S. Tegli, 2015. Virulence inhibiting peptides: an environmentally friendly and effective alternative to copper for the control of plant pathogenic bacteria. In: *Book of Abstracts, 4th International Workshop Conference on Expression, Structure and Function of Membrane Proteins*, June 28-July 2, 2015, Florence, Italy, 19.

Chaignon V., I. Sanchez-Neira, P. Herrmann, B. Jaillard and P. Hinsinger, 2003. Copper bioavailability and extractability as related to chemical properties of contaminated soils from a vine-growing area. *Environmental Pollution* 123, 229–238.

Chalal M., J.B. Winkler, K. Gourrat, S. Trouvelot, M. Adrian, J.P. Schnitzler, F. Jamois and X. Daire, 2015. Sesquiterpene volatile organic compounds (VOCs) are markers of elicitation by sulfated laminarine in grapevine. *Frontiers in Plant Science* 6, 350. DOI:10.3389/fpls.2015.00350.

Chouinard G., A. Firlej and D. Cormier, 2016. Going beyond sprays and killing agents: Exclusion, sterilization and disruption for insect pest control in pome and stone fruit orchards. *Scientia Horticulturae* 208, 13–27.

Chouinard G., J. Veilleux, F. Pelletier, M. Larose, V. Philion and D. Cormier, 2017. Impact of exclusion netting row covers on arthropod presence and crop damage to 'Honeycrisp' apple trees in North America: A five-year study. *Crop Protection* 98, 248–254.

Cicogna A., S. Dietrich, M. Gani, R. Giovanardi and M. Sandra, 2005. Use of meteorological radar to estimate leaf wetness as data input for application of territorial epidemiological model (downy mildew - *Plasmopara viticola*). *Physics and Chemistry of the Earth, Parts A/B/C* 30, 201–207.

Cohen S.R., 1974. A review of the health hazards from copper exposure. *Journal of Occupational and Environmental Medicine* 16, 621–624.

Cohen Y., W.O. Wang, B.H. Ben-Daniel and Y. Ben-Daniel, 2006. Extracts of *Inula viscosa* control downy mildew of grapes caused by *Plasmopara viticola*. *Phytopathology* 96, 417–424

Collins D.P. and B.J. Jacobsen, 2003. Optimizing a *Bacillus subtilis i*solate for biological control of sugar beet cercospora leaf spot. *Biological Control* 26, 153–161. DOI: org/10.1016/S1049-9644(02)00132-9.

Commission Regulation (EC) No 473/2002 of 15 March 2002 amending Annexes I, II and VI to Council Regulation (EEC) No 2092/91 on organic production of agricultural products and indications referring thereto on agricultural products and foodstuffs, and laying down detailed rules as regards the transmission of information on the use of copper compounds. OJ L 75, 16.3.2002, 21-24.

Commission Regulation (EC) No 889/2008 of 5 September 2008 laying down detailed rules for the implementation of Council Regulation (EC) No 834/2007 on organic production and labelling of organic products with regard to organic production, labelling and control. OJ L 250, 18.9.2008, 1-84.

Commission Directive 2009/37/EC of 23 April 2009 amending Council Directive 91/414/EEC to include chlormequat, copper compounds, propaquizafop, quizalofop-P, teflubenzuron and zeta-cypermethrin as active substances. OJ L 104, 24.4.2009, 23-32.

Commission Implementing Regulation (EU) No 85/2014 of 30 January 2014 amending Implementing Regulation (EU) No 540/2011 as regards the extension of the approval period of the active substance copper compounds. OJ L 28, 31.1.2014, 34-35.

Commission Implementing Regulation (EU) No 2015/232 of 13 February 2015 amending and correcting Implementing Regulation (EU) No 540/2011 as regards the conditions of approval of the active substance copper compounds. OJ L 39, 14.2.2015, 7-10.

Commission Implementing Regulation (EU) No 2015/408 of 11 March 2015 on implementing Article 80(7) of Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market and establishing a list of candidates for substitution. OJ L 67, 12.3.2015, 18-22.

Commission Implementing Regulation (EU) No 2018/84 of 19 January 2018 amending Implementing Regulation (EU) No 540/2011 as regards the extension of the approval periods of the active substances chlorpyrifos, chlorpyrifos-methyl, clothianidin, copper compounds, dimoxystrobin, mancozeb, mecoprop-p, metiram, oxamyl, pethoxamid, propiconazole, propineb, propyzamide, pyraclostrobin and zoxamide. OJ L 16, 20.1.2018, 8-10.

Cook P.J., P.J. Landschoot and M.J. Schlossberg, 2009. Inhibition of *Pythium* spp. and suppression of Pythium blight of turfgrasses with phosphonate fungicides. *Plant disease* 93(8), 809–814.

Cooksey D.A., 1990. Plasmid-determined copper resistance in *Pseudomonas syringae* from Impatiens. *Applied and Environmental Microbiology* 56, 13–16.

Council Directive 86/278/EEC of 12 June 1986 on the protection of the environment, and in particular of the soil, when sewage sludge is used in agriculture. OJ L 181, 4.7.1986, 6–12.

Dagostin S., A. Ferrari and I. Pertot, 2006. Integration of different control measures to maximise disease control of *Plasmopara viticola* in Italian organic viticulture. In: *Joint Organic Congress*, May 30–May 31, 2006, Odense, Denmark.

Dagostin S., T. Formolo and I. Pertot, 2008. Replacement of copper in organic viticulture: efficacy evaluation of new natural fungicides against downy mildew. *IOBC/wprs Bulletin* 36, 87–90.

Dagostin S., T. Formolo, O. Giovannini, I. Pertot and A. Schmitt, 2010. *Salvia officinalis* extract can protect grapevine against *Plasmopara viticola*. *Plant Disease* 94(5), 575–580.

Dagostin S., H.J. Schärer, I. Pertot and L. Tamm, 2011. Are there alternatives to copper for controlling grapevine downy mildew inorganic viticulture? *Crop Protection* 30, 776–788.

De Jong P.F. and B. Heijne, 2006. REPCO contribution to the development of products for apple scab control. In: *Joint Organic Congress*, May 30–May 31, Odense, Denmark.

Dell'Amico E., M. Mazzocchi, L. Cavalca, L. Allievi and V. Andreoni, 2008. Assessment of bacterial community structure in a long-term copper-polluted ex-vineyard soil. *Microbiological Research* 163, 671–683.

Deluisa A., P. Giandon, M. Aichner, P. Bortolami, L. Bruna, A. Lupetti, F. Nardelli and G. Stringari, 1996. Copper pollution in Italian vineyard soils. *Communications in Soil Science and Plant Analysis* 27, 1537–1548.

Deluisa A., L. Vincentini, V. Coletti and P. Sivilotti, 2007. Il rame nei vigneti biologici del Friuli Venezia Giulia. *Notiziario ERSA* 4, 43–49.

Demirci S., Z. Ustaoğlu, G.A. Yılmazer, F. Sahin and N. Baç, 2014. Antimicrobial properties of zeolite-X and zeolite-A ion-exchanged with silver, copper and zinc against a broad range of microorganisms. *Applied Biochemistry and Biotechnology* 172, 1652–1662.

Departments and Agencies of the federal government of the United States, 2018. *Electronic Code of Federal Regulations*. 7BIM205G. https://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&SID=9874504b6f1025eb0e6b67cadf9d3b40&rgn=div6&view=text&node=7:3.1.1.9.32.7&idno=7

Dietrich S., L. Baldini, F. Di Paola and E. Santorelli, 2007. Low rainfall optimization of operational radar measurements to support leaf wetness monitoring techniques. *Italian Journal of Agrometeorology* 12, 13–20.

Donnarumma L. and A. La Torre, 2000. Sali di rame in agricoltura biologica e possibili alternative. *Informatore Fitopatologico* 4, 27–31.

Dorn B., T. Musa, H. Krebs, P.M. Fried and H.R. Forrer, 2007. Control of late blight in organic potato production: evaluation of copper-free preparations under field, growth chamber and laboratory conditions. *European Journal of Plant Pathology* 119, 217–240.

Dorsey A., L. Ingerman and S. Swarts, 2004. *Toxicological profile for copper*. US Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, V. Weinsberg, Stuttgart, Deutschland, 106–109.

Dousset S., A.R. Jacobson, J. Dessogne, N. Guichard, P.C. Baveye and F. Andreux, 2007. Facilitated transport of diuron and glyphosate in high copper vineyard soils. *Environmental Science and Technology* 41, 8056–8061.

EFSA (European Food Safety Authority), M. Arena, D. Auteri, S. Barmaz, G. Bellisai, A. Brancato, D. Brocca, L. Bura, H. Byers, A. Chiusolo, D. Court Marques, F. Crivellente, C. De Lentdecker, M. Egsmose, Z. Erdos, G. Fait, L. Ferreira, M. Goumenou, L. Greco, A. Ippolito, F. Istace, S. Jarrah, D. Kardassi, R. Leuschner, C. Lythgo, J.O. Magrans, P. Medina, I. Miron, T. Molnar, A. Nougadere, L. Padovani, J.M. Parra Morte, R. Pedersen, H. Reich, A. Sacchi, M. Santos, R. Serafimova, R. Sharp, A. Stanek, F. Streissl, J. Sturma, C. Szentes, J. Tarazona, A. Terron, A. Theobald, B. Vagenende, A. Verani and L. Villamar-Bouza, 2018. Conclusion on the peer review of the pesticide risk assessment of the active substance copper compounds copper(I), copper(II) variants namely copper hydroxide, copper oxychloride, tribasic copper sulfate, copper(I) oxide, Bordeaux mixture. *EFSA Journal 2018* 16(1), 5152–5175.

EGTOP, 2014. Final Report On Plant Protection Products (II). In: *9th Plenary meeting* April 28–April 30 2014, European Commission, Directorate-General for Agriculture and Rural Development.

Eife R., M. Weiss, V. Barros, B. Sigmund, U. Goriup, D. Komb, W. Wolf, J. Kittel, P. Schramel and K. Reiter, 1999. Chronic poisoning by copper in tap water: I. Copper intoxications with predominantly gastrointestinal symptoms. *European Journal of Medical Research* 4, 219–223.

Eisler R. 1998. *Copper hazards to fish, wildlife, and invertebrates: A synoptic review*. U.S. Geological Survey, Biological Resources Division, Biological Science Report USGS/BRD/BSR-1997-0002, Washington, DC, 98 pp.

El Jarroudi M., L. Kouadio, C.H. Bock, M. El Jarroudi, J. Junk, M. Pasquali, H. Maraite and P. Delfosse, 2017. A threshold-based weather model for predicting stripe rust infection in winter wheat. *Plant Disease* 101(5), 693–703. DOI: 10.1094/PDIS-12-16-1766-RE.

El-Mougy N. and M. Abdel-Kader, 2009. Salts application for suppressing potato early blight. *Journal of Plant Protection Research* 49(4), 353–361. DOI: 10.2478/v10045-009-0055-8.

El-Mougy N., M. Abdel-Kader and D.E.H. Aly, 2012. Application of plant resistance inducers for controlling early and late blights of tomato under plastic houses conditions. *Journal of Applied Sciences Research* 8(7), 3406–3414.

El-Sharkawy H.H.A., S. Tohamey and A.A. Khalil, 2015. Combined Effects of *Streptomyces viridosporus* and *Trichoderma harzianum* on controlling wheat leaf rust caused by *Puccinia triticina*. *Plant Pathology Journal* 14, 182–188. DOI:10.3923/ppj.2015.182.188.

El-Sharkawy H.H.A, T.S.A. Abo-El-Wafa and S.A. Ibrahim, 2018. Biological control agents improve the productivity and induce the resistance against downy mildew of grapevine. *Journal of plant pathology* 100(3), 1–10. DOI: 10.1007/s42161-018-0007-0.

El-Sharouny H.M.M., M.M. Bagy and A.A. El-Shanawany, 1988. Toxicity of heavy metals to Egyptian soil fungi. *International biodeterioration* 24, 49–64.

Elvehjem C.A. and E.B. Hart, 1929. The relation of iron and copper to hemoglobin synthesis in the chick. *Journal of Biological Chemistry* 84, 131–141.

Enkelmann R. and P. Wohlfart, 1994. Aluminium residues on and in grapes as well as in must and wine after application of Ulmasud. *Angewandte Botanik* 68(5–6), 187–190.

EPA (United States Environmental Protection Agency), Office of Water, 2016. *Draft aquatic life ambient estuarine/marine water quality criteria for copper*. EPA-822-P-16-001.

Etebarian H.R., E.S. Scott and T.J. Wicks, 2000. *Trichoderma harzianum* T39 and *T. virens* DAR 74290 as potential biological control agents for *Phytophthora erythroseptica*. *European Journal of Plant Pathology* 106, 329–337.

Fage S.W., A. Faurschou and J.P. Thyssen, 2014. Copper hypersensitivity. *Denmark Contact Dermatitis* 71, 191–201. DOI:10.1111/cod.12273.

Federal Ordinance 910.181 on Organic Farming of the Federal Department of Economic Affairs, Education and Research of 22 September 1997 and further modifications.

Feliziani E., M. Santini, L. Landi and G. Romanazzi, 2013. Pre- and postharvest treatment with alternatives to synthetic fungicides to control postharvest decay of sweet cherry. *Postharvest Biology and Technology* 78, 133–138.

Fernández-Calviño D., J.C. Nóvoa-Muñoz, E. López-Periago and M. Arias-Estévez, 2008. Changes in copper content and distribution in young, old and abandoned vineyard acid soils due to land use changes. *Land Degradation and Development* 19, 165–177.

Fernández-Calviño D., C. Pérez-Novo, J.C., Nóvoa-Muñoz and M. Arias-Estévez, 2009. Copper fractionation and release from soils devoted to different crops. *Journal of Hazardous Materials* 167, 797-802.

Ferrari D., E. Bassignana and G. Pensabene, 2000. Efficacy evaluation of different low-rate copper formulations and acupric compounds against grapevine downy mildew (*Plasmopara viticola*) in Piedmont (North-Western Italy) during the period 1994-1999. In: *6th International Congress on Organic Viticulture*, August 25–August 26, 2000, Basel, Switzerland, 163–165.

Figueroa M., K.E. Hammond-Kosack and P.S. Solomon, 2018. A review of wheat diseases – a field perspective. *Molecular Plant Pathology* 19(6), 1523–1536. DOI: 10.1111/mpp.12618.

Flemming C.A. and J.T. Trevors, 1989. Copper toxicity and chemistry in the environment: a review. *Water, Air, and Soil Pollution* 44, 143–158.

Flores-Vélez L.M., J. Ducaroir, A.M. Jaunet and M. Robert, 1996. Study of the distribution of copper in an acid sandy vineyard soil by three different methods. *European Journal of Soil Science* 47, 523–532.

Flori P., M. Banorri and A. Cesari, 2006. Biological effect of the micronization and adjuvant addition on activity of fungicides controlling powdery mildew. In: *Atti Giornate Fitopatologiche* I, 535–542.

Foolad M., H. Merk and H. Ashrafi, 2008. Genetics, genomics and breeding of late blight and early blight resistance in tomato. *Critical Reviews in Plant Sciences* 27, 75–107.

FRAC, 2018. http://www.frac.info/docs/default-source/publications/frac-code-list/frac_code_list_2018-final.pdf?sfvrsn=6144b9a_2.

Franchi A., R. Bugani and A. Barani, 2010. Modelli previsionali: un aiuto contro la peronospora della vite. *L'Informatore Agrario* 21, 5–9.

Fregoni M. and L. Bavaresco, 1984. Il rame nel terreno e nella nutrizione della vite. *Vignevini* 11, 37–49.

Fregoni M. and G. Corallo, 2001. Il rame nei vigneti italiani; La dotazione in rame dei vigneti italiani. *Vignevini: Rivista Italiana di Viticoltura e di Enologia* 28, 35–43.

Gadd G.M., 1993. Interactions of fungi with toxic metals. *New Phytologist* 124, 25–60.

Galbignani M., S. Poni and A. Palliotti, 2014. Vite: posticipare la maturazione con la defogliazione tardiva. *L'Informatore Agrario* 18, 40–44.

Gallagher C.H. and V.E. Reeve, 1971. Copper deficiency in the rat effect on synthesis of phospholipids. *Australian Journal of Experimental Biology & Medical Science* 49, 21–31.

Gallegly M.E. and M.E. Marvel, 1955. Inheritance of resistance to tomato race O of *Phytophthora infestans*. *Phytopathology* 45, 103–109.

Garde-Cerdán T., V. Mancini, M. Carrasco-Quiroz, A. Servili, G. Gutiérrez-Gamboa, R. Foglia, E. P. Pérez-Álvarez and G. Romanazzi, 2017. Chitosan and Laminarin as alternatives to copper for *Plasmopara viticola* control: effect on grape amino acid. *Journal of Agricultural and Food Chemistry* 65(34), 7379–7386. DOI: 10.1021/acs.jafc.7b02352.

Gent D.H. and H.F. Schwartz, 2005. Management of Xanthomonas leaf blight of onion with a plant activator, biological control agents, and copper bactericides. *Plant Disease* 89, 631–639.

Gessler C. and I. Pertot, 2012. Vf scab resistance of *Malus*. *Trees* 26(1), 95–108.

Gilardi G., M.L. Gullino and A. Garibaldi, 2010. Evaluation of spray programmes for the management of leaf spot incited by *Pseudomonas syringae* pv. *syringae* on tomato cv. Cuore di bue. *Crop Protection* 29, 330–335.

Gilardi G., S. Demarchi, M.L. Gullino and A. Garibaldi, 2015. Management of leaf spot of wild rocket using fungicides, resistance inducers and a biocontrol agent, under greenhouse conditions. *Crop Protection* 71, 39–44.

Giller K.E., E. Witter and S.P. McGrath, 1998. Toxicity of heavy metals to microorganisms and microbial processes in agricultural soils: a review. *Soil Biology & Biochemistry* 30, 1389–1414. DOI: 0.1016/S0038-0717(97)00270-8.

Giosuè S., G. Spada, V. Rossi, G. Carli and I. Ponti, 2000. Forecasting infections of the leaf curl disease on peaches caused by *Taphrina deformans*. *European Journal of Plant Pathology* 106, 563–571.

Giovanale G., E. Fortunati, A. Mazzaglia and G.M. Balestra, 2017. Possibilities of copper reduction in control of tomato bacterial diseases. *Journal of Plant Pathology* 99, S27.

Gomez, C., M. Chovelon, I. Pertot and S. Dagostin, 2007. *Alternatives au cuivre dans la maitrise du mildiou de la vigne.* Bilan projet REPCO 2004-2007, 27 pp.

Gorell J.M., E.L. Peterson, B.A. Rybicki and C.C. Johnson, 2004. Multiple risk factors for Parkinson's disease. *Journal of the neurological sciences* 217, 169–174.

Goto M., A. Kodera, A. Fujita, M. Nakajima, S. Tsuyumu and Y. Takikawa, 1991. Copper resistance and plasmids in *Pseudomonas syringae* pv. *actinidiae* and *P. glumae*. *Annals of the Phytopathologal Society of Japan* 57, 444.

Grando M.S., 2007. Miglioramento genetico. In: *La vite e il vino* (Script Art S.p.a.–Bologna, ed.). *Coltura & Cultura*, Bayer CropScience, Milano, IT, 474–479.

Halliwell B., 1999. *Free Radicals in Biology and Medicine*. Oxford University Press, New York.

Harm, A., H.H. Kassemeyer, T. Seibicke and F. Regner, 2011. Evaluation of chemical and natural resistance inducers against downy mildew (*Plasmopara viticola*) in grapevine. *American Journal of Enology and Viticulture* 62, 184–192.

Heibertshausen D., O. Baus-Reichel, U. Hofmann, K.H. Kogel and B. Berkelmann-Loehnertz, 2007. Using copper in organic viticulture: doing it best with less? In: *3rd QLIF Congress* March 20–March 23, 2007, Hohenheim, Germany.

Heijne B., P.F. de Jong, J. Köhl, A.G.C.L. Speksnijder, J. Hockenhull, M. Bengtsson, H. Lindhard Pederson, K. Paaske, U. Eiben, L. Tamm and M. Trapman, 2006. Prevention and control of apple scab. In: *Proceedings of the European Joint Organic Congress "Organic farming and rural development"*, May 30–May 31, 2006, Odense, Denmark, 200–201.

Heijne, B., P.F. de Jong, P.H. Lindhard, K. Paaske, M. Bengtsson and J. Hockenhull, 2007. Field efficacy of new compounds to replace copper for scab control in organic apple production. In: *3rd QLIF Congress* March 20–March 23, 2007, Hohenheim, Germany. Archived at http://orgprints.org/view/projects/int_conf_qlif2007.htm

Heijne, B., H.H.M. Helsen, T. Caffi, V. Rossi, J. Strassemeyer, J. Köhl, M.M. Riemens, A. Alaphilippe, S. Simon, Y. Capowiez, I.J. Holb, J.S. Buurma and W.H.G.J. Hennen, 2015. PURE progress in innovative IPM in pome fruit in Europe. *Acta Horticulturae (ISHS)* 1105, 383–390.

Henrik H. and A. Frankm, 2002. tcrB, a gene conferring transferable copper resistance in *Enterococcus faecium*: occurrence, transferability, and linkage to macrolide and glycopeptide resistance. *Antimicrobial Agents and Chemotherapy* 46, 1410–1416.

Hill G. K., 1990. Plasmopara Risk Oppenheim – a deterministic computer model for the viticultural extension service. *Notiziario sulle Malattie delle Piante* 111, 182–194.

Hill G. K., 2000. Simulation of *Plasmopara viticola* oospore maturation with the model SIMPO. *IOBC/WPRS Bulletin* 23, 7–8.

Hobbelen P.H.F., J.E. Koolhaas and C.A.M. van Gestel, 2006. Bioaccumulation of heavy metals in the earthworms *Lumbricus rubellus* and *Aporrectodea caliginosa* in relation to total and available metal concentrations in field soils. *Environmental Pollution* 144, 639–646.

Hofmann U., 1996. Control of downy mildew in organic grape production. *Obstbau-Weinbau* 33(4), 105–107.

Hofmann U., 2002. Copper reduction and copper replacement - results and experiences of 12 years of on farm research [Verrringerung der Kupferaufwandmenge und Kupferersatz - langjährige Erfahrungen in praktischen Betrieben]. In: *10th International Conference on Cultivation Technique and Phytopathological Problems in Organic Fruit-Growing and Viticulture*, February 4–February 7, 2002, Weinsberg, Germany, 181–184.

Holb I.J. and S. Kunz, 2016. Integrated control of apple scab and powdery mildew in an organic apple orchard by combining potassium carbonates with wettable sulfur, pruning, and cultivar susceptibility. *Plant Disease* 100, 1894–1905.

Hough L.F., 1944. A survey of the scab reistance of the foliage on seedlings in selected apple progenies. *Proceedings of American Society of Horticulture Sciences* 44, 260–272.

Ibrahim Y.E, A.A. Saleh, M.H. El Komy and M.A. Al Saleh., 2016. *Bacillus subtilis* QST 713, copper hydroxide, and their tank mixes for control of bacterial citrus canker in Saudi Arabia. *Journal of Citrus Pathology*, 3(1), 1-6.

IFOAM, 2014. *The IFOAM NORMS for Organic Production and Processing (Version 2014)*. International Federation of Organic Agricoltura Movements, Germany, 77 pp.

Iglesias I. and S. Alegre, 2006. The effect of anti-hail nets on fruit protection, radiation, temperature, quality and profitability of 'Mondial Gala' apples. *Journal of Applied Horticulture* 8, 91–100.

Ilhan K., U. Arslan and O.A. Karabulut, 2006. The effect of sodium bicarbonate alone or in combination with a reduced dose of tebuconazole on the control of apple scab. *Crop Protection* 25, 963–967.

ISO 11466, 1995. Soil Quality - Extraction of Trace Elements Soluble in Aqua Regia. *International Organization for Standardization*, Geneva, Switzerland.

Jäger T., C. Scherr, D. Shah, V. Majewsky, U. Wolf, L. Betti and S. Baumgartner, 2015. The use of plant-based bioassays in homeopathic basic research. *Homeopathy* 104(4), 277–282.

Jamar L., B. Lefrancq and M. Lateur, 2007. Control of apple scab (*Venturia inaequalis*) with bicarbonate salts under controlled environment. *Journal of Plant Diseases and Protection* 114, 221–227.

Jamar L., B. Lefrancq, C. Fassotte and M. Lateur, 2008. A during-infection spray strategy using sulphur compounds, copper, silicon and a new formulation of potassium bicarbonate for primary scab control in organic apple production. *European Journal of Plant Pathology* 122, 481–493.

Jamar L, J. Song, F. Fauche, J. Choi and M. Lateur, 2017. Effectiveness of lime sulphur and other inorganic fungicides against pear scab as affected by rainfall and timing application. *Journal of Plant Diseases and Protection* 124(4), 383–391. DOI: 10.1007/s41348-017-0085-9.

James E.E., D.A. Mulholland, M.K. Langat, I. Kleeberg, J. Treutwein, H.M.T. Hokkanen, B. Thürig, H.J. Schärer and L. Tamm, 2016. Development of a botanical plant protection product from Larix by-products. *Planta Medica* 82(S01), S1–S381. DOI: 10.1055/s-0036-1596140.

Janik L.J., S.T. Forrester, J.M. Soriano-Disla, J.K. Kirby, M.J. McLaughlin and C. Reimann, 2015. GEMAS: Prediction of solid-solution partitioning coefficients (Kd) for cationic metals in soils using mid-infrared diffuse reflectance spectroscopy. *Environmental Toxicology and Chemistry* 34, 224–234.

Jansonius P.J., J. Bloksma, B. Heijne and R.H.N. Anbergen, 2000. Alternatives for copper fungicide against scab on Jonagold apple. In: *9. Internationaler Erfahrungsaustausch über Forschungsergebnisse zum Ökologischen Obstbau*: Beiträge zur Tagung vom 01. bis 02.02.2000- an der LVWO Weinsberg, 18–20 pp.

Karlsson T., P. Persson and U. Skyllberg, 2006. Complexation of copper (II) in organic soils and in dissolved organic matter – EXAFS evidence for chelate ring structures. *Environmental Science & Technology* 40, 2623–2628.

Kelderer M., C. Casera and E. Lardschneider, 2008. Formulated and unformulated carbonates to control apple scab (*Venturia inaequalis*) on organic apple. In: *13th International Conference on Cultivation Technique and Phytopathological Problems in Organic Fruit-Growing*. Fördergemeinschaft Ökologischer Obstbau e. V. Weinsberg, Stuttgart, Deutschland, 47–53.

Kelderer M., C. Casera, E. Lardschneider and A. La Torre, 2010. Preventative and curative applications of carbonates against apple scab (*Venturia inaequalis*) in organic apple orchards. *Proceedings of the 14th Ecofuit congress*, 52–60.

Kelderer M. and E. Lardschneider, 2010. Effect of different treatments with oil cakes, plant protection agents and potassium phosphite to control collar rot on Topaz. In: *14th International Conference in Organic Fruit-Growing* – Eco-fruit, Fördergemeinschaft Ökologischer Obstbau e. V. Weinsberg, Stuttgart, Deutschland, 106–109.

Kellerhals M., L. Franck, I.O. Baumgartner, A. Patocchi and J.E. Frey, 2011. Breeding for fire blight resistance in apple. *Acta Horticulturae* 896, 385–389.

Kim D.G., D.H. Kim, Ych Kim, G.H. Park, N.D. Sung and Y.G. Cho, 2000. *Process for producing pesticide compositions containing zeolite (S Korea)*. Repub Korean Kongkae Taeho Kongbo. KR 2000058598 A 20001005.

Klein O., 2011. *A field study to evaluate the effects of copper on the earthworm fauna in Central Europe*. Study code: 20031343/G1-NFEw. Eurofins Agroscience Services, EcoChem GmbH.

Köhl J., 2007. *Replacement of copper fungicides in organic production of grapevine and apple in Europe*. Publishable Final Activity Report. REPCO 501452. http://www.rep-co.nl.

Köhl J., W. Molhoek, L. Groenenboom-de Haas, H. Goossen-van de Geijn and U. Eiben, 2008. *Cladosporium cladosporioides* H39: A new antagonist for biological control of apple scab. In: *ENDURE International Conference 2008, Diversifying crop protection*, October 12–October 15, 2008, La Grande-Motte, France, No. 0.66 (contribution in proceedings).

Köhl J., C. Scheer, I.J. Holb, S. Masny and W. Molhoek, 2015. Toward an integrated use of biological control by *Cladosporium cladosporioides* H39 in apple scab (*Venturia inaequalis*) management. *Plant Disease* 99, 535–543.

Kolmer J., 2013. Leaf rust of wheat: pathogen biology, variation and host resistance. *Forests* 4, 70–84. DOI:10.3390/f4010070.

Komárek M., J. Száková, M. Rohošková, H. Javorská, V. Chrastný and J. Balík, 2008. Copper contamination of vineyard soils from small wine producers: a case study from Czech Republic. *Geoderma* 147, 16–22.

Komárek M., E. Čadková, V. Chrastný, F. Bordas and J.C. Bollinger, 2010. Contamination of vineyard soils with fungicides: a review of environmental and toxicological aspects. *Environment International* 36, 138–151.

Kopsell D.E. and Kopsell D.A., 2007. Copper. In: *Handbook of plant nutrition* (Barker A.V., D.J. Pilbeam, ed.), Taylor and Francis Group, 293–328.

Kovačič G.R., M. Lešnik and S. Vršič, 2013. An overview of the copper situation and usage in viticulture. *Bulgarian Journal of Agricultural Science* 19(1), 50–59.

Kowalska J., D. Remlein-Starosta and D. Drożdżyński, 2011. Efficacy of bioagents against apple scab in organic orchards, preliminary results. In: *Organic is Life-Knowledge for Tomorrow* (D. Neuhoff, S. Mok Sohn, C. Ssekyewa, N. Halberg, I.A. Rasmussen J. Hermansen, ed), ISOFAR, Namyangju, Korea, 587–590.

Krause R.A., L.B. Massie and R.A. Hyre, 1975. BLITECAST, a computerized forecast of potato late blight. *Plant Disease Reporter* 59, 95–98.

KRAV, 2017. *Standards for KRAV certified production*.

Kühne S., D. Roßberg, P. Röhrig, F. von Mehring, F. Weihrauch, S. Kanthak, J. Kienzle, W. Patzwahl, E. Reiners and J. Gitzel, 2017. The Use of Copper Pesticides in Germany and the Search for Minimization and Replacement Strategies. *Organic Farming* 3(1), 66–75.

Kunito T., K. Saeki, S. Goto, H. Hayashi, H. Oyaizu and S. Matsumoto, 2001. Copper and zinc fractions affecting microorganisms in long term sludge-amended soils. *Bioresource Technology* 79, 135–146.

Kunz S. and M. Hinze, 2014. Assessment of biocontrol agents for their efficacy against apple scab. In: *16th International conference on Organic Fruit-Growing, ed FÖKO*, 65–71.

Kushalappa A.C., 2001. BREMCAST: Development of a system to forecast risk levels of downy mildew on lettuce (*Bremia lactucae*). *International Journal of Pest Management* 47(1), 1–5. DOI: 10.1080/09670870150215540.

La Torre A., S. Alegi and G. Imbroglini, 2002. Mezzi di difesa in agricoltura biologica. *L'Informatore Agrario* 16, 4–42.

La Torre A., G. Spera, S. Talocci and G. Cargnello, 2007. Evaluation of the effectiveness of natural alternative copper products and low rate copper formulations against grape downy mildew in organic viticulture. In: *15th International Symposium GESCO*, June 20–June23, 2007, Porec, Croatia, 2, 1007–1015.

La Torre A., G. Spera, S. Talocci, R. Valori and S. Rosati, 2008. Prove triennali volte a valutare l'efficacia antiperonosporica di prodotti di origine naturale alternativi al rame. In: *2° Convegno Nazionale di Viticoltura*, July 14–July 19, 2008, Marsala, Italy.

La Torre A., V. Pompi and A. Coramusi, 2010. Natural products alone or with copper vs. grape downy mildew: efficacy, costs, Cu impact. *Communications in Agricultural and Applied Biological Sciences* 75, 730–737.

La Torre A., C. Mandalà, F. Caradonia and V. Battaglia, 2011. Pluriennal trials for the control of grapevine downy mildew with natural products. In: *Proceedings, 17th International Symposium GiESCO*, August 29–September 2, 2011, Asti-Alba, Italy, 107–110.

La Torre A., C. Mandalà, F. Caradonia and V. Battaglia, 2012a. Natural alternatives to copper and low-rate copper formulations to control grape downy mildew in organic farming. *Hellenic Plant Protection Journal* 5, 13–21.

La Torre A., C. Mandalà, F. Caradonia and V. Battaglia, 2012b. Pluriennal trials for the control of grapevine downy mildew with natural products. In: *17th International Symposium GiESCO Le Progrès Agricole et Viticole* 129, 35–41.

La Torre A., F. Caradonia, G. Cargnello and V. Battaglia, 2013. Activity of *Mimosa tenuiflora* extract for the control of *Plasmopara viticola*. *Le Progrès Agricole et Viticole* 130(11), 17–23.

La Torre A., C. Mandalà, L. Pezza, F. Caradonia and V. Battaglia, 2014a. Evaluation of essential plant oils for the control of *Plasmopara viticola*. *Journal of Essential Oil Research* 26, 282–291. DOI: 10.1080/10412905.2014.889049.

La Torre A., P. Menesatti, M. Fibiani, V. Picchi, C. Mandalà, F. Antonucci and R. Lo Scalzo, 2014b. Phytochemical concentrations and antioxidant capacity of grapes treated with low copper formulations against downy mildew. *American Journal of Enology and Viticolture* 65, 486–492.

Lamichhane J.R., E. Osdaghi, F. Behlau, J. Kohl, J.B. Jones and J.-N. Aubertot, 2018. Thirteen decades of antimicrobial copper compounds applied in agriculture. A review. *Agronomy for Sustainable Development* 38, 28. DOI: 10.1007/s13593-018-0503-9.

Lammerts van Bueren E.T., M. Tiemens-Hulscher and P.C. Struik, 2008. Cisgenesis does not solve the late blight problem of organic potato production: alternative breeding strategies. *Potato Research* 51, 89–99.

Lammerts van Bueren E.T., R. Hutten, M. Tiemens-Hulscher and N. Vos, 2009. Developing collaborative strategies for breeding for organic potatoes in the Netherlands. In: *Proceeding, First International IFOAM Conference on Organic Animal and Plant Breeding*, August 25–August 28, 2009, Santa Fe, New Mexico USA, 176–181 (contribution in proceedings).

Lammerts van Bueren E.T., 2010. A collaborative breeding strategy for organic potatoes in the Netherlands. *Ecology and Farming,* 50–53.

Langdon C.J., T.G. Piearce, A.A. Meharg and K.T. Semple, 2001. Survival and behaviour of the earthworms *Lumbricus rubellus* and *Dendrodrilus rubidus* from arsenate-contaminated and non-contaminated sites. *Soil Biology & Biochemistry* 33, 1239–1244.

Legler S.E., T. Caffi, M. Gatti and V. Rossi, 2013. La difesa del vigneto biologico: l'unione fa la forza! *BioAgricultura* 140-141, 39–41.

Lencioni V., V. Grazioli, B. Rossaro and P. Bernabò, 2016. Transcriptional profiling induced by pesticides employed in organic agriculture in a wild population of *Chironomus riparius* under laboratory conditions. *Science of the Total Environment* 557, 183–191.

Leonardi F., G. Mossi and M. Camani, 2002. Il rame dei vigneti. *Dati – Statistiche e Società* 3, 55–59.

Lespinasse Y., 1989. Breeding pome fruits with stable resistance to dieases. *IOBC Bulletin* XII, 100–115.

Levinskaitë L., 2001. Effect of copper sulphate on assimilation of various substrata by soil fungi. *Ekologija* 3, 9–13.

Lightner G.W. and P.W. Steiner, 1992. Maryblyt™: A computer model for predicting of fire blight disease in apples and pears. *Computers and Electronics in Agriculture* 7(3), 249–260. DOI: 10.1016/S0168-1699(05)80023-7.

Lin X., C. Liu and P. He, 2005. Study on the inhibitory effects of chlorogenic acid originated from the leaves of *Arctium lappa* L. on pathogenic fungi. *Plant Protection-Beijing* 31(3), 35-37.

Linder M.C. and M. Hazegh-Azam, 1996. Copper biochemistry and molecular biology. *American Journal of Clinical Nutrition* 63, 797S–811S.

Lizzi Y., C. Coulomb, C. Polian, P.J. Coulomb. and P.O. Coulomb, 1998. L'algue face au mildiou: quel avenir? Des résultats de laboratoire très encourageants [Seaweed and mildew: what does the future hold?]. *Phytoma* 508, 29–30.

Llorente I., P. Vilardell, R. Bugiani, I Gherardi and E. Montesinos, 2000. Evaluation of BSPcast disease warning system in reduced fungicide use programs for management of brown spot of pear. *Plant Disease* 84, 631–637.

Lo Scalzo R., M. Fibiani, P. Pietromarchi, C. Mandalà and A. La Torre, 2012. Effects of different fungicide treatments on grape, must and wine quality. *Communications in Agricultural and Applied Biological Sciences* 77, 151–161.

Lucas G.C., E. Alves, R.B. Pereira, F.J. Perina and R.M. Souza, 2012. Antibacterial activity of essential oils on *Xanthomonas vesicatoria* and control of bacterial spot in tomato. *Pesquisa Agropecuária Brasileira*, Brasília 47(3), 351–359.

Lugauskas A., L. Levinskaitë, D. Peèiulytë, J. Repeèkienë, A. Motuzas, R. Vaisvalavièius and L. Prosyèevas, 2005. Effect of copper, zinc and lead acetates on microorganisms in soil. *Ekologija* 1, 61–69.

Lukas K., G. Innerebne, M. Kelderer, M.R. Finckh and P. Hohmann, 2016. Efficacy of copper alternatives applied as stop-sprays against *Plasmopara viticola* in grapevine. *Journal of Plant Diseases and Protection* 123, 171–176.

MacHardy W.E. and D.M. Gadoury, 1989. A revision of Mills' criteria for predicting apple scab infection periods. *Phytopathology* 79, 304–310.

MacHardy W.E., D.M. Gadoury and C. Gessler, 2001. Parasitic and biological fitness of *Venturia inaequalis*: relationship to disease management strategies. *Plant Disease* 85, 1036–1051.

MacKenzie D.R., 1981. Scheduling fungicide applications for potato late blight. *Plant Disease* 65, 394–399.

MacKenzie D.R., 1984. Blitecast in retrospect a look at what we learned. *FAO Plant Protection Bulletin* 32, 45–49.

Mackie K.A., T. Müller and E. Kandeler, 2012. Remediation of copper in vineyards–a mini review. *Environmental Pollution* 167, 16–26.

Magalhães M.J., E.M. Sequeira and M.D. Lucas, 1985. Copper and zinc in vineyard of Central Portugal. *Water, Air and Soil Pollution* 26, 1–17.

Magnien C., D. Jacquin, N. Muckensturm and P. Guillemard, 1991. MILVIT: un modèle descriptif et quantitatif de la phase asexuée du mildiou de la vigne. Présentation et premiers résultats de validation. *EPPO Bulletin* 21(3), 451–459. DOI: 10.1111/j.1365-2338.1991.tb01275.x.

Maia A.J., C.D. Leite, R.V. Botelho, C.M.D.R. Faria C. and D. Machado, 2012. Chitosan as an option to control mildew in the sustainable vinegrowing. *Semina: Ciências Agrárias, Londrina* 33, 2519–2530.

Malcolmson J.F. and W. Black, 1966. New R genes in *Solanum* *demissum* Lindl. and their complementary races of *Phytophthora infestans* (Mont.) de Bary. *Euphytica* 15, 199–203.

Mantovi P., 2003. Rischi di accumulo del rame nei terreni. *L'Informatore Agrario* 59, 67–72.

Marchand P.A., 2016. Basic substances under EC 1107/2009 phytochemical regulation: experience with non-biocide and food products as biorationals. *Journal of Plant Protection Research* 56(3), 312–318.

Marco G.M. and R.E. Stall, 1983. Control of bacterial spot of pepper initiated by strains of *Xanthomonas campestris* pv. *vesicatoria* that differ in sensitivity to copper. *Plant Disease* 67, 779–781.

Maregalli T., 2017. *The effects of soil copper contamination on earthworms' cholinergic transmission, locomotion and muscle physiology*. Senior theses, Trinity College, Hartfort, CT.

Marschner H.,1995. *Mineral Nutrition of Higher Plants*. Academic, San Diego.

Martin M., 2009. Fitotossicità da rame in suoli acidi ex-vitati. In: Il rame è indispensabile per l'agricoltura biologica? Usi, problemi e possibili alternative a cura di C.R.A.B. S.c.r.l. In: *Atti, Workshop di agricoltura biologica Campus - Salone della nuova agricoltura* 26 marzo, 2009, Lingotto Fiere Torino, 19–24.

McBride M., K. Tiller and R. Merry, 1981. *Copper in Soils and Plants*. Academic Press, Sydney.

McIntyre J.K., D.H. Baldwin, J.P. Meador, and N.L. Scholz, 2008. Chemosensory deprivation in juvenile coho salmon exposed to dissolved copper under varying water chemistry conditions. *Environmental Science and Technology* 42, 1352–1358.

McIntrye J.K., D.H. Baldwin, D.A. Beauchamp and N.L. Scholz, 2012. Low-level copper exposures increase visibility and vulnerability of juvenile coho salmon to cutthroat trout predators. *Ecological Applications* 22:5, 1460–1471.

Menesatti P., F. Antonucci, C. Costa, C. Mandalà, V. Battaglia and A. La Torre, 2013. Multivariate forecasting model to optimize management of grape downy mildew control. *Vitis* 52, 141–148.

Mery A.B. and J.M. Joubert, 2012. Laminarin (Vacciplant®) against appple scab (*Venturia inaequalis*) and *Gloeosporium* on apple (*Gloeosporium album et Perenans*). In *10th Conférence Internationale sur les Maladies des Plantes*, 3 December-December 5, 2012, 630–639. Association Française de Protection des Plantes (AFPP), Tours, France.

Messgo-Moumene S., R. Boukhalfa, D. Belaïdi, L. Beninal, S. Haddadj-Hamdi and M. Bellatreche 2017. *In vitro* antifungal activity of different plant extracts against *Phytophthora infestans* the causal agent of potato late blight. *Tunisian Journal of Plant Protection* 12, 19–33.

Michelante D. and D. Haine, 2004. Evaluation of products for potato protection against late blight in order to replace copper-based fungicides in organic farming. In: *PPO-Special Report* No. 10, *Applied Plant Research, AGV Research Unit* (Westerdijk C.E., H.T.A.M. Schepers, ed.), Lelystad, The Netherlands, 303–310.

Mills W.D., 1944. Efficient use of sulfur dusts and sprays during rain to control apple scab. C*ornell Extension Bulletin* 630, 4.

Miotto A., C.A. Ceretta, G. Brunetto, F.T. Nicoloso, E. Girotto, J.G. Farias, T.L. Tiecher, L. De Conti and G. Trentin, 2014. Copper uptake, accumulation and physiological changes in adult grapevines in response to excess copper in soil. *Plant Soil* 374, 593–610. DOI: 10.1007/s11104-013-1886-7.

Mirlean N., A. Roisenberg and J.O. Chies, 2007. Metal contamination of vineyard soils in wet subtropics (southern Brazil). *Environmental Pollution* 149, 10–17.

Mohamed A., A. Hamza and A. Derbalah, 2016. Recent approaches for controlling downy mildew of cucumber under greenhouse conditions. *Plant Protection Science* 52(1), 1–9. DOI: 10.17221/63/2015-PPS.

Mohr H.D., J. Holder and B. Berkelmann-Löhnertz, 2007. Minimirung des Kupfereinsatzes im ökoligischen Weinbau unter basonderer Berücksichtigung der Blattbeläge und ihrer Wirkung gegen den Falschen Mehltau (*Plasmopara viticola*) - Teil 1: 2002 bis 2003. *Nachrichtenblatt des Deutschen Pflanzenschutzdienstes* 59, 49–58.

Mohr H.D., J. Holder and B. Berkelmann-Löhnertz, 2008. Minimization of copper use in organic viticulture with special emphasis on leaf spray deposits and their effect against down mildew (*Plasmopara viticola*) - Part 2: 2004 to 2006. *Nachrichtenblatt des Deutschen Pflanzenschutzdienstes* 60, 145–156.

Montag J., L. Schreiber and J. Schönherr, 2006. Die postinfektionelle Wirkung von Calciumhydroxid auf Konidien von *Venturia inaequalis*. In *Proceeding, ecofruit-12th International Conference on Cultivation Technique and Phytopathological Problems in Organic Fruit-Growing*, January 31–February 2, 2006, Weinsberg, Germany, 77–80.

Montesinos E., C. Moragrega, I. Llorente, P. Vilardell, A. Bonaterra, I. Ponti, R. Bugiani, P. Cavanni and A. Brunelli, 1995. Development and evaluation of an infection model for *Stemphylium vesicarium* on pear based on temperature and wetness duration. *Phytopathology* 85, 586–592.

Moreau P., P. Thoquet, J. Olivier, H. Laterrot and N. Grimsley, 1998. Genetic mapping of *Ph-2*, a single locus controlling partial resistance to *Phytophthora infestans* in tomato. *Molecular Plant-Microbe Interactions* 1(4), 259–269.

Mota L.J. and G.R. Cornelis, 2005. The bacterial injection kit: type III secretion systems. *Annals of Medicine* 37, 234–249.

Mozaffari M., A.K. Alva and E.Q. Chen, 1996. Relation of copper extractable from soil and pH to copper content and growth of two citrus rootstocks. *Soil Science* 161, 786–792.

Muccinelli M., 2006. *Prontuario degli Agrofarmaci*. 13th, Edagricole, Milano, Italy, 997 pp.

Musa-Steenblock T. and H.R. Forrer, 2005a. Bio-PhytoPRE a decision support system for late blight control in organic potato production in Switzerland. In: *8. Wissenschaftstagung Ökologischer Landbau* (Heß J., G. Rahmann G., ed.), Kassel University press GmbH, Kassel, Germany, 133–136.

Musa-Steenblock T. and H.R. Forrer, 2005b. Bio-PhytoPRE – ein Warn- und Prognosesystem für den ökologischen Kartoffelanbau in der Schweiz. In: *8. Wissenschaftstagung* Ökologischer *Landbau*. March 1- March 4, 2005. Kassel, Germany.

Musetti, R., A. Vecchione, L. Stringher, S. Borselli, L. Zulini., C. Marzani, M. D'Ambrosio., L. Sanità di Toppi and I. Pertot, 2006. Inhibition of sporulation and ultrastructural alterations of grapevine downy mildew by the endophytic fungus *Alternaria alternata*. *Phytopathology* 96, 689–698.

Nabrdalik M. and K. Grata, 2015. Assessment of antifungal activity of extracts from nettle (*Urtica dioica* L.) against *Alternaria solani*. *Proceedings of ECOpole* 9(2), 473–481.

NAS (National Academy of Sciences), 1977. *Copper. Committee on Medical and Biologic effects of environmental pollutants*. National Research Council. National Academy of Science, Washington D.C., 124 pp.

Neaman A., S. Huerta and S. Sauvé, 2012. Effects of lime and compost on earthworm (*Eisenia fetida*) reproduction in copper and arsenic contaminated soils from the Puchuncaví Valley, Chile. *Ecotoxicology and Environmental Safety* 80, 386–392. DOI: org/10.1016/j.ecoenv.2012.04.013.

Nechwatal J. and M. Zellner, 2015. Potential suitability of various leaf treatment products as copper substitutes for the control of late blight (*Phytophthora infestans*) in organic potato farming. *Potato Research* 58, 261–276.

Ng K.K. and J.M. Webster, 1997. Antimycotic activity of *Xenorhabdus bovieni*i (Enterobacteriaceae) metabolites against *Phytophthora infestans* on potato plants. *Canadian Journal of Plant Pathology* 19, 125–132.

Nóvoa-Muñoz J.C., J.M.G. Queijeiro, D. Blanco-Ward, C. Álvarez-Olleros, A. Martínez-Cortizas and E. García-Rodeja, 2007. Total copper content and its distribution in acid vineyards soils developed from granitic rocks. *Science of the Total Environment* 378, 23–27.

NRC (National Research Council), 1977. *Copper*. Washington, D.C.: National Academy of Sciences.

Odum E.P., 1971. *Fundamentals of Ecology*. Saunders Company, Philadelphia, PA.

Orlandini S., B. Gozzini, G. Maracchi and M. Rosa, 1993a. PLASMO: un modello per il controllo della peronospora della vite. In: *Atti Convegno "Informatica e Agricoltura"*, (G. Maracchi, M.A. Falchi, ed.), December 17–December 18, 1992, Firenze, Italia, 81–90.

Orlandini S., B. Gozzini, G. Maracchi, F. Miglietta, C. Palchetti, M. Rosa and L. Seghi,1993b. Use of simulation models for managing grapevine protection. In: *Atti Convegno "Models, Computer Programs and Expert Systems for Agricultural Mechanization"*, October 1–October 2, 1993, Firenze, Italia, 287–292.

Orlandini S., B. Gozzini, M. Rosa, E. Egger, P. Storchi, G. Maracchi and F. Miglietta, 1993c. PLASMO: a simulation model for *Plasmopara viticola* on grapevine. *EPPO Bulletin* 23, 619–626.

Orlandini S. and M. Rosa, 1997. A model for the simulation of grapevine downy mildew. *Petria* 7(1), 47–54.

Oruc H.H., M. Cengiz and A. Beskaya, 2009. Chronic copper toxicosis in sheep following the use of copper sulfate as a fungicide on fruit trees. *Journal of Veterinary Diagnostic Investigation* 21, 540–543.

Outten F.W., D.L. Huffman, J.A. Hale and T.V. O'Halloran, 2001. The independent cue and cus systems confer copper tolerance during aerobic and anaerobic growth in *Escherichia coli*. *Journal of Biological Chemistry* 276, 30670–30677.

Ozrenk K., F. Balta and F. Celik, 2012. Levels of fire blight (*Erwinia amylovora*) susceptibility of native apple, pear and quince germplasm from Lake Van Basin, Turkey. *European Journal of Plant Pathology* 132, 229–236.

Pacilly F.C.A., J.C.J. Groot, G.J. Hofstede, B.F. Schaap and E.T.L. van Bueren. 2016. Analysing potato late blight control as a social-ecological system using fuzzy cognitive mapping. *Journal of Agronomy for Sustainable Development* 36(2), 35. DOI:10.1007/s13593-016-0370-1.

Palmer C.L., R.K. Horst and R.W. Langhans, 1997. Use of bicarbonates to inhibit *in vitro* colony growth of *Botrytis cinerea*. *Plant Disease* 81, 1432–1438.

Palmieri M.C., M. Perazzolli, V. Matafora, M. Moretto, A. Bachi and I. Pertot, 2012. Proteomic analysis of grapevine resistance induced by *Trichoderma harzianum* T39 reveals specific defence pathways activated against downy mildew. *Journal of Experimental Botany* 63, 6237–6251.

Paoletti M.G., E. Lovane and M. Cortese, 1988. Pedofauna bioindicators and heavy metals in five agroecosystem in North East Italy. *Revue d'écologie et de biologie du sol* 25, 33–58.

Parat C., R. Chaussod, J. Lévéque, S. Dousset and F. Andreux, 2002. The relationship between copper accumulated in vineyard calcareous soils and soil organic matter and iron. *European Journal of Soil Scienc*e 53, 663–669.

Park E.W., D. Gadoury and R.C. Pearson, 1997. DMCast: a prediction model for grape downy mildew development. *Viticutural and Enological Science* 52, 182–189.

Parisi L., Y. Lespinasse, J. Guillaumes and J. Kruger, 1993. A new race of *Venturia inaequalis* virulent to apples with resistance due to the Vf gene. *Phytopathology* 83, 533–537.

Parveaud C.E., C. Gomez, M. Chovelon, J. Lambion, S. Dagostin and I. Pertot, 2010. Alternatives to copper-based treatments for the control of grapevine downy mildew (*Plasmopara viticola*): 5-year synthesis of trials in France and Italy. In: *28th International Horticultural Congress*, August 22–August 27, 2010, Lisbon, Portugal.

Pavloušek K., 2010. Experiences with the cultivation characteristics of new fungus-resistant varieties for red wine production. *Mitteilungen Klosterneuburg* 60, 355–362.

Pedneault K., M. Shan Ching Seong and P. Angers, 2012. Determination of quality attributes driving consumer acceptance for cold hardy grape wines produced in Quebec. In: *VitiNord*, November 28–December 1, 2012, Neubrandenberg, Germany.

Pedneault K. and C. Provost, 2016. Fungus resistant grape varieties as a suitable alternative for organic wine production: Benefits, limits and challenges. *Scientia Horticulturae* 208, 57–77.

Peil A., M.V. Hanke, H. Flachowsky, K. Richter, T. Garcia-Libreros, J.M. Celton, S. Gardiner, M. Horner and V.G.M. Bus, 2008. Confirmation of the fire blight QTL of Malus x robusta 5 on linkage group 3. *Acta Horticulturae* 793, 297–303.

Peil A, V.G.M. Bus, K. Geider, K. Richter K., H. Flachowsky and M.V. Hanke, 2009. Improvement of fire blight resistance in apple and pear. *International Journal of Plant Breeding* 3, 1–27.

Pellegrini A., D. Prodorutti, A. Frizzi, C. Gessler and I. Pertot, 2010. Development and evaluation of a warning model for the optimal use of copper in organic viticulture. *Journal of Plant Pathology* 92(1), 43–55.

Pertot I., T. Caffi, V. Rossi, L. Mugnai, C. Hoffmann, M.S. Grando, C. Gary, D. Lafond, C. Duso, D. Thiery, V. Mazzoni and G. Anfora, 2017. A critical review of plant protection tools for reducing pesticide use on grapevine and new perspectives for the implementation of IPM in viticulture. *Crop Protection* 97, 70–84.

Phillips S.L., C. Leifert, J. Santos, P. Juntharathep, L. Bodker, L. Tamm and A.B. Smit, 2002. Development of a systems approach for the management of late blight (*Phytophthora infestans*) in organic potato production: an update on the EU Blight-MOP project. *In:Proceeding, The BCPC Conference: Pests and Diseases,* November 18–November 21, 2002, Brighton, UK, 539–546.

Pietrzak U. and D.C. McPhail, 2004. Copper accumulation, distribution and fractionation in vineyard soils of Victoria, Australia. *Geoderma* 122, 151–166.

Plagge J. and S. Rommelt, 1997. Study on the effect of alternative control methods against blossom infection with fireblight (*Erwinia amylovora*) in apples. In: *4th Scientific Meeting on Ecological Agriculture,* March 3–March 4, 1997, Rheinische Friedrich Wilhelms Universitat Bonn 4, 199–203.

Pujos P., A. Martin, F. Farabullini and M. Pizzi, 2014. Romeo™, cerevisane-based biofungicide against the main diseases of grape and of other crops: general description. In: *Atti Giornate Fitopatologiche* 2, 51–56.

Puopolo G, O. Giovannini and I. Pertot, 2014a. *Lysobacter capsici* AZ78 can be combined with copper to effectively control *Plasmopara viticola* on grapevine. *Microbiological Research* 169, 633–642. DOI: 10.1016/j.micres.2013.09.013.

Puopolo G., A. Cimmino, M.C. Palmieri, O. Giovannini, A. Evidente and I. Pertot, 2014b. *Lysobacter capsici* AZ78 produces cyclo (l-Pro-l-Tyr), a 2, 5-diketopiperazine with toxic activity against sporangia of *Phytophthora infestans* and *Plasmopara viticola*. *Journal of applied microbiology* 117, 1168–1180. DOI: 10.1111/jam.12611.

Quattrucci A. and G.M. Balestra, 2011. Biocontrol of tomato bacterial speck by natural extracts. *Acta Horticulturae* 914, 369–371.

Quattrucci A., R. Cortesi, A. Tiezzi, M. Muganu and G.M. Balestra, 2011. Efficacia di microincapsulati contenenti acidi organici nel controllo di *Pseudomonas syringae* pv. *tomato*. In: *Abstract Book, I° Congresso Nazionale per la Ricerca in Agricoltura Biologica*, November 7–November 8, 2011, Catania, Italy, No. B10, 89 (abstract).

Rabea E.I., M.E.T. Badawy, C.V. Stevens, G. Smagghe and W. Steurbaut, 2003. Chitosan as antimicrobial agent: applications and mode of action. *Biomacromolecules* 4, 1457–1465. DOI: 10.1021/bm034130m.

Rajapaksha R.M., M.A. Tobor-Kaplon and E. Baath, 2004. Metal toxicity affects fungal and bacterial activities in soil differently. *Applied and Environmental Microbiology* 70, 2966–2973.

Ramesh K., D.D. Reddy, A.K. Biswas and A. Subbarao, 2011. Potential uses of zeolite in agriculture. *Advances in Agronomy* 113, 219–241.

Reháková M., S. Čuvanová, M. Dzivák, J. Rimár and Z. Gavaľová, 2004. Agricultural and agrochemical uses of natural zeolite of the clinoptilolite type. *Current Opinion in Solid State and Materials Science* 8, 397–404.

Rensing C. and G. Grass, 2003. *Escherichia coli* mechanisms of copper homeostasis in a changing environment. *FEMS Microbiological Reviews* 27, 197–213.

Reuveni M., D. Neifeld, D. Dayan and Y. Kotzer, 2009. BM- 608 - A novel organic product based on essential tea tree oil for the control of fungal diseases in tomato. *Acta Horticultura* 808, 129–132. DOI: 10.17660/ActaHortic.2009.808.18.

Richardson H.W., 1997. *Handbook of copper compound and applications*. Ed. Mark Dekker, New York, 432 pp.

Roberts P.D., M.T. Momol, L. Ritchie, S.M. Olson, J.B. Jones and B. Balogh, 2008. Evaluation of spray programs containing famoxadone plus cymoxanil, acibenzolar-S-methyl, and *Bacillus subtilis* compared to copper sprays for management of bacterial spot on tomato. *Crop Protection* 27, 1519–1526.

Robotic V., R. Bosancic and M. Mojic., 2000. Controlling vine powdery and downy mildews with *Urticum* preparation. In *Proceedings, 6th International Congress of Organic Viticulture*, 2000, Basel, 193–194.

Roelfs A.P., R.P. Singh and E.E. Saari, 1992. Rust. *Diseases of Wheat: Concepts and Methods of Disease Management*. Mexico, DF. CIMMYT.

Romanazzi G., V. Mancini, E. Feliziani, A. Servili, S. Endeshaw and D. Neri, 2016. Impact of alternative fungicides on grape downy mildew control and vine growth and development. *Plant Disease* 100(4), 739–748.

Rommelt S., J. Plagge, D. Treutter and W. Zeller, 1999. Fire blight control in apple using alternative products. *Gesunde Pflanzen* 51(3), 72–74.

Rosa M., R. Genesio, B. Gozzini, G. Maracchi and S. Orlandini, 1993. PLASMO: a computer program for grapevine downy mildew development forecasting. *Computers and Electronics in Agriculture* 9, 205–215.

Rosa M., B. Gozzini, G. Maracchi, S. Orlandini and L. Seghi, 1997. The PLASMO model for grapevine protection. *Viticultural and Enological Sciences* 52, 180–181.

Rosa M. and S. Orlandini, 1997. Structure and application of the PLASMO model for the control of grapevine downy mildew. *Petria* 7(1), 61–70.

Rossainz-Castro L.G., I. De la Rosa-Gomez, M.T. Olguín and D. Alcantara-Díaz, 2016. Comparison between silver- and copper-modified zeoliterich tuffs as microbicidal agents for *Escherichia coli* and *Candida albicans*. *Journal of Environmental Management* 183, 763–770.

Rossi V., 1995. Use of a simulation model "CERCODEP" in the control of cercospora leaf spot on sugar beet. *Proceedings of the 58th I.I.R.B. Congress*, 355–359.

Rossi V., P. Racca, D. Pancaldi and I. Alberti, 1996. Appearance of *Puccinia recondita* f.sp. *tritici* on winter wheat: a simulation model. *EPPO Bulletin* 26, 555–566.

Rossi V., P. Racca, S. Giosuè, D. Pancaldi and I. Alberti, 1997. A simulation model for the development of brown rust epidemics in winter wheat. *European Journal of Plant Pathology* 103, 453–465.

Rossi V., T. Caffi, S. Giosuè, B. Girometta, R. Bugiani, F. Spanna, D. Dellavalle, A. Brunelli and M. Collina, 2005. Elaboration and validation of a dynamic model for primary infections of *Plasmopara viticola*. *Rivista Italiana di Agrometeorologia* 10(3), 7–13.

Rossi V., R. Bugiani, T. Caffi and S. Giosuè, 2006. Dynamic simulation of grape downy mildew on grapevine. *Proceeding, 5th International Workshop on Grapevine Downy and Powdery Mildew*, June 18–June 23, San Michele all'Adige, Italy, 109–111.

Rossi V., S. Giosuè and R. Bugiani, 2007. A-scab (Apple-scab), a simulation model for estimating risk of *Venturia inaequalis* primary infections. *EPPO Bulletin* 37(2), 300–308. DOI: 10.1111/j.1365-2338.2007.01125.x.

Rossi V., T. Caffi, S. Giosuè and R. Bugiani, 2008. A mechanistic model simulating primary infections of downy mildew in grapevine. *Ecological Modelling* 212, 480–491.

Rousseau J., S. Chanfreau and É. Bontemps, 2013. *Les cépages* résistants aux *maladies cryptogamiques*. Groupe ICV, Bordeaux, 228 pp.

Roychoudhury S., S. Nath, P. Massanyi, R. Stawarz, M. Kacaniova and A. Kolesarova, 2016. Copper-induced changes in reproductive functions: *in vivo* and *in vitro* effects. *Physiological Research* 65, 11–22.

Rucksthul M. and H.R. Forrer, 1998. Main infection and sporulation periods (MISP): towards its use in an event-based DSS to control potato late blight. In: *PAV-Special Report* No. 3 (E. Bouma and H. Schepers, ed.), 67–76.

Rühling Å., E. Bååth, A. Nordgren and B. Söderström, 1984. Fungi in metal-contaminated soil near the Gusum brass mill, Sweden. *Ambio* 13, 34–36.

Runjić M. and H. Čustović, 2017. Copper in surface layer of vineyard soils on Island Hvar. *Agriculturae Conspectus Scientificus* 82(1), 13–17.

Rusjan D., M. Strlič M., D. Pucko and Z. Korošec-Koruza, 2007. Copper accumulation regarding the soil characteristics in Sub-Mediterranean vineyards of Slovenia. *Geoderma* 141, 111–118.

Sandahl J.F., D.H. Baldwin, J.J. Jenkins and N.L. Scholz, 2004. Odor-evoked field potentials as indicators of sublethal neurotoxicity in juvenile coho salmon (*Oncorhynchus kisutch*) exposed to copper, chlorpyrifos, or esfenvalerate. *Canadian Journal of Fisheries and Aquatic Sciences* 61, 404–413.

Sandahl J.F., D.H. Baldwin, J.J. Jenkins and N.L. Scholz, 2007. A sensory system at the interface between urban stormwater runoff and salmon survival. *Environmental Science and Technology* 41, 2998–3004.

Sanna F., A. Cossu, G. Roggero, S. Bellagarda, R. Deboli and A. Merlone, 2014. Evaluation of EPI forecasting model with inclusion of uncertainty in input value and traceable calibration. In: *17° Convegno Nazionale di Agrometeorologia,* June, 2014, AIAM, Rome.

Santić Z., Z. Puvacić, S. Radović and S. Puvacić, 2005. Higher mortality risk of lungs carcinoma in vineyard sprayers. *Bosnian journal of basic medical sciences* 5, 65–69.

Sawant S.D. and I.S. Sawant, 2008. Use of potassium bi-carbonates for the control of powdery mildew in table grapes. *Acta Horticulturae* 785, 285–291.

Scarascia-Mugnozza G., C. Sica and G. Russo, 2012. Plastic materials in European agriculture: actual use and perspectives. *Journal of Agricultural Engineering Research* 42, 15–28.

Scherf A., C. Schuster, P. Marx, U. Gärber, S. Konstantinidou-Doltsinis and A. Schmitt, 2010. Control of downy mildew (*Pseudoperonospora cubensis*) of greenhouse grown cucumbers with alternative biological agents. *Communications in Agricultural and Applied Biological Sciences* 75(4), 541–554.

Schiatti P. and S. Nutricato, 2006. Quali livelli di tossicità ha il rame che si accumula nel terreno? *Agricoltura (Regione Emilia Romagna)* 10, 124–126.

Schmitt A., S. Kunz, S. Nandi, B. Seddon and A. Ernst, 2002. Use of *Reynoutria sachalinensis* plant extracts, clay preparations and *Brevibacillus brevis* against fungal diseases of grape berries. In: *10th International Conference on Cultivation Technique and Phytopathological Problems in Organic Fruit-Growing and Viticulture*, February 4–February 7, 2002, Weinsberg, Germany, 146–151.

Schmitt A., A. Scherf, S. Mazzotta, S. Kühne, I. Pertot, J. Köhl, A. Markellou, D. Andrivon, R. Pellé, M. Bousseau, J.E. Chauvin, D. Thiéry, L. Delière, J. Kowalska, C.E. Parveaud, A. Petit, R. Giovinazzo, J. Brenner, M. Kelderer, E. Lammerts van Bueren, C. Bruns, M.R. Finckh, B. Kleinhenz, J. Smith, A. Simon-Levert, C. Bertrand, V. Andreu, P. Pujos, M. Trapman, J. Stark, P. van Cutsem, S. Neerakkal, H. Kleeberg, A. Peters and L. Tamm, 2017. CO-FREE Alternative Test Products for Copper Reduction in Agriculture. In: *Proceedings, 18th International Reinhardsbrunn Symposium*, April 24–April 28, 2016 Friedrichroda, Germany, 267–272.

Schulze K. and J. Schönherr, 2003. Calcium hydroxide, potassium carbonate and alkyl polyglycosides prevent spore germination and kill germ tubes of apple scab (*Venturia inaequalis*). *Journal of Plant Diseases and Protection* 110, 36–45.

Schuster C., S. Konstantinidou-Doltsinis and A. Schmitt, 2010. *Glycyrrhiza glabra* extract protects plants against important phytopathogenic fungi. *Communications in Agricultural and Applied Biological Sciences* 75, 531.

Segarra G., E. Casanova, D. Bellido, M.A. Odena, E. Oliveira and I. Trillas, 2007. Proteome, salicylic acid, and jasmonic acid changes in cucumber plants inoculated with *Trichoderma asperellum* strain T34. *Proteomics* 7, 3943–3952.

Segarra G., S. Van der Ent, I. Trillas and C.M.J. Pieterse, 2009. MYB72, a node of convergence in induced systemic resistance triggered by a fungal and a bacterial beneficial microbe. *Plant Biology* 11, 90–96.

Segarra G., M. Avilés, E. Casanova, C. Borrero and I.Trillas, 2013. Effectiveness of biological control of *Phytophthora capsici* in pepper by *Trichoderma asperellum* strain T34. *Phytopathologia Mediterranea* 52(1), 77–83.

Sévérac G. and M. Siegwart, 2013. Protection Alt'Carpo, nouvelles études sur trois ans. *Phytoma* 668, 33–37.

Sholberg P.L., K.E. Bedford, P. Haag and P. Randall, 2001. Survey of *Erwinia amylovora* isolates from British Columbia for resistance to bactericides and virulence on apple. *Canadian Journal of Plant Pathology* 23, 60–67.

Sivčev B.V., I.L. Sivčev and Z.Z. Ranković-Vasić, 2010. Natural process and use of natural matters in organic viticulture. *Journal of Agricultural Science* 55, 195–215.

Smith T.J. and P.L. Pusey, 2011. Cougarblight 2010, a significant update of the Cougarblight fire blight infection risk model. *Acta Horticulturae* 896, 331–336. DOI: 10.17660/ActaHortic.2011.896.45.

Solomon F., 2009. Impacts of Metals on Aquatic Ecosystems and Human Health. *Environment & Communities* 3, 25–28.

Speiser B., A. Berner, A. Häseli and L. Tamm, 2000. Control of downy mildew of grapevine with potassium phosphonate: Effectivity and phosphonate residues in wine. *Biological agriculture & horticulture* 17(4), 305–312.

Speiser B., L. Tamm, T. Amsler, J. Lambion, C. Bertrand, A. Hermansen, M.A. Russien, P. Haaland, J. Zarb, J. Santos, P. Shotton, S. Wilcockson, P. Juntharathep, R. Ghorbani and C. Leifert, 2006. Improvement of late blight management in organic potato production systems in Europe: field tests with more resistant potato varieties and copper-based fungicides. *Biological Agriculture & Horticulture* 23, 393–412.

Spera G., A. La Torre, S. Talocci, R. Valori and G. Cargnello, 2007. Difesa antiperonosporica su "Malvasia di candia" in un vigneto a conduzione biologica. In: *II Simposio Internazionale "Malvasie del Mediterraneo"*, October 2–October 6, 2007, Salina (Me), Italy.

Spitalny K.C., J. Brondum, R.L. Vogt, H.E. Sargent and S. Kappel, 1984. Drinking-water-induced copper intoxication in a Vermont family. *Pediatrics* 74, 1103–1106.

Stefanelli G., 1993. Utilizzo del rame in viticoltura: luci e ombre su uno dei più importanti anticrittogamici. In: *Atti dell'incontro tecnico su "Il controllo delle crittogame del melo e della vite con le tecniche più ecocompatibili"*, November 12–November 13, 1993, Gemona del Friuli, Italia.

Strizyk S., 1983. Modèle d'Etat Potentiel d'Infection. Application à *Plasmopara viticola*. *ACTA*, Paris.

Strumpf T., J. Strassemeyer, S. Krück, P. Horney, B. Hommel, D. Felgentreu and N. Herwig, 2015. Methodische Aspekte bei der Erhebung von Regenwurmlebensgemeinschaften im Qualitätsweinbau (Methodological aspects in the collection of earthworm communities in quality viticulture). *Journal für Kulturpflanzen* 67(1), 5–21.

Suciu I., L. Prodan, V. Lazar, E. Ilea, A. Cocîrla, L. Olinici, A. Paduraru, O. Zagreanu, P. Lengyel, L. Gyrffi and D. Andru, 1981. Research on copper poisoning. *La Medicina del Lavoro* 3, 190–197.

Sundin G.W., A.L. Jones and D.W. Fulbright, 1989. Copper resistance in *Pseudomonas syringae* pv. *syringae* from cherry orchards and its associated transfer *in vitro* and *in planta* with a plasmid. *Phytopathology* 79, 861–865.

Tamm L., J.G. Fuchs, N. Böger, L. Mühletaler, A. Amsler, D. Levite and A. Häseli, 2004. Eigenschaften von Tonerdepräparaten: Erfahrungen ausder Schweiz [Properties of acidified clay preparations: the Swiss experience]. In: *Internationales Symposium für ökologischen Weinbau*. Intervitis Stuttgart, Stuttgart, May 12-May 13, 2004, 27–36.

Tapwal A., S. Garg, N. Gautam and R. Kumar, 2011. *In vitro* antifungal potency of plant extracts against five phytopathogens. *Brazilian Archives of Biology and Technology* 54(6), 1093–1098.

Taub F.B., 2004. *Fish 430 lectures* (*Biological Impacts of Pollutants on Aquatic Organisms*). University of Washington College of Ocean and Fishery Sciences, Seattle, WA.

Tebbe C., C. Bruns, P. Racca, B. Kleinhenz, D. Werren, H. Schulz and M. Finckh, 2014. Reduktion der Anzahl Kupferapplikationen zur Kontrolle von *Phytophthora infestans* im ökologischen Kartoffelanbau durch das verbesserte Entscheidungshilfesystem Öko-SIMPHYT. *59. Deutsche Pflanzenschutztagung*, Julius-Kühn-Institut, Freiburg, 449 pp.

Tegli S., M. Cerboneschi, C. Biancalani, S. Macconi, F. Tadini-Buoninsegni, A. Sacconi, S. Smeazzetto, M.R. Moncelli, P. Bogani and S. Biricolti, 2015. Virulence inhibiting peptides for the environmentally friendly control of plant diseases caused by *Pseudomonas syringae*. In: *Book of Abstracts, 9th International Conference on Pseudomonas syringae and Related Pathogens,* June 2–June 5, 2015, Màlaga, Spain, 15 (abstract).

Thomidis T., V. Rossi and E. Exadaktylou, 2010. Evaluation of a disease forecast model for peach leaf curl in the Prefecture of Imathia, Greece. *Crop Protection* 29, 1460–1465.

Thuerig B., A. Binder, T. Boller, U. Guyer, S. Jiménez, C. Rentsch and L. Tamm, 2006. An aqueous extract of the dry mycelium of *Penicillium chrysogenum* induces resistance in several crops under controlled and field conditions. *European Journal of Plant Pathology* 114, 185–197.

Tomlin C.D.S., 2009. *The pesticide manual: a world compendium*. 10th ed. British Crop Production Council, Surrey, UK, 856 pp.

Torres K.C. and M.L. Johnson, 2001. Bioaccumulation of metals in plants, arthropods, and mice at a seasonal wetland. *Environmental Toxicology and Chemistry* 20, 2617–2626.

Toselli M., G. Marcolini, M. Quartieri, G. Sorrenti, D. Malaguti, E. Baldi and B. Marangoni, 2006. L'accumulo di rame nel suolo: risposta vegetativa del pero e della vite. *Agricoltura (Regione Emilia Romagna)* 31, 128–130.

Toth M., K. Kasa, M. Gondor, K. Honty and M. Hevesi, 2006. First results of fire blight resistance screening in a Hungarian breeding programme. *Acta Horticulturae* 704, 545–549.

Tóth G., T. Hermann, M.R. Da Silva and L. Montanarella, 2016. Heavy metals in agricultural soils of the European Union with implications for food safety. *Environment international* 88, 299–309.

Tran Manh Sung C., C. Strizyk and M. Clerjeau, 1990. Simulation of the date of maturity of *Plasmopara viticola* oospores to predict the severity of primary infections in grapevine. *Plant Disease* 74, 120–124. DOI: 10.1094/PD-74-0120.

Trapman M. and M. Polfliet, 1997. Management of primary infections of apple scab with the simulation program RIMpro: review of four years field trials. *IOBC-WPRS Bulletin* 20, 241–250.

Treutwein J., S. Cergel, J. Runte, A. Nowak, S. Konstantinidou-Doltsinis, H. Kleeberg and A. Schmitt, 2010. Effects of extract fractions from *Glycyrrhiza glabra* on plant pathogenic fungi. *Julius-Kühn-Archiv* 428, 82.

Trotel-Aziz P., M. Couderchet, G. Vernet and A. Aziz, 2006. Chitosan stimulates defense reactions in grapevine leaves and inhibits development of *Botrytis cinerea*. *European Journal of Plant Pathology* 114, 405–413.

Trouvelot S., A.L. Varnier, M. Allègre, L. Mercier, F. Baillieul, C. Arnould, V. Gianinazzi-Pearson, O. Klarzynski, J.M. Joubert, A. Pugin and X. Daire, 2008. A beta-1,3 glucan sulfate induces resistance in grapevine against *Plasmopara viticola* through priming of defense responses, including HR-like cell death. *Molecular Plant-Microbe Interactions* 21, 232–243. DOI: 10.1094/MPMI-21-2-0232.

Tschöpe B., B. Kleinhenz, S. Keil and M. Zellner, 2010. Öko-SIMPHYT: Ein praxisreifes Entscheidungshilfesystem zur gezielten Terminierung von Kupferpräparaten gegen die Kraut- und Knollenfäule. In Poster, *Deutsche Pflanzenschutztagung*, September 6-Semptember 9, 2010, Humboldt-Universität, Berlin; *Gesunde Pflanze, gesunder Mensch*, 448 (Poster).

Unger C., I. Wilhelm, R. Jünger and R. Thalmann, 2006. Evidence of induced resistance of tomato plants against *Phytophthora infestans* by a water extract of dried biomass of *Penicillium chrysogenum*. *Journal of Plant Diseases and Protection* 113(5), 225–233. DOI: org/10.1007/BF03356186.

Van der Meer M. and D. Lévite, 2010. Acceptation des vins de cépages résistants par les consommateurs. *Revue suisse de Viticulture Arboriculture Horticulture* 42, 147–150.

van Groenigen J.W., I.M. Lubbers, H.M.J. Vos, G.G. Brown, G.B. De Deyn and K.J. van Groenigen, 2014. Earthworms increase plant production: a meta-analysis. *Scientific Reports* 4, 6365. DOI: 10.1038/srep06365.

Van Zwieten M., G. Stovold and L. Van Zwieten, 2007. Alternatives to copper for disease control in the Australian organic industry (*A report for the Rural Industries Research and Development Corporation) R IR DC Publication No 07/110; RIRDC Project No DAN-208A*. Australian Government.

Vijver M.G., J.P.M. Vink, C.J.H. Miermans and C.A.M. van Gestel, 2003. Oral sealing using glue: a new method to distinguish between intestinal and dermal uptake of metal in earthworms. *Soil Biology & Biochemistry* 35, 125–132.

Wallhead M., H.P. Zhu and K. Broders, 2017. Hyperspectral evaluation of *Venturia inaequalis* management using the disease predictive model RIMpro in the Northeastern U.S. *Agricultural Sciences* 8, 1358–1371.

Wastie R.L., 1991. Breeding for resistance. In: *Phytophthora infestans: the cause of late blight of potato* (D.S. Ingram and P.H. Williams, ed.), Academic Press, San Diego, CA, 193–224.

Weihrauch F. and J. Schwarz, 2014. Versuche zur Minimierung des Einsatzes kupferhaltiger Pflanzenschutzmittel im ökologischen Hopfenanbau. In: *Angewandte Forschung und Beratung für den ökologischen Landbau in Bayern* (K. Wiesinger, K. Cais and S. Obermaier, ed.), Bayerische Landesanstalt für Landwirtschaft, D-Freising, Schriftenreihe der LfL 2, 174–180.

Wiedemann-Merdinoglu S. and C. Hoffmann, 2010. New resistant grape varieties. Bottlenecks and conditions for adoption in different European grapevine-growing regions. *From Science to Field. Endure Grapevine Case Study* – Guide Number 5.

Wightwick A., M.R. Mollah, D.L. Partington and G. Allinson G., 2008. Copper fungicide residues in Australian vineyard soils. *Journal of Agriculture and Food Chemistry* 56, 2457–2464.

Williams E.B., D.F. Dayton and J.R. Shay, 1966. Allelic genes in *Malus* for resistance to *Venturia inaequalis*. *Proceedings of American Society of Horticulture Sciences* 88, 52–56.

Williams L.E., J.K. Pittman and J.L. Hall, 2000. Emerging mechanisms for heavy metal transport in plants. *Biochimica et Biophysica Acta* 1465, 104–126. DOI: 10.1016/S0005-2736(00)00133-4.

Wojciechowska E., C.H. Weinert, B. Egert, B. Trierweiler, M. Schmidt-Heydt, B. Horneburg, S. Graeff-Hönninger, S.E. Kulling and R. Geisen, 2014. Chlorogenic acid, a metabolite identified by untargeted metabolome analysis in resistant tomatoes, inhibits the colonization by *Alternaria alternata* by inhibiting alternariol biosynthesis. *European Journal of Plant Pathology* 139(4), 735–747.

Wright D.A. and P. Welbourn, 2002. *Environmental Toxicology.* Cambridge University Press, Cambridge, UK.

Wszelaki A.L. and S.A. Miller, 2005. Determining the efficacy of disease management products in organically-produced tomatoes. Online. *Plant Health Progress*. DOI: 10.1094/PHP-2005-0713-01-RS.

Xiong Z.T. and H. Wang, 2005. Copper toxicity and bioaccumulation in Chinese cabbage (*Brassica pekinensis* Rupr.). *Environmental toxicology* 20, 188–194.

Yin Y., J. Gu, X. Wang, W. Song, K. Zhang, W. Sun, X. Zhang, Y. Zhang and H. Li, 2017. Effects of copper addition on copper resistance, antibiotic resistance genes, and intl1 during swine manure composting. *Frontiers in Microbiology* 8, 344.

Yruela I., 2005. Copper in plants. *Brazilian Journal of Plant Physiology* 17, 145–156.

Zini E., M. Raffeiner, B. Raifer, J. Terleth and T. Letschka, 2015. Ricerca su viti resistenti in Alto Adige. *Rivista di Frutticoltura e di ortofloricoltura* 12, 20–26.

Zuskin E., J. Mustajbegovic, E.N. Schachter, J. Kern and D. Pavicic, 1997. Respiratory function in vineyard and orchard workers. *American Journal of Industrial Medicine* 31, 250–255.

http://cordis.europa.eu/publication/rcn/11903_en.html

https://cordis.europa.eu/result/rcn/186831_en.html

http://life-evergreen.com/it/il-progetto/

http://organicrules.org/custom/differences.php?id=2bbc

http://orgprints.org/10650/12/leifert-wilcockson-2005-blight_mop-report-Annexes.pdf

http://research.ncl.ac.uk/nefg/blightmop/page.php?page=2

http://www.biofruitadvies.nl/rimpro/rimpr o_e.htm

http://www.co-free.eu/

http://www.demeter.it/wp-content/uploads/2015/08/STANDARD-PRODUZIONE-DEMETER-AGGIORNAMENTO-2016.pdf

http://www.ita-slo.eu/projects/projects_2000_2006/

http://www.lifeaftercu.com/

http://www.louisbolk.nl

http://www.naturland.de

http://www.organicexport.info/turkey.html

http://www.prolarix.eu

http://www.pure-ipm.eu/

http://www.sinab.it/ricerca/altrameinbio-strategie-la-riduzione-e-possibili-alternative-all%E2%80%99utilizzo-del-rame

http://www.vineman-org.eu

http://www.vineman-org.eu/nqcontent.cfm?a_id=11235&tt=t_law_market_www

http://www.zepp.info/ackerbau/75-kartoffel/61-oeko-simphyt

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