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Ecotoxicity of plant extracts and essential oils: A review☆

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ABSTRACT

Plant-based products such as essential oils and other extracts have been used for centuries due to their beneficial properties. Currently, their use is widely disseminated through a variety of industries and new applications are continuously emerging. For these reasons, they are produced industrially in large quantities and consequently they have the potential to reach the environment. However, the potential effects that these products have on the ecosystems' health are mostly unknown. In recent years, the scientific community started to focus on the possible toxic effects of essential oils and plant extracts towards non-target organisms. As a result, an increasing body of knowledge has emerged. This review describes the current state of the art on the toxic effects that essential oils and plant extracts have towards organisms from different trophic levels, including producers, primary consumers, and secondary consumers. The majority of the studies (76.5%) focuses on the aquatic environment, particularly in aquatic invertebrates (45.1%) with only 23.5% of the studies focusing on the potential toxicity of plant-derived products on terrestrial ecosystems.

While some essential oils and extracts have been described to have no toxic effects to the selected organisms or the toxic effects were only observable at high concentrations, others were reported to be toxic at concentrations below the limit set by international regulations, some of them at very low concentrations. In fact, $L(E)C_{50}$ values as low as 0.0336 $mg.L^{-1}$, 0.0005 $mg.L^{-1}$ and 0.0053 $mg.L^{-1}$ were described for microalgae, crustaceans and fish, respectively. Generally, essential oils exhibit higher toxicity than extracts. However, when the extracts are obtained from plants that are known to produce toxic metabolites, the extracts can be more toxic than essential oils.

Overall, and despite being generally considered "eco-friendly" products and safer than they synthetic counterparts, some essential oils and plant extracts are toxic towards non-target organisms. Given the increasing interest from industry on these plant-based products further research using international standardized protocols is mandatory.

1. Introduction

Essential oils and plant extracts have been used for centuries in traditional medicine, cooking (as flavour enhancers), perfumery and cosmetics due to their unique properties (Ríos, 2016). Essential oils are volatile liquids obtainable by distillation of any part of a plant or by a mechanical process when attained from the epicarp of a citrus fruit at ambient temperature. During the process to extract essential oils by distillation, hydrolates can also be obtained as a by-product. An hydrolate is, according to the International Organization for Standardization (ISO), the distilled water that remains after the distillation process and is usually rich in water-soluble components of the essential oil (ISO, 2013). Conversely, an extract is "a product obtained by treating a natural raw material with a solvent then, after filtration, removal of the solvent by distillation, except in the case of use of a non-volatile solvent" (ISO, 1997).

☆ This paper has been recommended for acceptance by Montes Marques.

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Plants produce essential oils naturally as secondary metabolites in response to stress, as a defence against pathogen attacks and to attract pollinators that play an essential role in the reproduction of the plant (Roohinejad et al., 2017). Variations in environmental conditions and ecological factors directly impact the ability of a plant to produce essential oils, affecting also the type of compounds produced, and the quality and quantity of the oils (Chrysargyris et al., 2020; Figueiredo et al., 2008).

Essential oils and plant extracts have been continuously used as a source of bioactive molecules. Due to the increasing interest from customers for natural and safer products, the demand for natural-based products has increased during the last few years. In fact, the applications of these plant-derived compounds are currently spread throughout almost all sectors of economic activity such as food, agriculture, pharmaceutical, cosmetic and textile (Jugreet et al., 2020). And industries are keeping up with this consumer demand for natural products. In 2007, the global production of essential oils was around 100 kilotons (Barbieri and Borsotto, 2018). In May 2020, a market size analysis on the global essential oils market by Grand View Research, estimated the global demand for these products to be around 247 kilotons in 2020 being expected to continue growing for the next years, with the same report estimating that the demand will almost double by 2027 to a whopping 473 kilotons (Grand_View_Research, 2020). By far, the most produced are orange, lemon and mint oils. These oils represent more than two-thirds of total essential crop production. In the EU (European Union), in 2016 the production of essential oils was about 41 kilotons, although the major producers around the world are Asian countries such as China, India and Indonesia (Barbieri and Borsotto, 2018).

This increased interest from the industry is also accompanied by increasing interest from academia. As depicted in Fig. 1, the number of publications has been steadily and continuously increasing from 74 in the early 2000s, to 508 in 2020, particularly in the pharmaceutical, biological, and medical areas.

This intensive research by the scientific community is responsible for the discovery of new compounds and new applications of compounds extracted from plants (Rana and Das, 2017; Zhang et al., 2020). Among these new applications, some are addressing the most pressing health care problems of our society, as are, for instance, antimicrobial resistance (AMR), vector-borne diseases and cancer. Recently, natural products (including essential oils) have been revealed as an important ally in developing products with antibacterial properties that can be used instead of antibiotics (Abdelli et al., 2018; Alonso-Esteban et al., 2019; Reid et al., 2020; Tavares et al., 2020). Another growing concern is the resistance of insects, particularly those acting as disease vectors, to synthetic chemical pesticides and the environmental issues linked to the widespread usage of these chemicals that often result in long-term contamination of soils and water bodies, with severe consequences to ecosystems and human health. Essential oils and extracts of some plants have been studied for their potential to be used as biopesticides which can have similar effects as chemical pesticides with the advantage of, most of the time, having high degradability in the environment and being relatively safe to non-target organisms (Benelli et al., 2020a; Pavela et al., 2020; Pintong et al., 2020). Besides antimicrobial properties and the potential use as biopesticides, essential oils and plant extracts have also been intensively studied for their cytotoxic activity in tumour cells, which can lead to new cancer therapies or the enhancement of the effectiveness of existing cancer drugs (El-Garawani et al., 2019; Saleh et al., 2017; Salehi et al., 2020).

As previously mentioned, most of the studies published on plant extracts and essential oils focus on pharmaceuticals, agriculture, medicine and biochemistry with over 75% of all research published (Fig. 2).

Overall, most of the research focuses on industrial applications of these products, including antibacterial and antifungal properties, potential development of new biopesticides, applications in new drugs and therapies or even applications in anti-corrosion chemicals. Remarkably, despite all the increasing interest in these resources, and the consequent expected increase in their production, possible environmental impacts of essential oils and plant extracts received far less attention from the scientific community. In fact, in a period of 20 years, only 2% of the studies (n = 320) were published in the environmental sciences category (c.f. Fig. 2). The general idea that plants and their components are generally natural and safe, could explain this lack of studies. However, some plants can produce metabolites that have the potential to be highly toxic (Falkowski et al., 2020; Zárybnický et al., 2018) and therefore the evaluation of their possible toxic effects on non-target organisms needs to be performed.

This review aims to describe and critically evaluate the available data on the ecotoxicological effects of plant extracts and essential oils towards different organisms across aquatic and terrestrial trophic chains. To achieve this goal, a literature search was performed on

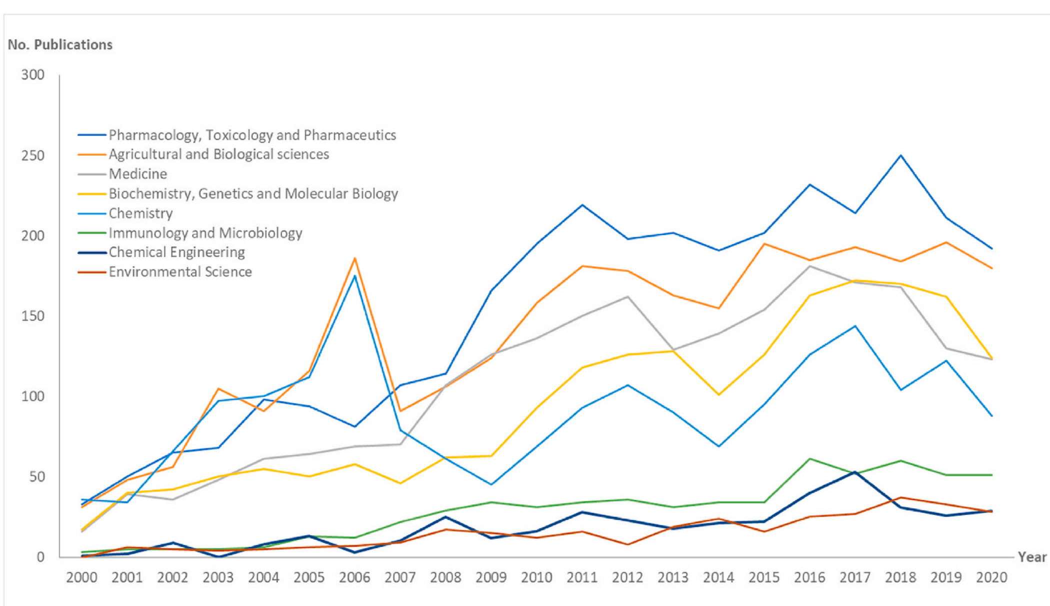

Fig. 1. Evolution of the number of papers published between 2000 and 2020 according to the Scopus database. Search performed on December 18th, 2020 using the keywords: essential oil(s), plant extract(s).

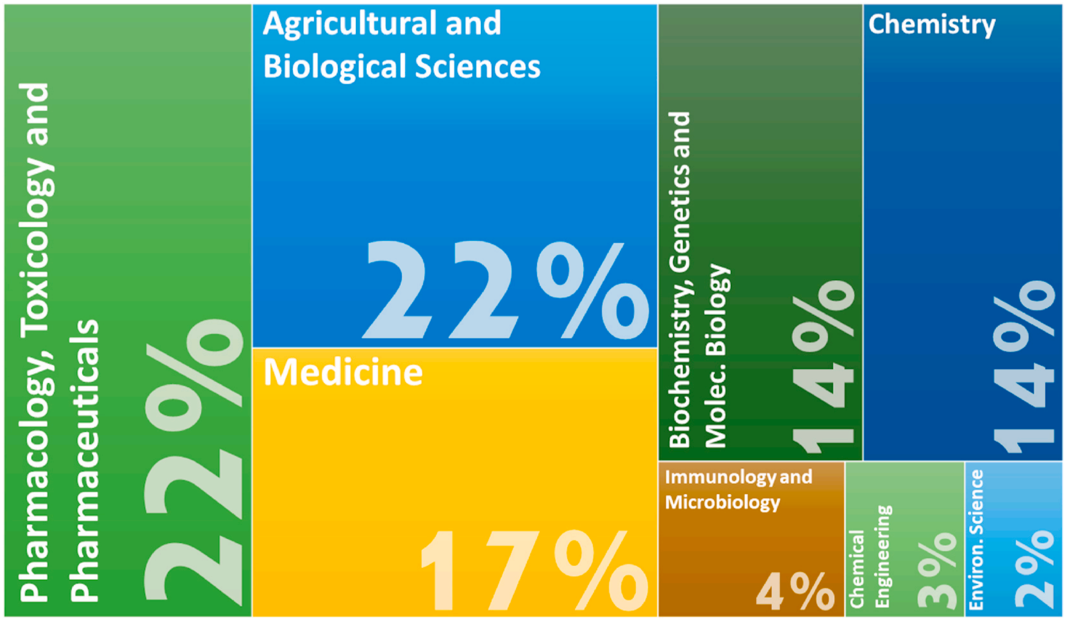

Fig. 2. Relative distribution of the number of papers published between 2000 and 2020 across eight main categories. Data retrieved from Scopus Database on December 18th, 2020 using the keywords: Plant extract(s); Essential oil(s).

Scopus, PubMed, and Web of Science databases in December 2020, using the following search string: Essential oil(s) AND Plant extract(s) AND Toxicity AND ecotoxicity. Of the 1207 papers retrieved, the vast majority were not related to the effects that these products may exert on non-target organisms, namely phytoplankton, zooplankton, macroalgae, aquatic vertebrates (fish and mammals), soil (micro)organisms, terrestrial vertebrates, and plants, and therefore, they were excluded (n = 1156). Fig. 3 summarizes the search methods and the workflow of this review. Of the 51 selected publications, the vast majority focus on the effects of plant extracts and essential oils on crustaceans, particularly *Daphnia magna*, followed by fishes, phytoplankton, and plants.

2. Toxicity towards microalgae

In general, the available data concerning the toxicity of essential oils and other plant extracts towards phytoplankton is very scarce, although algae, tend to be one of the most sensitive organisms (Rawlings et al., 2019). Despite the importance of phytoplankton towards the entire ecosystem, as these organisms are at the base of the aquatic food chain, only six studies evaluated the toxicity towards microalgae, namely *Raphidocelis subcapitata* (3 studies), *Chlorella vulgaris* (2 studies), *Scenedesmus quadricauda* (1 study) and *Chlamydomonas reinhardtii* (1 study). The higher number of studies with *R. subcapitata* (formerly known as *Pseudokirchinella subcapitata, formerly known as Selenastrum capricornutum*) is most probably due to the fact that this species is a standard test organism in ecotoxicological tests being reported to be very sensitive to many common toxic compounds (Geis et al., 2000; OECD, 2011). The available data regarding toxicity of essential oils and extracts on microalgae is presented in Table 1.

Concerning the essential oils and plant extracts evaluated in these papers: three studies used plant extracts; one study used oleoresins; one essential oils, and; one study used a hydrolate. Generally, most of the 5

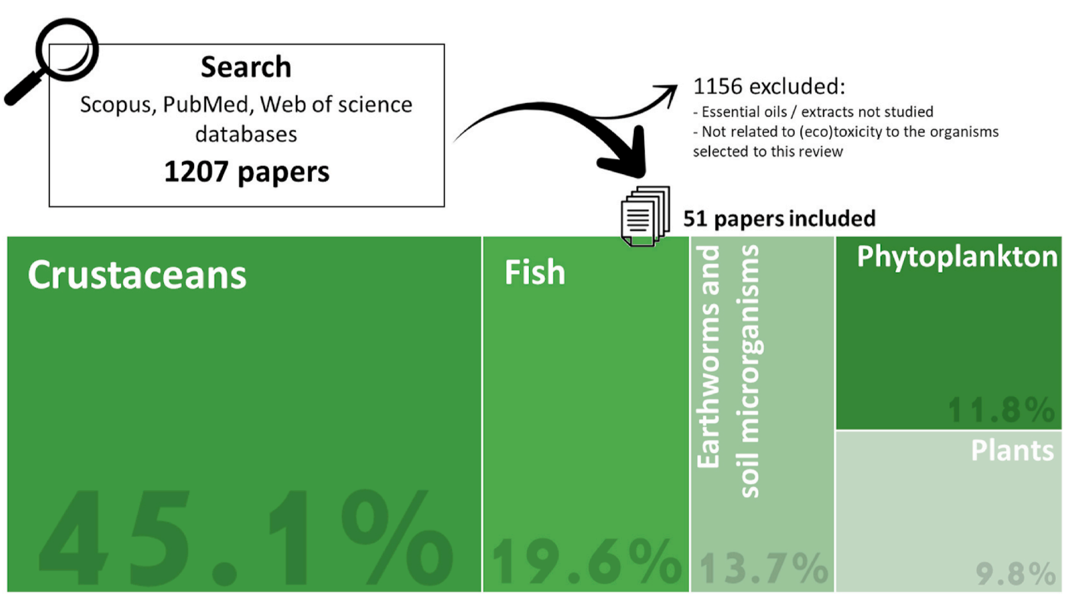

Fig. 3. Schematic representation of the study selection process.

Table 1

Essential oils and plant extracts tested towards microalgae and their toxicological categorization according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) by the United Nations. N. S. – Not specified; N. C. – Not classifiable; N. D. – Not determined; Acute 3 in the range of 10–100 $mg.L^{-1}$; Acute 2 in the range of 1–10 mg.L-1; Acute 1 ≤ 1 $mg.L^{-1}$.

Plant				Toxicity evaluation					Major compound(s) identified	Reference
Family	Species	Part(s) used	Type of Extract	Test species	Endpoint	EC_{50} ($mg.L^{-1}$)		GHS Classification		
Asteraceae	*A. absinthium*	N. S.	Hydrolate	*C. reinhardtii*	Photosynthetic activity	16.49% (1 h)		N. C.	(−)-(Z)-2,6-dimethylocta-5,7-diene-2,3-diol[a]	Pino-Otín et al. (2019a)
Cupressaceae	*J. occidentalis*	Leaves	Essential oil	*R. subcapitata*	Algal cell density biomass growth	1.7 (96 h) 1.7 (96 h) 2.0 (96 h)		Acute 2	l-borneol acetate, 4-terpineol, sabinene	Duringer et al. (2010)
	C. lawsoniana	Heartwood	Essential oil		Algal cell density biomass growth	>5 >5 >5		N. C.	A-terpineol, borneol, fenchol	
Fabaceae	*P. emarginatus*	Fruits	Oleoresin (in nanoemulsion)	*C. vulgaris*	Algal density, growth	N. D.		N. C.	Methyl 6α,7β-dihydroxyvouacapan-17-β-oate, geranylgeraniol, β-caryophyllene	Oliveira et al. (2016)
Malvaceae	*A.rosea*	Leaves	Aqueous extract + nanoparticles		biomass Chlorophyll *a*	0.0336 N. D.		Acute 1[b]	N. D.	Khoshnamvand et al. (2020)
Papaveraceae	*C. majus*	Roots	Aqueous	*R. subcapitata* (1); *S. quadricauda* (2)	Growth	(1) 96 h 60.87	(2) 96 h 78.01	Acute 3	Copsitine[a]	Jancula et al. (2007)
	D. lactucoides					21.27	20.61	Acute 3	Sanguinarine, chelerythrine[a]	
	M. microcarpa					>600	>600	N. C. (not toxic)		
	S. canadensis					23.90	29.05	Acute 3	Sanguinarine, chelerythrine[a]	
	S. lasiocarpum					114.10	117.48	N. C. (not toxic)	Copsitine[a]	
Pinaceae	*P. radiata*	Bark	Methanolic (polyflavonoids extracts)	*R. subcapitata*	Growth	N. D.		N. C.	Polyflavonoids	García et al. (2017)

[a] This compound was identified by the authors as the one responsible for the observed toxicity.
[b] Acute 1 may be subdivided for some regulatory systems to include a lower band at $L(E)C_{50} \leq 0.1$ $mg.L^{-1}$.

plant species studied belong to the Papaveraceae family. Other species studied belong to the Pinaceae, Fabaceae, Malvaceae and Cupressaceae families.

The hydrolate obtained from *Artemisia absinthium* caused a reduction in the photosynthetic activity of the unicellular green algae *C. reinhardtii*, with an EC_{50} value of 16.49% of hydrolate dilution and the major bioactive compound isolated from the hydrolate was (−)-(Z)-2,6-dimethylocta-5,7-diene-2,3-diol. The authors reported that this compound and another compound related to (−)-*cis*-epoxyocimene could be responsible for the hydrolate toxicity (Pino-Otín et al., 2019a).

Essential oils obtained from the leaves of *Juniperus occidentalis* and the heartwood of *Chamaecyparis lawsoniana* (Cupressaceae) were tested for the potential toxic effects in the microalgae *R. subcapitata*. Commonly known as western juniper, *Juniperus occidentalis* is a plant of the Cupressaceae family, and is an encroaching species spreading fast in the North American rangelands (Sankey et al., 2010). Belonging to the same family, *Chamaecyparis lawsoniana*, commonly known as Port Orford cedar, is exploited for its high-value timber (Hansen et al., 2000). The essential oils were studied for their potential acute toxicity towards *R. subcapitata* for 96 h of exposure. For the *J. occidentalis* essential oil, the 72 and 96 h EC_{50} was 1.7 $mg.L^{-1}$ and the NOEC (no observable effect concentration) was 0.63 $mg.L^{-1}$. The authors considered the *J. occidentalis* essential oil to be moderately toxic to *R. subcapitata* causing a significant reduction in algal cell density. Concerning the oil from *C. lawsoniana*, the EC_{50} for algal cell growth was reported to be > 5 $mg.L^{-1}$, as a reduction in 50% of cells growth was not observed, leading the authors to conclude that there were no expected acute toxic effects of the release of this oil into the environment in organisms of the same trophic level as *R. subcapitata* (Duringer et al., 2010).

Aqueous extracts obtained from the roots of five plants from the Papaveraceae family were tested for their effects on *R. subcapitata* and *S. quadricauda*: the greater celandine *Chelidonium majus*, the eastern horned poppies *Dicranostigma lactucoides*, *Macleaya microcarpa* known as plume poppies, the bloodroot *Sanguinaria canadensis* and the Chinese celandine poppy *Stylophorum lasiocarpum*. The results showed that after 96 h of exposure, the extracts from *D. lactucoides* and *S. canadensis* were the most toxic towards both algae (EC_{50} of 21.27 and 23.90 $mg.L^{-1}$, for *R. subcapitata* and 20.61 and 29.05 $mg.L^{-1}$, for *S. quadricauda,* respectively). The extract from *C. majus* was also toxic to both algae (EC_{50} of 60.87 and 78.01 $mg.L^{-1}$, respectively). *S. lasiocarpum* presented EC_{50} of 114.10 to R. *subcapitata* and 117.48 $mg.L^{-1}$ to *S. quadricauda*. The least toxic extract was the one obtained from *M. microcarpa* with EC_{50} values above 600 $mg.L^{-1}$ for both species. The authors linked the toxicity observed to the content of sanguinarine and chelerythrine, important alkaloids common in plants from the Papaveraceae family, present in the extracts of *D. lactucoides* and *S. canadensis*. For the *C. majus* and *S. lasiocarpum* the toxicity was thought to be caused by the presence of coptisine, the major alkaloid found in both extracts (Jancula et al., 2007).

Polyflavonoids of a methanolic extract obtained from the bark of *Pinus radiata* (Pinaceae) the radiate pine tree, seem to favour the growth of *R. subcapitata* at concentrations up to 100 $mg.L^{-1}$. Only after 160 h of exposure, some inhibition in algal growth was registered, but this could be a consequence of nutrient deficiency or changes in the static medium conditions after the exponential growth phase. However, derivates from these flavonoids (itaconic-, maleic- and citraconic-based) caused different effects on algae growth. For example, itaconic-based derivate caused growth inhibition at the concentrations of 0.01, 0.1 and 0.5 $mg.L^{-1}$, but at concentrations above 1 $mg.L^{-1}$ growth appeared to be favoured. The maleic-based anhydride had a modest effect on growth, except after 120 h of exposure when a slight growth inhibition was observed at the concentrations of 0.5 and 1 $mg.L^{-1}$. On the other hand, citraconic-based derivates showed a remarkable growth enhancement at the concentrations of 0.01, 0.1 and 0.5 $mg.L^{-1}$ although at 1 $mg.L^{-1}$ some inhibition was observed. These results present good evidence on how dose and slight changes in chemical structure may influence toxic effects (García et al., 2017).

Recently, the combination of plant extracts and essential oils into nanoemulsions or biosynthesized nanoparticles is in vogue. A recent study assessed the potential toxicity of these products – generally regarded as "green products" – towards the microalgae *Chlorella vulgaris*. The nanoparticles, synthesized with $AgNO_3$ and the hollyhock *Alcea rosea* aqueous leaf extract, showed effects in algae biomass in a dose-dependent way, being the highest concentration tested (0.05 $mg.L^{-1}$) the one that produced the greatest biomass reduction. The 72 h LC_{50} was 33.63 $\mu g.L^{-1}$. The nanoparticles also caused aggregation of the microalgae cells which can also lead to toxicity (Khoshnamvand et al., 2020). Similarly, a decrease in *C. vulgaris* cell concentration was observed when the cells were exposed to a nanoemulsion prepared with oleoresin obtained from the fruits of *Pterodon emarginatus*. The suppression of growth was registered for concentrations above 25 $mg.L^{-1}$ and can be attributed to a deleterious synergistic effect of all the constituents of the nanoemulsion (Oliveira et al., 2017).

In order to classify the toxicity of the essential oils and plant extracts, the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) proposed by the United Nations was used (UN, 2019). As described in Table 1, the silver nanoparticles produced with the aqueous extract from *A. rosea* showed the highest toxicity to phytoplankton. The EC_{50} value obtained (below 1 $mg.L^{-1}$) can be categorized as highly toxic under the acute 1 category. The essential oil from *J. occidentalis* presented EC_{50} values within 1 and 10 $mg.L^{-1}$ which can be classified in the acute 2 category. With EC_{50} values between 10 and 100 $mg.L^{-1}$, the aqueous extracts from *C. majus*, *D. lactucoides* and *S. canadensis* can be categorized under the acute 3 category. For the other studies reported, the information given is not sufficient to characterize the product under the categories of the GHS. This lack of information, noticeable in several studies, turns the comparison between toxicities very difficult, and future studies should report all toxicity data, including 48 h LC_{50} values. By failing to do so, these limitations preclude a better understanding of the relative toxicity of the different plant extracts and essential oils.

3. Toxicity towards crustaceans

Crustaceans like *Daphnia magna*, *Daphnia pulex*, *Scapholeberis kingi* and *Artemia salina* (Anostraca) have been studied regarding the toxic effects of plant extracts and essential oils. Of all the retrieved papers, the most studied species was *D. magna*, with 78% of studies on the effects of essential oils or extracts using this species, followed by *A. salina* (14.8%), *D. pulex* (5.8%) and finally *S. kingi* (1.4%, used in only one study). Organisms from the *Daphnia* genus, particularly *D. magna*, are recommended for the execution of ecotoxicity tests of chemicals and other substances by international organizations like ASTM and OECD (ASTM, 1997; OECD, 2004) to assess the risk of materials and chemicals to aquatic organisms. The European Union under the Regulation (EC) nº 1907/2006 of the European Parliament and Council recommends the use of organisms from the *Daphnia* genus to perform acute and chronic toxicity tests to provide information regarding ecotoxicity towards aquatic organisms (EU, 2006). When the acute toxicity is evaluated, young *Daphnia*, less than 24 h old, are exposed to the test substance for 48 h. Immobilisation is recorded after 24 h and after 48 h and compared with the control group. The immobilisation observed after 48 h of exposure is used to calculate the EC_{50} value (concentration estimated to cause immobilisation in 50% of the organisms) (OECD, 2004). The 48 h EC_{50} is used to determine the effect of a substance when performing acute toxicity tests with *D. magna* or other *Daphnia* species. However, and despite the fact that international organizations recommend using 48 h EC_{50} values, some studies report the EC_{50} for 24 h or even 72 h or 96 h, and don't include the 48 h EC_{50} (see Table 2). Additionally, some studies report the results in units that cannot be translated into classification systems such as percentage of mortality or concentrations in percentage of dilution. By adopting different toxicity units than the ones

Table 2
Essential oils and plant extracts tested towards crustaceans and categorization according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) by the United Nations. (The reported values that do not follow the recommendations were considered not classifiable). N. S. – Not specified; N. C. – Not classifiable; N. D. – Not determined; N. R. – Not reported.

Plant				Toxicity evaluation				Major compound(s) identified	Reference
Family	Species	Part(s) used	Type of Extract	Test species	Test/Endpoint	48 h EC_{50}/ LC_{50} ($mg.L^{-1}$)	GHS Classification		
Amaranthaceae	*Amaranthus retroflexus*	Leaves	Ethanolic	*D. magna*	Acute toxicity	1053 (24 h)	N. C.	N. D.	Dinu et al. (2017)
Apiaceae	*Anthriscus sylvestris*	Aerial parts	Aqueous			483.7 (24 h)	N. C.	deoxypodophyllotoxin[a]	Olaru et al. (2016)
			Hydroethanolic			102.4 (24 h)			
			Ethanolic			106.9 (24 h)			
	Ferula assa-foetida	Oleo-gum-resin	Essential oil			N. D.	N. C.	Sec-butyl (*Z*)-propenyl disulfide, sec-butyl (*E*)-propenyl dissulfide	Pavela et al. (2020)
	Ferula gummosa	Oleo-gum-resin	Essential oil			N. D.	N. C.	α-pinene, β-phellandrene	
	Trachyspermum ammi	Seeds	Essential oil			8.53	Acute 2	thymol[a]	Seo et al. (2012)
Asteraceae	*Achillea millefolium*	Aerial parts	Essential oil			13.6	Acute 3	N. D.	Zanfirescu et al. (2020)
	Artemisia absinthium	N. S.	Ethanolic			0.093 (24 h)	N. C.	(−)-(Z)-2,6-dimethylocta-5,7-diene-2,3-diol[a]	Pino-Otín et al. (2019a)
			Hexane			0.103 (24 h)	N. C.		
			Hydrolate			0.236%	N. C.		
	Petasites hybridus	Roots	Methanolic			178.6 (72 h)	N. C.	pyrrolizidine alkaloids[a]	Seremet et al. (2018)
	Senecio vernalis	Aerial parts	Methanolic			83.31 (72 h)	N. C.	pyrrolizidine alkaloids[a]	
	Solidago canadensis	N. S.	Ethanolic		Acute and chronic toxicity (reproduction)	>1000	Not toxic	N. D.	Huang et al. (2014)
	Tussilago farfara	Leaves	Methanolic			189.97 (72 h)	N. C.	pyrrolizidine alkaloids[a]	Seremet et al. (2018)
Berberiaceae	*Berberis vulgaris*	Bark	Ethanolic			201.3 (24 h)	N. C.	N. D.	Gîrd et al. (2017)
Boraginaceae	*Symphytum officinale*	Roots	Methanolic			801.0 (72 h)	N. C.	pyrrolizidine alkaloids[a]	Seremet et al. (2018)
Cupressaceae	*Chamaecyparis lawsoniana*	Heartwood	Essential oil			1.9	Acute 2	α-terpineol, borneol, fenchol	Duringer et al. (2010)
	Juniperus occidentalis	Leaves	Essential oil			>5	N. C.		
	Taxodium distichum	Female cones	Essential oil			10.9	Acute 3	N. D.	Zanfirescu et al. (2020)
	Tetraclinis articulata	Wood	Aqueous		Acute toxicity Chronic toxicity (reproduction)	6.49 EC_{50} 8.17 NOEC 0.49 LOEC 0.83	Acute 2 Acute 2	N. D.	Montassir et al. (2017)
Ericaceae	*Ledum palustre*	Aerial parts	Essential oil		Acute toxicity	N. D	N. C.	N. D.	Benelli et al. (2020a)
Euphorbiaceae	*Hura crepitans*	Bark	Aqueous			0.036	Acute 1[b]	Hurin, crepitin[a]	Iannacone et al. (2014)
Fabaceae	*Medicago sativa*	Aerial parts	Ethanolic			1008 (24 h)	N. C.	N. D.	Gîrd et al. (2017)
	Myroxylon pereira	Resin	Essential oil			3.89	Acute 2	Benzyl benzoate, benzyl cinnamate[a]	Seo et al. (2012)
	Robinia pseudoacacia	Leaves	Aqueous			4290 (96 h)	N. C.	N. D.	Alonso et al. (2020)
	Tephrosia vogelii	Leaves	Aqueous			0.00047 (24 h)	N. C.	Rotenone[a]	Li et al. (2015)

(*continued on next page*)

Table 2 (*continued*)

Plant				Toxicity evaluation				Major compound(s) identified	Reference
Family	Species	Part(s) used	Type of Extract	Test species	Test/Endpoint	48 h EC_{50}/ LC_{50} ($mg.L^{-1}$)	GHS Classification		
Geraniaceae	*Pelargonium gravolens*	Flowering aerial parts	Dry extract			203.3	Not toxic	N. D.	Neagu et al. (2018)
Humiriaceae	*Humiria balsamifera*	Bark	Ethyl acetate			N. D	N. C.	N. D.	Falkowski et al. (2020)
Lamiaceae	*Origanum vulgare*	Aerial parts	Ethanolic			364.4	Not toxic	N. D.	Gîrd et al. (2016)
Lythraceae	*Trapa japonica*	Leaves	Methanolic			4.7–22.0	Acute 2/3	N. D.	Ishimota et al. (2019)
Monimiaceae	*Peumus boldus*	Leaves	Essential oil			N. D.	N. C.	1,8-cineole, *p*-cymene	Pavela et al. (2019)
Myrtaceae	*Eucalyptus gobulus*	N. S. (commercial)	Essential oil			143.96	Not toxic	1,8-cineole	Park et al. (2011)
	Melaleuca dissitiflora	N. S. (commercial)	Essential oil			103.35	Not toxic	Terpinen-4-ol	
	Melaleuca linariiflora	N. S. (commercial)	Essential oil			1.84	Acute 2	Terpinen-4-ol	
	Melaleuca quinquenervia	N. S. (commercial)	Essential oil			8.94	Acute 2	1,8-cineole, *(E)*-nerolidol	
Oleaceae	*Fraxinus angustifolia*	Leaves	Aqueous			9500 (96 h)	N. C.	N. D.	Alonso et al. (2020)
Papaveraceae	*Chelidonium majus*	Aerial parts	Ethanolic			258.1	Not toxic	copsitine	Jancula et al. (2007)
	Dicranostigma lactucoides	Roots	Aqueous			31.25	Acute 3	Sanguinarine, chelerythrine[a]	
	Macleaya microcarpa	Roots	Aqueous			>1000	Not toxic	N. D.	
	Sanguinaria canadensis	Roots	Aqueous			62.0	Acute 3	Sanguinarine, chelerythrine[a]	
	Stylophorum lasiocarpum	Roots	Aqueous			>400	Not toxic	copsitine	
Plantaginaceae	*Plantago lanceolata*	Leaves	Ethanolic			375.0	Not toxic	N. D.	Zanfirescu et al. (2020)
Polygonaceae	*Fallopia aubertii*	Flowers	Aqueous			3019.95 (24 h)	N. C.	N. D.	Olaru et al. (2015)
			Hidroethanolic			2398.83 (24 h)		N. D.	
			Ethanolic			2951.20 (24 h)		N. D.	
	Fallopia convulvulus	Stems, Leaves, Flowers and fruits	Hydroethanolic			N. D.	N. C.	N. D.	
	Fallopia dumetorum		Hydroethanolic			4073.8 (24 h)	N. C.	N. D.	
Salicaceae	*Popolus alba*	Leaves	Aqueous			9500 (96 h)	N. C.	N. D.	Alonso et al. (2020)
Sapindaceae	*Aesculus hippocastanum*	Seeds	Ethanolic			7.5	Acute 2	N. D.	Zanfirescu et al. (2020)
	Mataya arborescens	Fruits	Ethyl acetate			N. D.	N. C.	N. D.	Falkowski et al. (2020)
Simaroubaceae	*Ailanthus altissima*	Leaves	Aqueous			10,100 (96 h)	N. C.	N. D.	Alonso et al. (2020)
Solanaceae	*Solanum nigrum*	Leaves	Ethyl acetate			N. D.	N. C.	N. D.	(Rawani et al., 2014b)a
			Petroleum ether			N. D.	N. C.	N. D.	(Rawani et al., 2014a)b
			Benzene			N. D.	N. C.	N. D.	(Rawani et al., 2014a)b

(continued on next page)

Table 2 (*continued*)

Plant				Toxicity evaluation				Major compound(s) identified	Reference
Family	Species	Part(s) used	Type of Extract	Test species	Test/Endpoint	48 h EC_{50}/LC_{50} ($mg.L^{-1}$)	GHS Classification		
			Chloroform/Methanol			N. D.	N. C.	N. D.	Rawani et al. (2017)
			Ethanolic			N. D.	N. C.	N. D.	(Rawani et al., 2014a)[b]
Quillajaceae	*Quillaja saponaria*	Bark	Commercial extract			27.3	Acute 3	Saponins	Jiang et al. (2018a)
Asteraceae	*Artemisia absinthium*	Aerial parts	Ethanolic	*D. pulex*		150–200	N. C.	Flavone	Andreu et al. (2018)
	Artemisia vulgaris	Aerial parts	Ethanolic			50–100	N. C.	Hydroxycinnamic acid	
Equisetaceae	*Equisetum arvense*	Bark + leaves	Ethanolic			50–100	N. C.	Flavonols	
Salicaceae	*Salix alba*	Bark + leaves	Ethanolic			150–200	N. C.	Flavonols	
Lythraceae	*Trapa japonica*	Leaves	Methanolic	*S. kingi*		1.2–6.9	Acute 2	N. D.	Ishimota et al. (2019)
Asteraceae	*Petasites hybridus*	Roots	Methanolic	*A. salina*		296.48 (24 h)	N. C.	pyrrolizidine alkaloids[a]	Seremet et al. (2018)
	Senecio vernalis	Aerial parts	Methanolic			131.22 (24 h)	N. C.		
	Tussilago farfara	Leaves	Methanolic			222.33 (24 h)	N. C.		
Boraginaceae	*Symphytum officinale*	Roots	Methanolic			707.95 (24 h)	N. C.		
Eleagnaceae	*Eleagnus angustifolia*	Flowers	Essential oil			2.25	Acute 2	E-ethyl cinnamate	Torbati et al. (2016)
		Leaves				11.0	Acute 3	E-ethyl cinnamate, phytol	
Polygonaceae	*Fallopia aubertii*	Flowers	Aqueous			2239.55	Not toxic	N. D.	Olaru et al. (2015)
		Stems + leaves	Hydroethanolic			2576.36		N. D.	
		Flowers	Ethanolic			1872.16		N. D.	
	Fallopia convulvulus	Stems, Leaves, Flowers and fruits	Hydroethanolic			N. D.	N. C.	N. D.	
	Fallopia dumetorum	Stems, Leaves, Flowers and fruits	Hydroethanolic			2689.09	Not toxic	N. D.	

[a] This compound was identified by the authors as the one responsible for the observed toxicity.
[b] Acute 1 may be subdivided for some regulatory systems to include a lower band at $L(E)C_{50} \leq 0.1$ $mg.L^{-1}$.

recommended in the international guidelines, the comparison and classification of the toxic effects of essential oils and plant extracts is difficult to perform. Table 2 summarizes the available toxicity data for crustaceans and a brief description of the available studies is here provided.

An aqueous extract from the leaves of *Tephrosia vogelii* (Fabaceae) was studied for the potentially toxic effects it could have in non-target aquatic organisms. The extract showed remarkable acute toxicity towards *D. magna* after 24 h of exposure (LC_{50} of 0.47 $\mu g.L^{-1}$/0.00047 $mg.L^{-1}$) (Li et al., 2015). This plant has been used in tropical areas of India and other tropical regions as a fish-poison, insecticide or for soil enrichment, and various studies have shown the potential of the essential oils of *T. vogelii* to be used as bioinsecticides and larvicides (Bravim dos Santos et al., 2021; Touqeer et al., 2013). An aqueous extract from the bark of *Hura crepitans* (Euphorbiaceae) also showed to be acutely toxic towards *D. magna*, although to a lesser extent with 48 h LC_{50} = 0.036 $mg.L^{-1}$ (36 $\mu g.L^{-1}$) (Iannacone et al., 2014). Like *T. vogelii*, *H. crepitans* is a tree known for its toxicity, especially the latex it produces which is rich in huratoxin (Trinel et al., 2018; Vassallo et al., 2020).

A commercial extract from the bark of *Quillaja saponaria* (Quillajaceae) was tested for its toxicity towards *D. magna*. The extract was toxic to the daphnids with a 48 h EC_{50} value of 27.3 $mg.L^{-1}$. The authors concluded that the high saponin content of the extract was the main responsible for the registered toxicity (Jiang et al., 2018a). Jiang et al. have reported a EC_{50} of 18.3 $mg.L^{-1}$ of saponins from *Q. saponaria*'s bark to *D. magna* (Jiang et al., 2018b). *Q. saponaria* extracts and their physically modified derivatives are of restricted use in the European Union under the European Chemicals Agency EC/List no. 273-620-4. These saponin extracts are used as an active ingredient in biopesticides and its hazards to aquatic environments are known (Jiang et al., 2018b). An aqueous extract from *Tetraclinis articulata* (Cupressaceae), commonly known as Thuya, also showed acute toxicity in *D. magna* (48 h EC_{50} = 6.49 $mg.L^{-1}$) and chronic toxicity was observed as well – the extract affected both survival and reproduction of the organisms in a dose-response and time-dependant manner (NOEC of 1.42 and LOEC of 2.41 $mg.L^{-1}$ for mortality; NOEC of 0.49 and LOEC of 0.83 $mg.L^{-1}$ for reprotoxicity) (Montassir et al., 2017). Ethyl acetate extracts obtained from the fruits of *Matayba arborescens* (Sapindaceae) and the bark of *Humiria balsamifera* (Humiriaceae) showed acute toxicity towards *D. magna* at the concentrations of 100 $mg.L^{-1}$ and 80 $mg.L^{-1}$, respectively. These extracts caused almost 100% of mortality in the organisms, and the authors considered these extracts to be highly toxic (Falkowski et al., 2020).

A heartwood oil from the Port Orford cedar *C. lawsoniana* showed acute toxic effects in *D. magna* after 48 h of exposure (EC_{50} = 1.9 mg. L^{-1}). In the same study an essential oil from the leaves of another Cupressaceae, western Juniper, *Juniperus occidentalis* showed no acute toxicity to *D. magna* up to 5 mg.L^{-1}, the concentration which the authors describe as being the limit of solubility (Duringer et al., 2010), but according to international classifications for acute toxicity of mixtures (in which oils obtained from plants are included) to aquatic organisms, a product is considered nontoxic when no effects are observable only at concentrations above 100 mg.L^{-1} (UN, 2019). Essential oils from the common yarrow, *Achillea millefolium* (Asteraceae) aerial parts and the female cones of the bald cypress, *Taxodium distichum* (Cupressaceae), also showed acute toxicity towards *D. magna* (48 h LC_{50} of 13.6 and 10.9 mg.L^{-1}, respectively). In the same study, an ethanolic extract obtained from the seeds of the horse chestnut tree, *Aesculus hippocastanum* (Sapindaceae) was also acutely toxic towards *D. magna* with a 48 h LC_{50} value of 7.5 mg.L^{-1}, and an ethanolic extract from the leaves of *Plantago lanceolata* (Plantaginaceae), commonly referred to as ribwort plantain, showed low toxicity (LC_{50} = 375 mg.L^{-1}) (Zanfirescu et al., 2020).

Other studies reported toxic effects of essential oils on *D. magna*. For example, an essential oil obtained from wild rosemary *Ledum palustre* (Ericaceae), caused mortality to this organism at the concentration of 80 mg.L^{-1} (45% mortality after 24 h of exposure and 47.5% after 72 h of exposure) (Benelli et al., 2020a). The authors do not report results after 48 h of exposure and the same happening for the LC_{50} value, which makes categorization or comparison with other studies impossible. An essential oil obtained from the leaves of *Peumus boldus* (Monimiaceae), an evergreen tree native to Chile used in traditional medicine, at the concentration of 96.2 mg.L^{-1}, caused 46.2% of mortality after 24 h of exposure and 66.2% mortality after 48 h of exposure to *D. magna* (Pavela et al., 2019). Again, no LC_{50} values were reported by the authors, rendering any comparison impossible. Commercial essential oils from four species of the Myrtaceae family were also studied regarding their acute toxicity to *D. magna*. Essential oils of *Melaleuca dissitiflora*, *Melaleuca linariiflora*, *Melaleuca quinquenervia* and *Eucalyptus globulus* were toxic towards D. magna, with 48 h EC_{50} for immobilisation of 1.84, 8.94, 103.35 and 143.96 mg.L^{-1}, respectively. In this study, it was also reported that the *M. dissitiflora* and *M. linariiflora* essential oils were mainly composed of terpinene-4-ol and ϒ-terpinene, while the essential oil from *M. quinquenervia* was rich in *(E)*-nerodiol, ρ-cymene and linalool. The essential oil from *E. globulus* was mainly composed of 1, 8-cineole. The persistence of these essential oils in water was also assessed and after 7 days the residues of all the essential oils were below 22% indicating a high susceptibility to hydrolysis (Park et al., 2011). The same analysis was performed in another study that evaluated the acute toxicity of essential oils from the seeds of *Trachyspermum ammi* (Apiaceae) and the resin of *Myroxylon pereira* (Fabaceae). The essential oils showed to be acutely toxic to *D. magna* with 48 h EC_{50} values of 8.53 and 3.89 mg.L^{-1}, respectively. Moreover, the degradability in water was also shown to be low after 7 days (below 35% for both essential oils). The authors reported that the *T. ammi* essential oil was mainly composed of thymol, ϒ-terpinene and ρ-cymene while the *M. pereira* essential oil was mostly entirely composed of benzyl benzoate and benzyl cinnamate (Seo et al., 2012). These last two studies are a good example of a complete assessment of the potential of using essential oils as biopesticides: the authors studied the larvicidal potential against mosquito larvae, the ecotoxicological risk to a non-target organism and the persistence of the test substances in the environment.

To better understand the effect that the introduction of exotic species can have in the surrounding ecosystem, aqueous extracts from the leaves of four three species (two endemic to Europe, *Populus alba* (Salicaceae) and *Fraxinus angustifolia* (Oleaceae) and two introduced exotic species, *Robinia pseudoacacia* (Fabaceae) and *Ailanthus altissima* (Simaroubaceae)) were studied for their ecotoxicological risk to aquatic organisms, particularly *D. magna*. All extracts showed low toxicity to *D. magna* with the authors indicating 96 h EC_{50} values of 1.77 g.L^{-1} (1770 mg.L^{-1}) for *P. alba* extract, 9.50 g.L^{-1} (9500 mg.L^{-1}) for *F. angustifolia* extract, 4.29 g.L^{-1} (4290 mg.L^{-1}) for *R. pseudoacacia* extract and 10.1 g.L^{-1} (10,100 mg.L^{-1}) for the extract of *A. altissima*. The reported 96 h EC_{50} values indicate very low toxicity of these extracts to *D. magna* as all of them are above 1000 mg.L^{-1} (Alonso et al., 2020). However, according to international guidelines, the observed effect used to calculate the $L(E)C_{50}$ values and to categorize the toxicity in the GHS should be obtained after 48 h of exposure. Therefore, it is not possible to apply the GHS categorization and comparison with other studies is also difficult.

A dry extract obtained from the leaves, flowers and aerial parts of *Pelargonium graveolens* (Geraneaceae) was also tested for the potential acute toxicity to *D. magna* organisms. The 48 h LC_{50} value obtained was 203.3 mg.L^{-1} (Neagu et al., 2018) and therefore this extract can be classified as not toxic to *D. magna*. A hydro-ethanolic obtained from the leaves of *Amaranthus retroflexus* (Amaranthaceae) had a 24 h LC_{50} of 1053 mg.L^{-1}, and was considered of low risk to *D. magna* (Dinu et al., 2017). However, because only 24 h LC_{50} values were reported, it remains unknown what are the toxicity levels after 48 h of exposure. Ethanolic extracts obtained from the aerial parts of *Chelidonium majus* (Papaveraceae), *Medicago sativa* (Fabaceae) and from the bark of *Berberis vulgaris* (Berberidaceae) were tested for their potential toxicity to *D. magna*. The authors presented only 24 h results of the toxicity tests, with LC_{50} values of 258.1, 1008 and 201.3 mg.L^{-1} for the extracts of *C. majus*, *M. sativa* and *B. vulgaris*, respectively (Gîrd et al., 2017). Since the recommendation from OECD (OECD, 2004) is not followed (reporting EC_{50} values for 48 h), it is not possible to compare the results obtained in this study with others using extracts from the same plant. Another study reported that an ethanolic extract from the aerial parts of *Origanum vulgare* (Lamiaceae) showed low toxicity towards *D. magna* (48 h LC_{50} = 364.4 mg.L^{-1}) and the authors attribute the toxicity to the high phenolic content of the extract (Gîrd et al., 2016).

Olaru et al. studied the toxicity of extracts obtained from the aerial parts of *Anthriscus sylvestris* (Apiaceae) an edible plant commonly known as wild chervil. The aqueous, hydroethanolic and ethanolic extracts exhibited 24 h LC_{50} values of 483.70, 102.40 and 106.90 mg.L^{-1}. The authors suggest that the toxicity of the hydroethanolic and ethanolic extracts could be related to the presence of deoxypodophyllotoxin and related lignans which can induce cytotoxicity (Olaru et al., 2016). It would be interesting to have information regarding the 48 h LC_{50}'s, especially for the hydroethanolic and ethanolic extracts since at 24 h the values are very close to 100 mg.L^{-1} (classification limit for toxicity proposed by the (UN, 2019)). In another study, extracts from three species of the *Fallopia* genus (Polygonaceae): *F. convolvulus*, *F. dumetorum* and *F. aubertii* were tested for their potential toxicity towards crustaceans. Different extracts were prepared: for *F. convolvulus* and *F. dumetorum*, stems, leaves, flowers and fruits were used to obtain a hydroethanolic extract, whereas for *F. aubertii*, flowers were used to obtain an aqueous, a hydroethanolic and an ethanolic extract, and the leaves were used to obtain a hydroethanolic extract. Toxicity tests with *D. magna* and *A. salina* were performed for all the extracts, and the results (24 h LC_{50} values were all above 1000 mg.L^{-1} (Olaru et al., 2015)) showed that the extracts present no risk to both aquatic organisms, except for those of *F. convolvulus* for which toxicity was not determined. In another experiment, an ethanolic extract from the Canada goldenrod *Solidago canadensis* (Asteraceae) also showed low acute toxicity towards *D. magna* with a 48 h LC_{50} above 1000 mg.L^{-1}, but regarding long-term (chronic) effects, the number of offspring per animal decreased significantly when the animals were exposed to concentrations over 20 mg. L^{-1}, survival of parent animals was affected when exposed to concentrations over 30 mg.L^{-1} and exposure to 50 mg.L^{-1} resulted in no offspring produced by the parent animals that survived, throughout their entire life cycle (Huang et al., 2014). This study shows that despite having no acute toxicity up to very high concentrations, this extract is able to cause effects when the exposure is longer, resulting in alterations in the animal's life cycle.

Aqueous extracts from five species of the Papaveraceae family, *Chelidonium majus*, *Dicranostigma lactucoides*, *Macleaya microcarpa*, *Sanguinaria canadensis* and *Stylophorum lasiocarpum*, were evaluated for their potential toxicity towards aquatic organisms. The extract from *D. lactucoides* showed the highest toxicity regarding immobilisation of *D. magna* after 48 h of exposure (EC_{50} = 31.25 mg.L^{-1}) followed by *S. canadensis* extract (EC_{50} = 62.00 mg.L^{-1}). All the other extracts showed low toxicity towards this organism with EC_{50} values above 400 mg.L^{-1} (Jancula et al., 2007). As mentioned before, the study by Gîrd et al. (2017) has reported a 24 h EC_{50} for an ethanolic extract from *C. majus* of 258.1 mg.L^{-1} and, although a direct comparison between EC_{50} values for 24 h and 48 h is not possible, it seems that the aqueous extract is less toxic than the ethanolic extract. This could be due to numerous reasons: the environmental conditions from which the plant was obtained, the developmental stage of the plant (Ishimota et al., 2019) and also the solvent that was used to obtain the extract. Different solvents ultimately will extract different amounts and even different compounds produced by the plant (Feng et al., 2020).

The volatile oils from the oleo-gum-resins of *Ferula assa-foetida* and *Ferula gummosa* exhibited toxic effects towards *D. magna* (Pavela et al., 2020). These plants, belonging to the Apiaceae family, produce an oleo-gum-resin composed of volatile oils, gum and resin, rich in sulphurous compounds and monoterpenes. Both oils caused mortality to *D. magna*, being the *F. assa-foetida* oil the most toxic (100% mortality after 48 h of exposure to 10 mg.L^{-1} of essential oil), while that obtained from *F. gummosa* showed less toxic effects (70% mortality after 48 h of exposure to 10 mg.L^{-1} of essential oil). The authors did not report LC_{50} values (Pavela et al., 2020) wich precludes any toxicity categorization or comparison with other studies.

Methanolic extracts from leaves of the water plant *Trapa japonica* (Trapaceae) commonly known as Japanese water chestnut, collected in different stages of development were studied for the potential acute toxicity towards the cladocerans *D. magna* and *Scapheloberis kingi*. The 48 h EC_{50} values obtained varied from 4.7 to 22 g of leaves. L^{-1} wet mass in *D. magna* and 1.2–6.9 g of leaves. L^{-1} wet mass in *S. kingi*. The extracts obtained from yellow leaves with grazing damage induced the highest toxicity in both organisms, and the authors also acknowledged that leaves in this stage had the highest amount of bioactive compounds (probably due, at least in part, to the induction of defence mechanisms against grazing animals), which can explain the higher acute toxicity when compared with the extracts from the leaves in different stages of development (Ishimota et al., 2019). In this study, although the authors reported 48 h EC_{50} values, the units used (weight of leaves used per volume) impairs comparison with other studies that do not use the same reference units. In another study, methanolic extracts of the aerial parts of *Senecio vernalis* (Astereaceae), leaves of *Tussilago farfara* (Astereaceae), roots of *Petasites hybridus* (Astereaceae) and *Symphytum officinale* (Boriginaceae) were tested for their acute toxicity towards *D. magna* and *A. salina*. After 72 h the LC_{50} values obtained were 83.31, 189.97, 178.6 and 801.0 mg.L^{-1}, respectively, in *D. magna*. Again, because the authors did not present 48 h LC_{50} results any comparison with other studies becomes impossible, the same happening to the toxicity categorization according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). In *A. salina*, the 24 h LC_{50} results were 131.22, 222.33, 296.48 and 707.95 mg.L^{-1}, respectively. For both organisms, the *S. vernalis* extract was the most toxic. The authors attribute the toxicity of the extract to the high content of pyrrolizidine alkaloids present, namely senecivernine, senecionine, seneciphylline, integerrimine and senkirkine (Seremet et al., 2018). Once again, due to methodological differences (EC_{50} obtained after 24 h of exposure instead of the recommended 48 h), it is not possible to compare these results with those obtained for other species.

Polyflavonoid extracts obtained from *Pinus radiata* (Pinaceae) bark showed to be toxic to *D. magna*. Maleic- and Itaconic-derivates of the polyflavonoids showed the highest toxicity (48 h LC_{50} of 10.09 and 16.94 mg.L^{-1}, respectively) while citraconic-derivate and unmodified polyflavonoids had similar toxicity (LC_{50} of 52.06 and 56.64 mg.L^{-1}, respectively). Interestingly, there were differences in toxicity between citraconic- and itaconic-anhydrides which are interchangeable isomers, showing a significant effect of the esterification in the extracts' toxicity (García et al., 2017).

Extracts obtained from *Solanum nigrum* (Solanaceae) leaves appear to have no toxicity to *D. magna* organisms, at least at low concentrations. Two studies assessed the potential toxicity of different extracts (chloroform:methanol and ethyl acetate). For both *S. nigrum* extracts, no acute toxic effects were observed. In these studies, the extracts were tested for their potential effectiveness as bioinsecticides and the concentrations tested on the non-target organism *D. magna* were the concentrations that were found to be the most effective against 3rd instar larvae of *Culex vishnui* and *Anopheles subpictus* (15 mg.L^{-1} for the chloroform:methanol extract) and *Culex quinquefasciatus* (25 mg.L^{-1} for the ethyl acetate extract) (Rawani et al., 2014b; Rawani et al., 2017). Therefore, the information provided regarding the acute toxicity of the extracts to *D. magna* was limited. While no effects were detected up to the maximum concentrations tested, the effects at higher concentrations still remain unknown including those that are categorized as toxic to aquatic organisms (100 mg.L^{-1}) (UN, 2019).

Essential oils obtained from the flowers and leaves of *Elaeagnus angustifolia* (Elaeagnaceae) were tested for their general toxicity using *A. salina*. The essential oil from the flowers was the most toxic (24 h LC_{50} = 2.25 mg.L^{-1}) and the essential oil from the leaves showed high toxicity as well (24 h LC_{50} = 11.00 mg.L^{-1}). The authors link the toxicity of the oils to the high content of ester compounds, specially E-ethyl cinnamate (Torbati et al., 2016).

An ethyl acetate extract obtained from the leaves of *Pistia stratiotes* was reported to have low toxicity towards *A. salina* at a concentration of 602.03 mg.L^{-1} (Ma et al., 2019) however the time of exposure was not reported. This study was focused on the effectiveness of different fractions of the extract against *Anopheles* mosquitoes and so the concentrations that showed to be the most effective towards the mosquito was the one tested towards *A. salina* as a non-target species. Because only one concentration was tested it was impossible to calculate the EC_{50}. Furthermore, by not disclosing the duration of the test any comparison between the results obtained and the ones reported for other species is impossible.

Ethanolic extracts from the bark and leaves of *Salix alba* (Salicaceae), *Equisetum arvense* (Equisetaceae), aerial parts of *Artemisia absinthium* and aerial parts of *Artemisia vulgaris* from the Asteraceae family, were tested for the potential ecotoxicity using *Daphnia pulex*. The most toxic extracts were the ones obtained from *E. arvense* and *A. vulgaris* with EC_{50} values for immobilisation between 50 and 100 mg.L^{-1}. Both *S. alba* extracts EC_{50} was between 100 and 150 mg.L^{-1} and *A. absinthium* extract was the least toxic -EC_{50} between 150 and 200 mg.L^{-1} (Andreu et al., 2018). Interestingly, Pino-Otín et al. have reported high toxicity of three extracts from *A. absinthum* to *D. magna*. The ethanolic extract resulted in a 24 h LC_{50} of 0.093 mg.L^{-1} and the hexane extract of 0.103 mg.L^{-1}, besides these extracts, a hydrolate presented a 24 h LC_{50} of 0.236% (Pino-Otín et al., 2019a). The difference between these studies relies on the *Daphnia* species used, one used *D. pulex* and the other *D. magna*, but the differences in toxicity observed should not be down to this fact as similarities in toxicities of many toxicants have been reported between the two species (Lewis and Horning II, 1991; Lilius et al., 1995) and both are suitable for acute toxicity tests according to the OECD guideline (OECD, 2004). The difference could be due to environmental factors that can affect the production of secondary metabolites and, particularly concerning the differences in the hydrolate, it is noticeable that one of the studies reports EC_{50} values and the other LC_{50}, which usually mean the measurement of different parameters (e.g., immobilisation vs lethality), and the units used are also different (mg.L^{-1} and percentage of dilution). Differences in how the authors report their toxicity results can lead to difficulties in comparing different studies of the same product and therefore future harmonization on results reporting is very important.

Isolated compounds from plants used in the agro-food industry were tested towards *Daphnia similis*. Piplartine was isolated from a methanolic extract from the roots, stems, leaves and fruits of *Piper tuberculatum* (Piperaceae). The isolated compound was then tested for its toxicity towards *D. similis*, showing high acute toxicity to this organism (48 h EC_{50} of 7.32 $mg.L^{-1}$ for immobilisation) (Rapado et al., 2013). It should be considered that only the toxicity of piplartine was reported and not of the methanolic extract as a whole.

More recently, the addition of extracts from plants has been emerging as an “eco-friendlier” way to produce metal nanoparticles. The bioactive properties of molecules that can be extracted from plants combined with nanoparticles can eventually lead to some innovative therapies and applications (Ahmad et al., 2021). Interestingly, their possible effects on aquatic organisms are mostly unknown, and only sparsely has research addressed this subject. One study addressed the possible acute toxic effects of biosynthesized silver nanoparticles with an aqueous extract from the leaves of *Alcea rosea* (Malvaceae) to *D. magna*. The nanoparticles showed high acute toxicity (48 h LC_{50} = 1.86 $\mu g.L^{-1}$) to the test organisms, which the authors attribute to the effect of Ag^{+} ions which can cause ROS generation and oxidative stress, among other effects like DNA and mitochondrial damage or membrane lipid peroxidation. This product has been shown to have toxic effects on organisms across the aquatic trophic chain – phytoplankton, crustaceans and fish. (Khoshnamvand et al., 2020). Controversially, Sharma et al. report no toxicity of nanocomposites, synthesized with aqueous extract from the leaves of *Achyranthes aspera* (Amaranthaceae) with 4 mM $AgNO_3$, on *D. magna* and *Moina macrocopa* organisms after 48 h of exposure up to 5.82 $mg.L^{-1}$ (Sharma et al., 2020) and Zahir et al. also reported no toxicity towards *D. magna* and *C. dubia*, of nanoparticles synthesized with 1 mM $AgNO_3$ and an aqueous extract from the leaves of *Euphorbia prostrata* (Euphorbiaceae) at 10 $mg.L^{-1}$ (Zahir and Rahuman, 2012). The ecotoxicological effects of silver nanoparticles on several organisms were recently reviewed by Tortella et al. The authors concluded that these man-made products can cause changes to biodiversity, but the effects still remain mostly unknown especially regarding the nanoparticles internalization and bioaccumulation in aquatic and terrestrial systems (Tortella et al., 2020).

As previously highlighted a comparison between all studies published is impossible, nevertheless, to be able to compare the relative toxicity between the different plants and types of extracts, we have compiled all the results that described the 48 h $L(E)C_{50}$ values towards *D. magna*, the most extensively studied species (Fig. 4). For most of the available data, the 48 h $L(E)C_{50}$ values reported can be categorized as toxic to *D. magna*, except for the *P. gravolens* dry extract, the *O. vulgare* ethanolic extract, *C. majus* ethanolic extract and *P. lanceolata* ethanolic extract as well as the essential oils from *M. dissitiflora* and *E. globulus* that showed $E(L)C_{50}$ values above 100 $mg.L^{-1}$. Moreover, the aqueous extract from *H. crepitans* was highly toxic to *D. magna* with an $L(E)C_{50}$ value below 1 $mg.L^{-1}$.

In order to be able to compare the relative toxicity of the essential oils *versus* other plant extracts and considering that this information for the same plant under the same conditions is not available we computed all the reported $L(E)C_{50}$ values (including 24, 48, 72 and 96 h) in the scheme depicted in Fig. 5. It is noticeable that essential oils tend to cause effects at lower concentrations. There are some exceptions, though. Extracts from plants that are known to produce toxic metabolites such as *Tephrosia vogelii* (rotenone), *Hura crepitans* (huratoxin) (Iannacone et al., 2014; Li et al., 2015) or even from plants that are not known to produce toxic metabolites such as the studied extracts from *Artemisia absinthium* (ethanolic and hexane) (Pino-Otín et al., 2019a), that showed high acute toxicity to *D. magna* at low concentrations (Table 2). A link between the

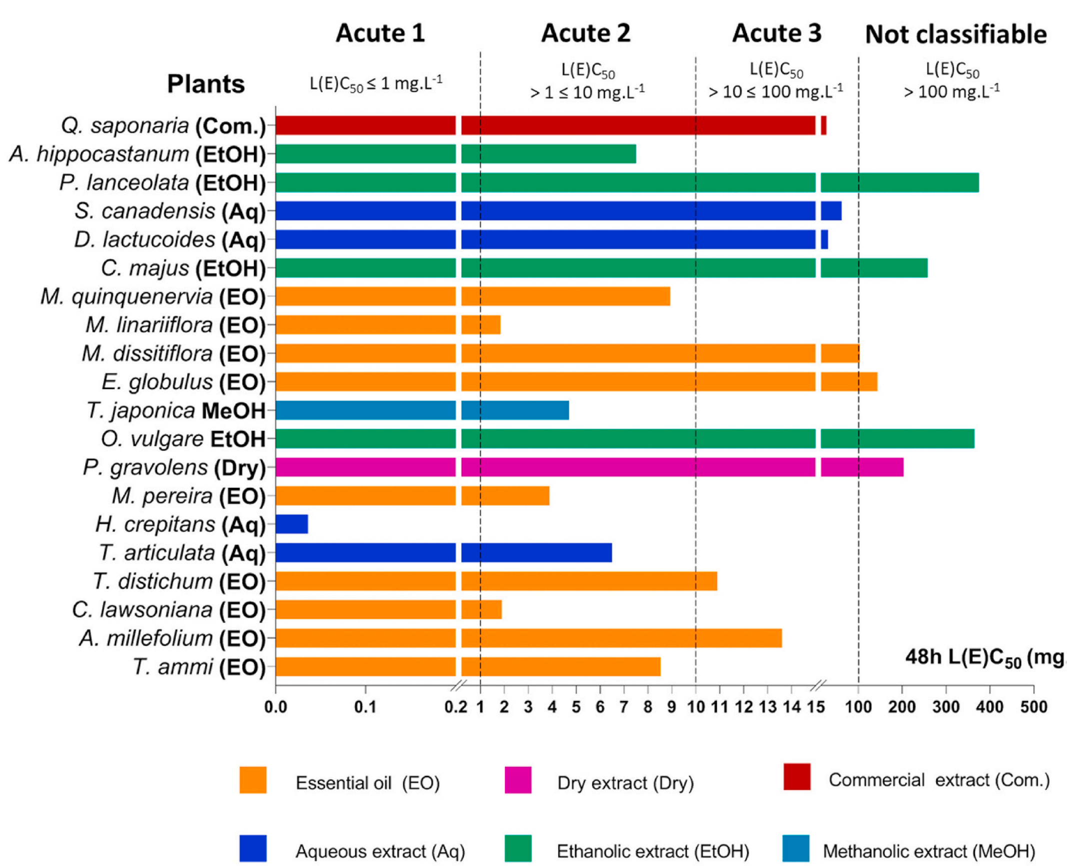

Fig. 4. Comparison of reported 48 h $L(E)C_{50}$ values towards *D. magna* with the indication of the United Nations Globally Harmonized System of Classification and Labelling of Chemicals (GHS) categorization.

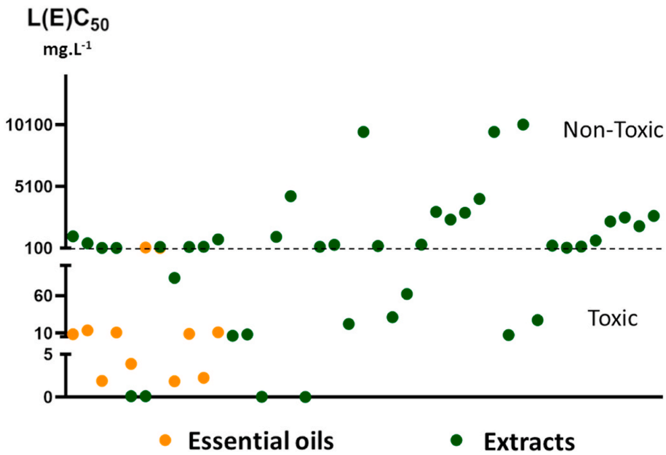

Fig. 5. Comparison of the toxicity towards crustaceans reported for essential oils *versus* other extracts.

toxicity observed and the compounds responsible for this effect, is often hard to establish. Some studies have reported the compounds that could be responsible for the observed effect (as previously described and highlighted in Tables 2–5) but, as these products, especially essential oils, are a complex mixture of compounds it becomes difficult to pin point the compound responsible for the observed toxicity. Furthermore, the chemical characterization of the oils and plants extracts is often not provided.

4. Toxicity towards fish

The use of fish larvae for early life stage toxicity tests has been going on for years. This practice has become growingly more restricted due to regulations directing the use of vertebrates as models for toxicity testing. The European Union's regulation on Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) clearly states that fish testing should only be used when no other options are available (CEC, 2006). To avoid restrictions, zebrafish embryotoxicity tests present a promising alternative approach (Lammer et al., 2009), and presently most of the fish studies regarding the toxicity of essential oils and plant extracts use zebrafish (*Danio rerio*). Other species include the rainbow trout *Oncorhynchus mykiss* (Salmoniformes), the Nile tilapia *Oreochromis*

Table 3
Essential oils and plant extracts tested towards fish. N. D. – not determined; hpf – hours postfertilization.

Plant				Toxicity evaluation			Major compound(s) identified	Reference
Family	Species	Part(s) used	Type of extract	Test species	Endpoint(s)	LC_{50} (mortality)		
Apocynaceae	*Cascabela thevetia*	Fruits	Methanolic	*D. rerio*	Mortality; Developmental abnormalities; Coagulation; Embryonic movements and heart rate; Length; Failure to straighten; Oedema	(72 h) 1000 mg. L^{-1}	N. D.	Haldar et al. (2015)
Asteraceae	*Solidago canadensis*	N. S.	Ethanolic		Mortality	(72 h) 320 mg. L^{-1}	N. D.	Huang et al. (2014)
Lamiaceae	*Leonurus japonicus*	Aerial parts	Essential oil		Mortality; Developmental abnormalities; Embryo hatching rate; Embryo heartbeat	(24 hpf) ~10 mg.L^{-1}; (48 hpf) ~60 mg. L^{-1}	Alkaloids	He et al. (2018)
Piperaceae	*Piper kadsura*	Stems	Methanolic		Mortality; Body adnormalities; Abnormal swimming; Hemorrhaging	43 mg.L^{-1} NOEC = 31 mg. L^{-1}	Pellitorine, chingchengenamide A, piperone	Seo et al. (2021)
	Piper turbeculatum	Roots	Piplartine isolated from the methanolic extract		Mortality; Swimming activity; Developmental abnormalities	1.69 mg.L^{-1}	Piplartine	Rapado et al. (2013)
Zingiberaceae	*Zingiber cassamunar*	Rhizomes	Essential oil		Mortality; Developmental abnormalities	N. D.	Sabinene, terpinene-4-ol	Mektrirat et al. (2020)
Apiaceae	*Heracleum sprengelianum*	Leaves	Essential oil	*G. affinis*	Mortality; Swimming activity	4219 mg.L^{-1}	Lavandulyl acetate, bicyclogermacrene	Govindarajan and Benelli (2016b)
Zingiberaceae	*Zingiber nimmonii*	Leaves	Essential oil		Mortality	(48 h) 9250.12 mg.L^{-1}	Myrcene, β-caryophyllene, α-humulene, α-cadinol	Govindarajan et al. (2016a)
Cupressaceae	*Chamaecyparis lawsoniana*	Leaves	Essential oil	*O. mykiss*	Mortality	(96 h) > 5 mg. L^{-1}	l-borneol acetate, 4-terpineol, sabinene	Duringer et al. (2010)
	Juniperus occidentalis	Heartwood	Essential oil		Mortality	(96 h) > 5 mg. L^{-1}	A-terpineol, borneol, fenchol	Duringer et al. (2010)
Fabaceae	*Tephrosia vogelii*	Leaves	Aqueous	*O. niloticus*	Mortality	5.31 μg.L^{-1}	Rotenone[a]	Li et al. (2015)

[a] This compound was identified by the authors as the one responsible for the observed toxicity.

Table 4
Essential oils and plant extracts tested towards plants. N. D. – Not determined; N. S. – Not specified.

Plant				Toxicity evaluation				Major compound(s) identified	
Family	Species	Reference	Type of extract	Test species	Family	Endpoint	EC_{50} (mg. L^{-1})		
Amaranthaceae	*Amaranthus retroflexus*	Leaves	Hydroalcoholic	*T. aestivum*	Poaceae	Cytotoxicity and genotoxicity	N. D.	N. D.	Dinu et al. (2017)
Asteraceae	*Achillea biebersteinii*	Flowering aerial parts	Essential oil and extracts (n-		Amaranthaceae	Germination, root growth and seedling growth	N. D	Camphor, 1,8-cineole, viridiflorol, ethyl oleate	Çakır et al. (2015)
Acetone, methanolic)	*A. retroflexus*		hexane,	*A. retroflexus*	Camphor, 1,8-cineole, viridiflorol, ethyl oleate				
	Achillea biserrate			*C. album*	Chenopodiaceae				
				C. juncea	Asteraceae				
	Achillea coarctata			*L. serriola*					
				T. officinale					
	Achillea wilhelmsii			*R. crispus*	Polygonaceae				
	Artemisia absinthium	N. S.	Hydrolate	*A. cepa*	Amaryllidaceae	Root growth	3.87% (v/v)	(−)-(Z)-2,6-dimethylocta-5,7-diene-2,3-diol[a]	Pino-Otín et al. (2019b)
Papaveraceae	*Chelidonium majus*	Roots	Aqueous	*L. minor*	Araceae	Growth	484.69	copsitine	Jancula et al. (2007)
	Stylophorum lasiocarpum	Roots	Aqueous				>500	copsitine	
Pinaceae	*Pinus radiata*	Bark	Extract of polyflavonoids	*L. sativa*	Asteraceae	Percentage of germination and radicle length	N. D.	Polyflavonoids	García et al. (2017)

[a] This compound was identified by the authors as the one responsible for the observed toxicity.

Table 5
Essential oils and plant extracts tested towards earthworms. N. D. – Not determined; N. S. – Not specified.

Plant				Toxicity evaluation			Major compound(s) identified	Reference
Family	Species	Part(s) used	Type of extract	Test species	Endpoint	EC_{50} (mg. L^{-1})		
Asteraceae	*Artemisia absinthium*	N. S.	Hydrolate	*E. fetida*	Mortality	0.07	(−)-(Z)-2,6-dimethylocta-5,7-diene-2,3-diol[a]	Pino-Otín et al. (2019b)
	Stevia rebaudiana	Flowering branches	Essential oil			N. D.	Caryophyllene oxide, spathulenol	Benelli et al. (2020b)
Apiaceae	*Cuminum cyminum*	Seeds	Essential oil			N. D.	γ-terpinen-7-al, cumin aldehyde, α-terpinen-7-al	Benelli et al. (2018a)
	Ferula assa-foetida	Oleoresin	Essential oil			N. D.	Sec-butyl *(Z)*-propenyl dissulfide, Sec-butyl *(E)*-propenyl dissulfide	Pavela et al. (2020)
	Ferula gummosa	Oleoresin	Essential oil			N. D.	α-pinene, β-phellandrene	
	Foeniculum vulgare	N. S.	Commercial essential oil			N. D.	*Trans*-anethole, fenchone	Pavela (2018)
	Pimpinella anisum	Seeds	Essential oil			N. D.	*(E)*-anethole	Benelli et al. (2018a)
Meliaceae	*Swietenia mahagoni*	Leaves	Methanolic	*E. eugeniae*		N. D.	Bis (2-ethylhexyl) phthalate	Dinesh-Kumar et al. (2018)
Pieraceae	*Piper betle*	Leaves	Essential oil			N. D.	Eudesm-7 (11)-en-4-ol	Vasantha-Srinivasan et al. (2016)

[a] This compound was identified by the authors as the one responsible for the observed toxicity.

niloticus (Cichliformes), the mosquitofish *Gambusia affinis* (Cyprinodontiformes) and the Japanese rice fish *Oryzias latipes* (Beloniformes). *Oncorhynchus mykiss* and *Danio rerio* are recommended by OECD for ecotoxicity tests. The OECD guideline 203 also recommends *Pimephales promelas* and *Oryzias latipes* for fresh water toxicity tests and *Cyprinodon variegatus* and *Menidia* sp. for saltwater toxicity tests (OECD, 2013a).

Several studies reported that essential oils are toxic towards fish, some assessed embryotoxicity and others used juvenile fishes, while others do not report this information. According to the OECD guideline 203, the selected test organisms should be juveniles of the same age and the exposure period should be 96 h after which the LC_{50} (median lethal concentration) should be calculated (OECD, 2019). For embryotoxicity tests, the OECD guideline 236 recommends *D. rerio* as the test species and the embryos should be exposed to the test substances for 96 h immediately after fertilisation and the selected endpoints should be observed every 24 h (OECD, 2013b).

Table 3 compiles the available studies on the toxicity of essential oils and plant extracts towards fish. An essential oil obtained from the aerial parts of *Leonurus japonicus* (Lamiaceae), commonly known as motherwort, had toxic effects on embryos of *D. rerio* when exposed to concentrations above 6.25 mg.L^{-1}. Several endpoints were assessed: mortality, developmental abnormalities (yolk sac, axis, eye, head, tail, snout, jaw, brain, pericardial oedema, somites, pigmentation and circulatory system), embryo hatching rate and embryo heartbeat. The heartbeat rate decreased in the embryos treated with the essential oil. From the lowest concentration tested, the egg hatching was significantly reduced (77%) and at concentrations of 6.25 or 12.5 $mg.L^{-1}$ embryos developed dysplastic heads and tails, incomplete heart formation, partial or complete lack of eye formation. Embryos exposed to concentrations of 25, 50 and 100 $mg.L^{-1}$ at 2 h post-fertilization (hpf), 10 hpf and 24 hpf showed signs of cardiotoxicity and entered cardiac arrest, and eventually, total mortality occurred. Some of the embryos exposed to 100 $mg.L^{-1}$ of essential oil at 48 hpf survived but the heads and tails of the embryos did not form properly. The LC_{50} values obtained were significantly lower and similar for embryos treated at 2 hpf, 10 hpf and 24 hpf (around 10 $mg.L^{-1}$), than the LC_{50} observed for the embryos treated at 48 hpf (above 60 $mg.L^{-1}$). The TC_{50} (median teratogenic concentration) was much lower for the embryos treated at 2 hpf indicating more serious abnormalities. The authors concluded that the essential oil from *L. japonicus* was toxic to the zebrafish embryos, causing death and malformations on the fish especially before the pharyngula stage when the major organs start to form (He et al., 2018). An essential oil obtained from the rhizomes of *Zingiber cassamunar* (Zingiberaceae) was also toxic towards *D. rerio* embryos. The embryotoxicity of the essential oil was dose dependant, with the concentration of 500 $mg.L^{-1}$ of essential oil causing the highest mortality rate (15 ± 5.77%) after 24 h of exposure. Regarding teratogenic effects, concentrations above 10 $mg.L^{-1}$ caused developmental abnormalities, especially at the concentration of 100 $mg.L^{-1}$ which caused malformations of the yolk sac, head and tail development abnormalities, pericardial sac oedema, spinal column abnormalities and poor reabsorption of the yolk sac. Moreover, coagulation of the embryos exposed to 100 $mg.L^{-1}$ was observed after 96 h of exposure, causing 100% mortality. Concentrations below 10 $mg.L^{-1}$ caused no mortality or embryonic malformations (Mektrirat et al., 2020). Essential oils obtained from *J. occidentalis* e *C. lawsoniana* showed no toxic effects to juveniles of the rainbow trout *O. mykiss* at concentrations up to 5 $mg.L^{-1}$ (the authors consider this concentration as the solubility limit for the oils). The essential oils were considered safe towards organisms on the same trophic level as *O. mykiss* (Duringer et al., 2010). Leaf essential oil from *Heracleum sprengelianum* (Apiaceae) and *Zingiber nimmonii* (Zingiberaceae) rhizomes essential oil showed very low toxicity to *G. affinis* after 10 days of exposure for the *H. sprengelianum* essential oil, and 48 h of exposure to *Z. nimmonii* essential oil (LC_{50} values of 4219 and 9250.12 $mg.L^{-1}$, respectively) but the authors did not report the age of the test organisms (Govindarajan and Benelli, 2016b; Govindarajan et al., 2016a).

Besides essential oils, different types of plants extract were also evaluated in terms of their potential toxicity towards fish (*D. rerio* and *O. niloticus*). A methanolic extract obtained from the stems of *Piper kadsura* (Piperaceae) showed acute toxicity to *O. latipes*. The authors reported a 96 h LC_{50} of 43 $mg.L^{-1}$ and a NOEC of 31 $mg.L^{-1}$ but no results regarding other endpoints such as body abnormalities or abnormal swimming were reported in detail (Seo et al., 2021). Another methanolic extract obtained from the fruits of *Cascavela thebetia* (Apocynaceae), an ornamental and poisonous plant, was tested for developmental toxicity and behavioural safety in *D. rerio* embryos. The extract caused developmental abnormalities at concentrations above 200 $mg.L^{-1}$ on embryos treated at 72 hpf, showing eye, tail and head development abnormalities, as well as a decrease in pigmentation. The authors reported an LC_{50} value of 1000 $mg.L^{-1}$ of the methanolic extract to the zebrafish embryos (Haldar et al., 2015). Piplartine isolated from a methanolic extract from the roots of *Piper tuberculatum* (Piperaceae) was also tested for potentially toxic effects towards *D. rerio*. This compound showed high toxicity (LC_{50} = 1.69 $mg.L^{-1}$) and other abnormalities were observed as transient effects after 48 h of exposure, such as erratic swimming, extended abdomen, body hemorrhaging, red-pigmented spots, exophthalmia, and abnormal head shape (Rapado et al., 2013). An ethanolic extract obtained from *Solidago canadensis* (Asteraceae) induced mortality in *D. rerio* with an LC_{50} value after 72 h of exposure of 320 $mg.L^{-1}$ which can be considered of low to no risk to this organism (Huang et al., 2014).

Aqueous extract from the leaves of *Tephrosia vogelii* (Fabaceae) showed high toxicity to *O. niloticus*, with a 24 h LC_{50} of 5.31 $\mu g.L^{-1}$. This extract was shown to be highly toxic to different organisms including *D. magna* as previously described (Li et al., 2015).

Recent studies also studied the potential toxicity of new preparation of plant extracts, namely Nano formulations. Biosynthesized silver nanoparticles with aqueous extract from *Alcea rosea* (Malvaceae) was reported to be highly toxic towards *D. rerio* (96 h LC_{50} of 10.09 $\mu g.L^{-1}$) (Khoshnamvand et al., 2020). In another study, biosynthesized silver nanoparticles with an aqueous extract from the leaves of *Achyranthes aspera* (Amaranthaceae) showed no toxic effects on the fish *G. affinis* up to concentrations of 5.82 $mg.L^{-1}$ after 48 h of exposure (Sharma et al., 2020). The reported results of toxicity observed in these studies makes it impossible to make comparisons of the effects observed as most do not follow the same duration of exposure, or, regarding embryotoxicity, the exposure started hours after the fertilisation of the embryos.

5. Toxicity towards plants and soil organisms

Plants have a major influence on the ecosystem. Besides being able to generate local micro-climates, preventing the erosion of the soils or affecting the water yielded, plants and vegetation influence the fauna around them and support a wide diversity of other organisms (Hamilton, 2013). Despite their importance, they are disregarded in most of the studies concerning the possible toxic effects of essential oils and other plant extracts on the ecosystem. Only five studies included plants in their toxicity assessments, being most of them published after 2015. Different target plants were used in all studies: edible plants such as the common onion *Allium cepa* (Amaryllidaceae), common wheat *Triticum aestivum* (Poaceae) and the garden lettuce *Lactuca sativa* (Asteraceae); different weeds, that are also edible but only in some cultures or specific areas of the world such as the red-rooted pigweed *Amaranthus retroflexus* (Amaranthaceae), the rush skeletonweed *Chondrilla juncea* (Asteraceae), the prickly lettuce *Lactuca serriola* (Asteraceae), the white goosefoot *Chenopodium album* (Chenopodiaceae) and the curly dock *Rumex crispus* (Polygonaceae) or the dandelion *Taraxacum officinale* (Asteraceae). One study also used the aquatic plant *Lemna minor* (Araceae) commonly known as duckweed to evaluate the possible toxic effects of extracts towards aquatic plants, but it was the only study that focused on this species, even though this plant is a recommended test species for aquatic toxicity tests (OECD, 2006) and it is commonly used in ecotoxicological risk assessment (Amy-Sagers et al., 2017; de Alkimin et al., 2020; Sackey et al., 2020). Besides plants, earthworms and soil microorganisms play an important role in the general soil health and can affect the biodiversity of entire ecosystems (Fründ et al., 2011; Saccá et al., 2017). Few studies focus on the potentially toxic effects of essential oils and other plant extracts on these types of soil organisms, and in general, these effects remain mostly unknown, and even though these organisms play such an important role in the ecosystem, only eight papers studied the effects of these products towards earthworms and three to soil microorganisms.

6. Plants

As previously mentioned only one study evaluated the effects of plant extracts in aquatic plants (Table 4). In this study, aqueous extracts from the roots of *Chelidonium majus* and *Stylophorum lasiocarpum* showed low toxic effects to *L. minor*, with 7 days EC_{50} values above 450 $mg.L^{-1}$, and therefore, these extracts did not cause significant growth inhibition in this aquatic plant. These extracts were tested for their acute toxicity to several organisms (*L. minor*, *R. subcapitata*, *S. quadricauda* and *D. magna*) (Jancula et al., 2007). The *S. lasiocarpum* extract does not seem to pose risk to aquatic organisms as the EC_{50} values obtained were above 100

$mg.L^{-1}$ to all tested organisms. Concerning the *C. majus* extract, the EC_{50} values obtained were also above 100 $mg.L^{-1}$ for all tested organisms, except for both microalgae (*R. subcapitata* and *S. quadricauda*) for which the EC_{50} values obtained were below 100 $mg.L^{-1}$, and thus are considered to be in the acute 3 category of the GHS (see Table 1). As it seems, microalgae are the most sensitive organisms to this *C. majus* aqueous extract.

Most of the studies conducted in terrestrial plants tested the effects of extracts and only one evaluated the toxicity of the essential oil (Çakır et al., 2015). In this last study, the toxicity of essential oils and three different extracts (*n*-hexane, acetone and methanolic) of four plants from the *Achillea* genus were studied in *Amaranthus retroflexus*, *Chondrilla juncea*, *Chenopodium album*, *Lactuca serriola*, *Rumex crispus* and *Taraxacum officinale* to evaluate their effects in terms of seed germination, root growth and seedling growth. The essential oils and n-hexane extracts were obtained from the flowering aerial parts of *A. biebersteinii*, *A. coarctata*, *A. wilhelmsii* and *A. biserrata*. The acetone and methanolic extracts were obtained from the flowers only. At 1.0 mg mL^{-1}, all the essential oils caused inhibition of germination, root growth and seedling growth, on all tested species. For the extracts, some inhibition occurred but with minor effects. The minor effects caused by the extracts was attributed to the lower content of volatile compounds when compared to the essential oils (Çakır et al., 2015). This study shows that the essential oils were more toxic to all the target plants while the respective extracts tended to be less toxic. It would be interesting to have more studies that compare the toxicity of essential oils and extracts obtained from the same plant to ascertain if essential oils are always more toxic than extracts or not. Generally, most studies focus on the effects of essential oils or extracts and not both. This could be because there are very few studies focusing solely on the ecotoxicological effects of these products, being the ecotoxicological evaluations performed to assess the safety of a specific essential oil or an extract that has the potential to be used industrially as, for example, a bioinsecticide or bioherbicide or for their properties to be used in the enhancement of cosmetics, and food industry products or as new therapeutical agents. While it is important that the awareness to the necessity of studying the effects on the ecosystems of new potential products to be introduced commercially is rising, such partial assessments make comparisons and trend establishment difficult.

The hydroalcoholic extract obtained from the leaves of *A. retroflexus* displayed low toxicity towards *Triticum aestivum*, with inhibitory effects in root length due to mitosis inhibition, only being found at the highest concentration tested of 1%. Accordingly, the authors concluded that the extract was cytotoxic and genotoxic to *T. aestivum* only at high concentrations (Dinu et al., 2017). In another study, polyflavonoids extracted from the bark of *Pinus radiata* appeared to slightly influence the growth of *Lactuca sativa* roots, while modified itaconic- and maleic-derivate polyflavonoids did not seem to have any toxic effects on the radicle growth of *L. sativa.* (García et al., 2017).

In contrast, toxic effects of an hydrolate obtained from *Artemisia absinthium* were observed in *Allium cepa.* The hydrolate caused significant inhibition of root after 72 h at low concentrations (LC_{50} of 3.87% v/v) which can ultimately affect the ability of the plant to get nutrients. This study also evaluated the toxicity of this extract towards organisms belonging to different trophic levels, namely, the annelid *Eisenia fetida* and soil bacteria as described in the next subsection.

7. Earthworms

Earthworms are important soil invertebrates due to their ability to break down organic matter being considered good indicators of soil quality. They can also influence soil structure and chemistry which influences entire soil ecosystems (Fründ et al., 2011; Römbke et al., 2005). The OECD guideline 207 recommends *Eisenia fetida* as the preferred test organism to perform toxicity tests in earthworms due to its susceptibility to chemicals and resembling response of “true soil-inhabiting species” although other species can be used if the necessary methodology is available (OECD, 1984, 2016).

Table 5 describes the available studies on the essential oils and extracts tested towards earthworms. The hydrolate from *A. absinthium* was tested towards different organisms and the results showed high toxicity to *E. fetida* after 14 days of exposure (LC_{50} of 0.07 $mg.L^{-1}$) having an important impact on the survival of this species (Pino-Otín et al., 2019b). This hydrolate was reported to be highly toxic towards different organisms, including the aquatic species *D. magna* and *C. reinhardtii* as well as the terrestrial species *A. cepa* and *E. fetida*.

Contrastingly, the essential oils from the oleo-gum-resins of *Ferula assa-foetida* and *Ferula gummosa* showed no toxic effects on *E. fetida* after 14 days of exposure (Pavela et al., 2020). Three other studies focused on the potentially toxic effects of essential oils on *E. fetida*. In these studies, the essential oils from the flowering branches of *Stevia rebaudiana* (up to 200 $mg.Kg^{-1}$), from the seeds of *Cuminum cyminum* and *Pimpinella anisum* (up to 100 $mg.Kg^{-1}$), and a commercial essential oil of *Foeniculum vulgare* (at a concentration of 240.7 $mg.Kg^{-1}$) showed no significant effects to the earthworms after 14 days of exposure (Benelli et al., 2020b; Benelli et al., 2018a; Pavela, 2018). Similar results were obtained with the essential oil from the leaves of the betel *Piper betle* towards *Eudrilus eugeniae*, a large-sized earthworm native from the African continent (Blakemore et al., 2009). The essential oil from *P. betle* showed no toxicity to *E. eugeniae* after 14 days of exposure (Vasantha-Srinivasan et al., 2016). A methanolic extract obtained from the leaves of *Swietenia mahagoni* was also tested for the potentially toxic effects to *E. eugeniae* as a non-target organism, showing low mortality after 14 days of exposure at doses up to 200 ppm. Kg^{-1} (Dinesh-Kumar et al., 2018).

8. Soil microbiome

Few studies evaluated the effects of plant extracts on the soil microbial community. One study evaluated the effects of an aqueous extract from the leaves of neem (*Azadirachta indica*), a plant used to obtain the neem essential oil, which main component, azadirachtin, is used commercially as a biopesticide (Campos et al., 2019). The aqueous extract reduced soil microorganism’s activity *in vitro* at the concentrations of 100,000 and 400,000 $mg.L^{-1}$ in short-term exposure, but significantly increased the presence of microorganisms after two months of soil supplementation with the neem extract. The authors compared the response when using the neem extract and azadirachtin and observed that the same long-term response did not occur with the biopesticide (Sarawaneeyaruk et al., 2015).

To assess the effects of plant-derived products on soil bacteria, Pino-Otín et al. (2019b) studied a hydrolate obtained from *A. absinthium* (var. Candial), a product that has been reported to possess nematicidal activity, in a microbial community obtained from soil from an experimental crop field free of pesticides or other contaminants in North-eastern Spain. The soil samples were characterized mainly by Proteobacteria (76.06%), Bacteroidetes (11.29%) and Firmicutes (4.86%). The authors used the Biolog EcoPlate™ to determine the ability of the microbial community to degrade different carbon sources after being exposed to the *A. absinthium* hydrolate in different concentrations. Their results showed that in all the concentrations tested (up to 100%) the hydrolate did not exert significant differences in the physiological diversity of soil bacteria, but concentrations above 25% v/v decreased the metabolism of soil bacteria significantly. Interestingly, at lower concentrations (1% v/v) the hydrolate caused an enhancement in the metabolism which the authors think could be due to the usage of the hydrolate as a source of nutrients or even the elimination of other competitors such as fungi (Pino-Otín et al., 2019b). This effect has been observed in other soil pesticides such as Glyphosate and Carbendazin (Ratcliff et al., 2006; Tortella et al., 2013).

9. New perspectives on the use of essential oils and plants extracts

One of the most studied potential applications of essential oils and plant extracts addresses the replacement of chemical pesticides by biopesticides. This area has received increasing attention over the past few years with numerous studies addressing the toxicity of essential oils and plant extracts towards insects that affect crops and their potential use as biopesticides (see review by (Pavela, 2016). A complete description of the toxicity of essential oils and extracts towards insects that are disease vectors or that affect crops is not under the scope of the present review that focuses on non-target organisms, nevertheless, considering the importance of this topic, a brief compilation of studies that focus on the potential effectiveness of essential oils and other plant extracts to be used as biopesticides against these insects is provided in Table 6.

Several compounds that can be obtained from plants have been identified as bioinsecticides such as nicotine, azadirachtin, rotenone, limonene and pyrethrin, while carvacrol, berberine, ethylicin can be used to prevent plant diseases (Liu et al., 2021). Currently, the most commercially used plant-based pesticides are derived from neem (*Azadirachta indica*) and neem-based formulations, and these are used to control bollworms, aphids, jassids, thrips, whitefly, diamonblack moth, among others. Pyrethrium, rotenone and ryanodine obtained from *Chrysanthemum cinerariaefolium*, *Lonchocarpus* spp. and *Ryania* spp. are used against crawling and flying insects such as cockroaches, ants, mosquitoes, and termites. Essential oils from *Artemisia annua* and *Vinca rosea* are also used against the bollworm *Helicoverpa armigera*, a pest that can attack several crops (Rajamani and Negi, 2021).

Biopesticides mechanisms of action, their effects and their potential to be used as a replacement for synthetic pesticides were recently reviewed (see for example Chaudhary et al., 2017; Liu et al., 2021; Luz et al., 2020; Rajamani and Negi, 2021; Samada and Tambunan, 2020; Singh et al., 2019). In comparison to synthetic pesticides, biopesticides have several advantages: (1) they are often less toxic than conventional pesticides and their toxicity tends to be species-specific and with fewer effects on non-target species, while broad spectrum pesticides can affect a wide variety of organisms, (2) they can be effectively used in integrated pest management (IPM) programs decreasing the need to use conventional pesticides and (3) they are often quickly degraded in the ecosystem (Leahy et al., 2014). This is in fact one of the main advantages of using essential oils and extracts as biopesticides instead of synthetic pesticides. Essential oils are mainly composed of volatile compounds such as mono- and sesquiterpenes which have been reported to be rapidly biodegradable (Jenner et al., 2011; Prasanna, 2018).

The comparison of the toxicity profile of biopesticides *versus* synthetic ones is not straightforward, as there is still a scarcity of data for biopesticides and because the toxicity of plant-based products ultimately depends on the composition of the essential oil or extract.

One of the few studies that evaluated the potential use of essential oils as a biopesticide with larvicidal activity against *Aedes aegypti* also evaluated the toxicity on *D. magna* organisms as a non-target species. The studied essential oils from *E. globulus*, *M. dissitiflora*, *M. linariiflora* and *M. quinquenervia* showed larvicidal activity while also presenting an LC_{50} value to the non-target organism much lower than one of the most used synthetic pesticides against larvae of *A. aegypti*, the organophosphate temephos, which is reported to have a 48 h LC_{50} of 0.00015 mg.L^{-1} to *D. magna* (Abe et al., 2014). The essential oil from *M. linariiflora* showed the lowest EC_{50} to *D. magna* of 1.84 mg.L^{-1}, which is still more than 12,000 times the value reported of temephos. Fig. 6 describes the toxicities (in terms of $L(E)C_{50}$) of the most widely used synthetic pesticides and essential oils and extracts towards *D. magna* (the test species for which more data is available).

Essential oils and plant extracts have been intensively studied for their potential use as biopesticides and, in general, they often pose less risk to non-target organisms although some acute effects can still occur at low concentrations. Due to their volatile character, compounds extracted from plants usually tend to be rapidly biodegradable, but studies that address the persistence or even studies that focus on chronic toxicity to non-target organisms are still very scarce.

10. Conclusions

Essential oils and plant extracts are an important part of plant-derived products with a wide range of applications in various types of industries, including food, agriculture, pharmaceuticals, cosmetics, and textiles. The demand for these products is expected to increase as the call for more natural products continues to rise. Therefore, it will become more and more important to evaluate their safety in the ecosystem. Although some work has already been performed, much more is necessary not only due to the expected increasing demand and consequent large-scale industrial production but also due to regulatory issues. Most of the work performed so far focused on the evaluation of acute toxicity of essential oils, extracts or selected ingredients obtained from plants towards organisms from different trophic levels, mainly crustaceans. Interestingly, several studies evaluated the potential toxicity of endemic plant species, however, no studies on the effects of the most common industrially produced essential oils (orange, lemon, and mint) are available. Overall, essential oils are more toxic than extracts and most of the highly toxic extracts are derived from plants that are known to be toxic as is the case of the aqueous extracts from *Thephrosia vogelii*, *Hura crepitans* or *Quillaja saponaria*. Toxicity has also been reported for extracts obtained from plants that are not known to have highly toxic metabolites such as the ethanolic and hexane extracts from *Artemisia absinthium*. Furthermore, some of these products exhibited toxic effects in some organisms and no effects on others, as was the case with the essential oil from *Juniperus occidentalis* that caused relatively high toxicity to microalgae while registering no effects on crustacea, while the contrary effect was observed with the oil obtained from *Chamaecyparis lawsoniana* that caused toxicity at low concentrations to crustacea but not on microalgae. Despite the general perception that plant-based products are “greener” and safer alternatives to their chemical counterparts, there is a lack of empirical data that can sustain it, creating an imperative obligation to widen the assessment of their safety to better understand their effects in the ecosystem. As international regulations become tighter regarding environmental impacts of chemicals, mixtures of chemicals and new products, such as REACH in the European Union or more globally the GHS put in place by the UN, we expect that more studies will generate scientific data about the effects of essential oils, hydrolates and other extracts obtained from plants as new sources of bioactive compounds.

Presently, data regarding the effects of plant-based products is still scarce (most of the studies focus on aquatic systems and in a particular organism, *Daphnia magna*) and the possible effects on other aquatic organisms or even to marine or terrestrial systems remain still largely unknown. Although many international guidelines regarding acute toxicity testing to organisms are in place, the way that experiments are conducted and the way that results are presented often do not follow the requested criteria, which renders the subsequent comparison and classification impossible. Future studies should strictly follow standardized guidelines in order to allow a broader comparison between studies and to allow future ranking of plant-based extracts according to their eco-safety potential.

We hope that this review, which describes the current state of the art on this emerging topic, can launch the basis for further studies on the environmental safety of plant essential oils and extracts. Of particular emerging interest are the studies regarding the use of essential oils and plant extracts as a replacement for synthetic pesticides. In this line, it becomes even more important to evaluate the eco-safety of essential oils and extracts to non-target organisms of different trophic levels, as they will be intentionally released into the environment. This evaluation should focus in, not only acute, but also in chronic toxicity tests the study of the effects of complex mixtures of multiple oils and extracts, as

Table 6
Examples of Essential oils and extracts that have been studied for their biopesticide potential against important disease vectors and crop pests.

	Insect family	Scientific name	Plant family	Plant	Part(s) used	Type of extract	Effect	Reference
Disease vectors	Culicidae	*Aedes aegypti*	Apiaceae	*Petroselium crispum*	Fruits	Essential oil	Larvicidal/Adulticidal	Intirach et al. (2016)
			Asteraceae	*Foeniculum vulgare*	Fruits	Essential oil	Larvicidal	Intirach et al. (2016)
			Euphorbiaceae	*Ageratum conyzoides*	Flowers and leaves	Essential oil +	Adulticidal	Pintong et al. (2020)
			Fabaceae	*Artemisia absinthium*	Leaves	extracts	Larvicidal	Govindarajan and Benelli (2016a)
			Lamiaceae	*Blumea eriantha*	Leaves	Essential oil	Larvicidal	Benelli et al. (2017)
			Myristicaceae	*Croton tetradenius*	Leaves	Essential oil	Larvicidal/Adulticidal	Carvalho et al. (2016)
			Piperaceae	*Acacia nilotica*	Leaves	Essential oil	Larvicidal	Vivekanandhan et al. (2018)
			Plantaginaceae	*Pogostemon cablin*	Leaves	Essential oil	Larvicidal	Santos et al. (2019)
			Schisandraceae	*Salvia apiana*	Aerial parts	Essential oil	No effect	Ali et al. (2015a)
			Zingiberaceae	*Salvia elegans*	Aerial parts	Essential oil	Larvicidal	Ali et al. (2015a)
				Salvia leucantha	Aerial parts	Essential oil	Larvicidal	Intirach et al. (2016)
				Myristica fragans	Mace	Essential oil	Larvicidal	Intirach et al. (2016)
				Piper sarmentosum	Stems and leaves	Mace oil +	Larvicidal	Govindarajan et al. (2016b)
				Kadsura heteroclita	Leaves	extracts	Larvicidal	Intirach et al. (2016)
				Limnophila aromantica	Whole plant	Essential oil	Larvicidal	(Intirach et al., 2016)/(Ali et al., 2015b)
				Curcuma longa	Rhizomes/	Essential oil	LarvicidalLarvicidal	AlShebly et al. (2017)
				Hedychium larsenii	LeavesRhizomes	Essential oil	Larvicidal	Govindarajan et al. (2016a)
				Zingiber nimmonii	Rhizomes	Essential oil		
						Essential oil		
		Aedes albopictus	Asteraceae	*Blumea eriantha*	Leaves	Essential oil	Larvicidal	Benelli et al. (2017)
				Artemisia absinthium	Leaves			Govindarajan and Benelli (2016a)
				Heracleum sprengelianum	Leaves			Govindarajan and Benelli (2016b)
		Culex quinquefasciatus	Asteraceae	*Artemisia absinthium*	Leaves	Essential oil	Larvicidal	Govindarajan and Benelli (2016a)
			Fabaceae	*Baccharis dracunculifolia*	Leaves			Alves et al. (2018)
			Lamiaceae	*Blumea eriantha*	Leaves			AlShebly et al. (2017)
			Monimiaceae	*Echinops giganteus*	Rhizomes			Pavela et al. (2016)
			Schisandraceae	*Helichrysum faradifani*	Aerial parts			Benelli et al. (2018b)
			Zingiberaceae	*Acacia nilótica*	Seeds			Vivekanandhan et al. (2018)
				Afromomum daniellii	Fruits			Pavela et al. (2016)
				Dichrostachyl cinerea	Fruits, leaves, seeds			Pavela et al. (2016)
				Nepeta cadmea	Aerial parts			Öz et al. (2018)
				Peumus boldus	Leaves			de Castro et al. (2016)
				Kadsura heteroclita	Leaves			Govindarajan et al. (2016b)
				Hedychium larsenii	Rhizomes			AlShebly et al. (2017)
				Zingiber nimmonii	Rhizomes			Govindarajan et al. (2016a)
		Culex tritaeniorhynchus	Asteraceae	*Artemisia absinthium*	Leaves	Essential oil	Larvicidal	Govindarajan and Benelli (2016a)
				Blumea eriantha	Leaves			Benelli et al. (2017)
				Heracleum sprengelianum	Leaves			Govindarajan and Benelli (2016b)
		Culex pipens		*Nepeta cadmea*	Aerial parts	Essential oil	Larvicidal	Öz et al. (2018)
				Pimpinella anisum	Seeds			
		Anopheles gambiae	Lamiaceae	*Satureja montana*	Leaves	Essential oil	Adulticidal	Deletre et al. (2013)
			Lauraceae	*Thymus vulgaris*	Leaves			
			Poaceae	*Cinnamomum zeylanicum*	Bark			
				Cymbopogon winterianus	Leaves			
					Leaves			
		Anopheles stephensi	Asteraceae	*Artemisia absinthium*	Leaves	Essential oil	Larvicidal	Govindarajan and Benelli (2016a)
			Fabaceae	*Blumea eriantha*	Leaves			Benelli et al. (2017)
			Schisandraceae	*Acacia nilótica*	Seeds			Vivekanandhan et al. (2018)
			Zingiberaceae	*Kadsura heteroclita*	Leaves			Govindarajan et al. (2016b)
				Hedychium larseni	Rhizomes			AlShebly et al. (2017)
				Zingiber nimmonii	Rhizomes			Govindarajan et al. (2016a)
		Anopheles subpictus	Asteraceae	*Artemisia absinthium*		Essential oil	Larvicidal	
			Apiaceae	*Blumea eriantha*				

(*continued on next page*)

Table 6 (*continued*)

	Insect family	Scientific name	Plant family	Plant	Part(s) used	Type of extract	Effect	Reference
				Heracleum sprengelianum	Leaves			(Govindarajan and Benelli, 2016a;
					Leaves			Govindarajan et al., 2016a)
					Leaves			Govindarajan and Benelli (2016b)
		Anopheles quadrimaculatus	Lamiaceae	*Salvia leucantha*	Aerial parts	Essential oil	Larvicidal	Ali et al. (2015a)
			Zingiberaceae	*Curcuma longa*	Leaves			Ali et al. (2015b)
Crop pests	Anobiidae	*Lasioderma serricorne*	Rutaceae	*Evodia lenticellata*	Fruits	Essential oil	Fumigant and contact toxicity, repellent	Cao et al. (2018)
	Curculionidae	*Sitophylus oryzae*	Lamiaceae	*Nepeta cataria*	Aerial parts	Essential oil	Repellent and fumigant toxicity	Amini et al. (2019)
				Nepeta pogonosperma				(Koutsaviti et al., 2018)
				Nepeta glomerulosa				
				Nepeta binaloudensis				
				Salvia pomifera				
				Thymbra capitata				
		Sitophylus zeamais	Sapindaceae	*Paullinia pinnata*	Leaves	Essential oil	Fumigant toxicity	Ogunwande et al. (2017)
				Mosla soochowensis	Aerial parts		Contact + fumigant toxicity	Chen et al. (2017)
	Liposcelididade	*Liposcelis bostrychophila*	Rutaceae	*Evodia lenticellata*	Fruits	Essential oil	Fumigant and contact toxicity, repellent	Cao et al. (2018)
	Margarodidae	*Drosicha mangiferae*	Meliaceae	*Azadirachta indica*	Leaves and fruits	Methanolic extract	Contact toxicity	Ghafoor et al. (2019)
			Poaceae	*Cymbopogon citratus*	Leaves	Essential oil		
			Solanaceae	*Datura alba*	Leaves and seeds	Essential oil		
			Sapindaceae	*Dodonaea viscosa*	Tender stems	Methanolic extract		
			Rubiaceae	*Gardenia jasminoides*	Leaves and stems	Methanolic extract		
			Apocynaceae	*Nerium indicum*	Leaves	Methanolic extract		
			Asteraceae	*Parthenium hysterophorus*	Leaves and tender stems	Methanolic extract		
			Myrtaceae	*Syzygium aromaticum*	Buds	Essential oil		
	Tenebrionidae	*Tribolium castenum*	Rutaceae	*Evodia lenticellata*	Fruits	Essential oil	Fumigant and contact toxicity, repellent	Cao et al. (2018)
			Asteraceae	*Artemisia annua*	Leaves	Essential oils + extracts	Fumigant and contact toxicity, repellent	Deb and Kumar (2020)
		Tribolium confusum	Meliaceae	*Azadirachta indica*	Seeds	Ethanolic extracts	Adulticidal	Zaka et al. (2019)
			Euphorbiaceae	*Ricinus communis*	Seeds			
			Brassicaceae	*Eruca sativa*	Seeds			
			Myrtaceae	*Eucalyptus globulus*	Seeds			
			Myrtaceae	*Syzygium cumini*	Peel + seeds			
			Rutaceae	*Citrus reticulata*	Peel + seeds			

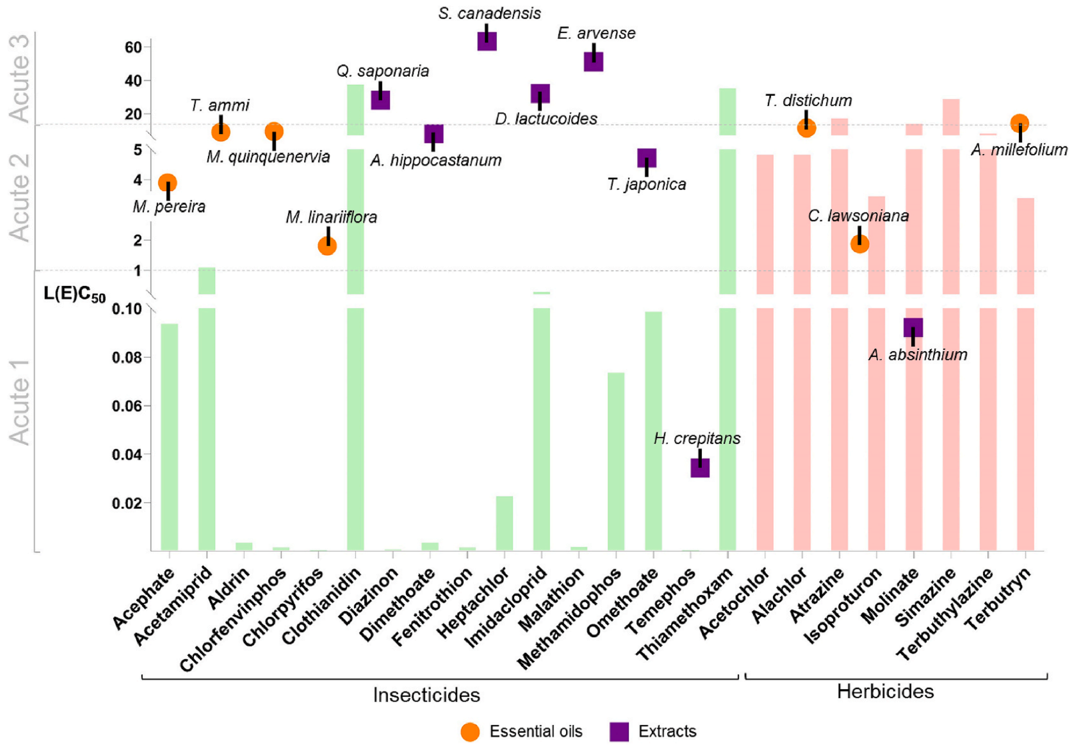

Fig. 6. 48 h L(E)C_{50} values (in mg.L^{-1}) of common insecticides and herbicides *vs* reported 48 h L(E)C_{50} values of essential oils and extracts towards *D. magna*.

well as potential multi and transgenerational effects in the biota.

Author statement

Celso Afonso Ferraz: Investigation, Visualization, Writing – original draft preparation. **M. Ramiro Pastorinho**: Supervision, Methodology, Writing – review & editing. **Ana Palmeira de Oliveira**: Funding acquisition, Writing – review & editing. **Ana Catarina Sousa**: Conceptualization, Methodology, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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