agronomy

MDPI

Article

Phytotoxic Effects of Three Natural Compounds: Pelargonic Acid, Carvacrol, and Cinnamic Aldehyde, against Problematic Weeds in Mediterranean Crops

Marta Muñoz [1,2], Natalia Torres-Pagán [1], Rosa Peiró [3], Rubén Guijarro [2], Adela M. Sánchez-Moreiras [4,5] and Mercedes Verdeguer [1,*]

1 Instituto Agroforestal Mediterráneo (IAM), Universitat Politècnica de València, Camino de Vera s/n, 46022 Valencia, Spain; mmunoz@seipasa.com (M.M.); natorpa@etsiamn.upv.es (N.T.-P.)
2 SEIPASA S.A. C/Ciudad Darío, Polígono Industrial La Creu naves 1-3-5, L'Alcudia, 46250 Valencia, Spain; rguijarro@seipasa.com
3 Centro de Conservación y Mejora de la Agrodiversidad Valenciana (COMAV), Universitat Politècnica de València, Camino de Vera s/n, 46022 Valencia, Spain; ropeibar@btc.upv.es
4 Department of Plant Biology and Soil Science, Faculty of Biology, University of Vigo, Campus Lagoas-Marcosende s/n, 36310 Vigo, Spain; adela@uvigo.es
5 CITACA. Agri-Food Research and Transfer Cluster, Campus da Auga. University of Vigo, 32004 Ourense, Spain
* Correspondence: merversa@doctor.upv.es; Tel.: +34-9-6387-7000

Received: 28 April 2020; Accepted: 27 May 2020; Published: 2 June 2020

check for updates

Abstract: Weeds and herbicides are important stress factors for crops. Weeds are responsible for great losses in crop yields, more than 50% in some crops if left uncontrolled. Herbicides have been used as the main method for weed control since their development after the Second World War. It is necessary to find alternatives to synthetic herbicides that can be incorporated in an Integrated Weed Management Program, to produce crops subjected to less stress in a more sustainable way. In this work, three natural products: pelargonic acid (PA), carvacrol (CV), and cinnamic aldehyde (CA) were evaluated, under greenhouse conditions in postemergence assays, against problematic weeds in Mediterranean crops *Amaranthus retroflexus*, *Avena fatua*, *Portulaca oleracea,* and *Erigeron bonariensis*, to determine their phytotoxic potential. The three products showed a potent herbicidal activity, reaching high efficacy (plant death) and damage level in all species, being PA the most effective at all doses applied, followed by CA and CV. These products could be good candidates for bioherbicides formulations.

Keywords: weeds; abiotic stress; natural herbicides; secondary metabolites; postemergence; phytotoxicity

1. Introduction

One of the main challenges for the agriculture in this 21st century is to be capable to feed the increasing world population in a sustainable way, because natural resources are becoming even more scarce [1]. Crop protection measures can prevent yield losses due to pests [2]. Herbicides have been the most used method to control weeds since their development, at the end of the Second World War because they are effective and economical [3,4].

Herbicides cause stress in crops and can make them more susceptible to other pests [5]. Other problems derived from the overuse of herbicides are environmental pollution, toxicity for nontarget organisms, and the development of herbicide-resistant weed biotypes [6]. In the latest 10 years, integrated weed management (IWM) strategies have been promoted worldwide [7,8] to control weeds. They consist of a combination of methods: cultural, mechanical, physical, biological, biotechnological, and chemical. In Europe, IWM has been promoted through the European Union Directive 2009/128/EC [8].

The society is demanding new solutions for weed control and "greener" weed management products. The use of natural products as bioherbicides could be one alternative to reduce the stress that synthetic herbicides promote in crops and all their negative impacts aforementioned. Bioherbicides could be incorporated in IPM programs as an innovative weed control method. They are less persistent than synthetic herbicides and are potentially more environmentally friendly and safe [9] and also, they have different modes of action, which can prevent the development of herbicide-resistant weed biotypes [10].

Bailey [11] defined bioherbicides as products of natural origin for weed control. The EPA (USA Environmental Protection Agency), considers three categories of biopesticides: (1) biochemical pesticides, which include naturally occurring substances that control pests; (2) microbial pesticides or biocontrol agents, which are microorganisms that control pests; and (3) plant-incorporated protectants, or PIPs, which are pesticide substances produced by plants that contain added genetic material) [10]. In recent years, the search for natural substances that can act as bioherbicides has been very extensive.

The weeds selected for this study were *Amaranthus retroflexus* L., *Avena fatua* L., *Portulaca oleracea* L., and *Erigeron bonariensis* L. because of their importance in many crops worldwide and their difficult management. *A. fatua* is a very important weed mainly in cereals and also in other crops around the world [12], and this weed is on the fourth position in resistance to herbicides worldwide, having developed resistance to nine different modes of action [13]. *A. retroflexus* is a serious and aggressive weed in summer crops, with cosmopolite distribution [14]. It has developed resistance to five modes of action and is on the eight position worldwide in resistance to herbicides [13]. *E. bonariensis*, which can be found both in summer or winter crops, especially with no-tillage practices [15], is on the ninth position in resistance to herbicides worldwide, with resistance to four modes of action. *P. oleracea*, which is a summer weed difficult to control in Mediterranean crops [16], has developed resistance only to two modes of action [13]. *A. fatua* and *E. bonariensis* have developed resistance to glyphosate, which is the herbicide most commonly used around the world [13,17].

There are several examples of natural products that have been tested as potential bioherbicides to control *A. fatua*, *A. retroflexus*, *E. bonariensis*, and *P. oleracea*, mainly essential oils (EOs) [14,18–26], or extracts from plants with different solvents [27–29], or their isolated compounds [30,31]. Most studies have been carried out only in in vitro conditions. Of the weeds considered, *A. retroflexus* has been the most tested. In vitro studies with EOs from *Artemisia vulgaris*, *Mentha spicata*, *Ocimum basilicum*, *Salvia officinalis*, and *Thymbra spicata* from Turkey demonstrated high phytotoxic effects on seed germination and seedling growth of *A. retroflexus*, with stronger effects with higher doses [18]. EOs from *Tanacetum* species growing in Turkey, rich in oxygenated monoterpenes, inhibited completely *A. retroflexus* germination in in vitro assays [19]. In addition, EOs from *Nepeta meyeri*, with high content in oxygenated monoterpenes controlled completely *A. retroflexus* germination [20]. The phytotoxic potential of 12 EOs was studied in vitro against *A. retroflexus* and *A. fatua*, and the most phytotoxic EOs were those constituted mainly by oxygenated monoterpenes [21]. Other EOs which showed strong herbicidal potential against *A. retroflexus* seed germination and seedling growth were *Rosmarinus officinalis*, *Satureja hortensis*, and *Laurus nobilis* [14], and a nanoemulsion of *S. hortensis* EO was tested against *A. retroflexus* in greenhouse conditions killing the weed at 4000 µL/mL dose [22]. *P. oleracea* germination was completely inhibited by *Eucalyptus camaldulensis* EO in in vitro conditions [23]. The application of leaf extracts (obtained using water, methanol, and ethanol as solvents) of cultivated *Cynara cardunculus* in in vitro bioassays inhibited seed germination and germination time in *A. retroflexus* and *P. oleracea* [27].

Different natural compounds have demonstrated herbicidal potential against the germination and seedling growth of *A. fatua*, such as EOs from *Artemisia herba-alba* [24] and *Eucalyptus citriodora* EOs [25] and extracts from *Sapindus mukorossi*, which inhibited *A. fatua* and *A. retroflexus* growth in vitro and in pots [28] or from *Iris sibirica* rhizomes [29].

EOs from *Thymbra capitata*, *Mentha piperita*, *Eucalyptus camaldulensis*, and *Santolina chamaecyparissus* were tested in vivo against *E. bonariensis*. *T. capitata* EO, with high content in carvacrol, was the most effective to control *E. bonariensis*, showing an excellent potential to develop bioherbicide formulations [26].

Some studies carried out in recent years relate the herbicidal activity of plant extracts or EOs to their composition in monoterpenes, and these substances are postulated as the future of natural herbicide components [32–35]. For example, eugenol, a monoterpene that can be found in many EOs as the major compound, like in *Syzygium aromaticum* EO, has shown strong phytotoxic potential against *A. retroflexus* [30] and *A. fatua* [31]. In *A. fatua*, eugenol inhibited its seedling growth, affecting more the roots than the coleoptiles. In addition, sesquiterpenes, secondary metabolites in plants, present in some EOs, have demonstrated strong herbicidal activity [36,37].

The natural products studied on this work for their potential as bioherbicides were pelargonic acid, trans-cinnamaldehyde and carvacrol. Pelargonic acid (PA) ($CH_3(CH_2)_7CO_2H$, n-nonanoic acid), which is present as esters in the EO of *Pelargonium* spp., is a saturated fatty acid with nine carbons in its structure [28–40]. PA and its salts are used like active ingredients in bioherbicide formulations for garden and professional uses worldwide. They are applied as burndown herbicides, which in a short time, attack cell membranes, causing cell leakage, followed by breakdown of membrane acyl lipids [41], and finally causing visible effects of desiccation of green areas of the weeds [38]. All the symptoms caused by PA on weeds involve extreme phytotoxicity for the plants and their cells, which rapidly begin to oxidize, causing necrotic lesions on aerial parts of plants [42,43].

Herbicidal fatty acids have been used for a long time in weed management, and some of them are used as natural herbicides. Still, the high dosage and the high cost are some of the drawbacks of its practical application in the current agriculture. In 2015, the bioherbicide Beloukha® was authorized as plant protection product to be marketed in Europe [44]. It is derived from oleic acid from different origin. Actually, it is authorized also for markets in USA and Canada. This work aims to find an optimal formulation of PA capable to be effective at reduced doses compared to the existing products in the market.

Trans-cinnamaldehyde (CA) (C_9H_8O) is one of the major components of two different cinnamon species (*Cinnamomum zeylanicum* and *Cinnamomum cassia*) and their EOs [45–48]. This compound has shown strong antioxidant properties and is responsible for various observed biological activities of cinnamon like bactericidal, fungicidal, or acaricidal [49–52]. The antimicrobial activity of CA is well known, however, its potential as bioherbicide has been less studied. Despite that, recent research demonstrated the herbicidal activity of CA against *Echinochloa crus-galli* by reducing the fresh weight and growth of this important weed [53]. To our knowledge, the mode of action of CA on weeds has not been elucidated.

The third natural compound evaluated was carvacrol (CV), a phenolic monoterpene frequently present on EOs obtained from many species belonging to Lamiaceae family like *Thymus* spp., *Thymbra* spp., and *Origanum* spp. [34]. CV presents antimicrobial properties that make it helpful for controlling diseases in crop protection [54–58]. In relation to its mode of action, CV exhibited membrane-disrupting activity that was dependent on long exposure at high concentration [33]. Postemergence exposure of plants to high concentrations of CV causes severe phytotoxicity. One of the effects associated with the mode of action of CV is the reduction of weed growth [22,41,54].

This work is a collaboration between the Universitat Politècnica de València (UPV) and the company Seipasa S.A., which develops and commercializes biopesticides, with the purpose to manage agricultural ecosystems in a more sustainable way. The objective of the present study was to evaluate the herbicidal potential of the natural compounds pelargonic acid, trans-cinnamaldehyde, and carvacrol against important cosmopolite weeds (*Amaranthus retroflexus* L., *Portulaca oleracea* L., *Erigeron bonariensis* L., and *Avena fatua* L.) as an alternative to synthetic herbicides to reduce the abiotic stress that they cause on crops. Effective compounds were formulated as emulsifiable concentrates (ECs) by Seipasa S.A., and evaluated for their postemergence herbicidal activity in greenhouse conditions in the UPV (Spain).

2. Materials and Methods

2.1. Postemergence Herbicidal Assays against Targeted Weed Species

2.1.1. Weeds

Seeds of *Amaranthus retroflexus* L., *Portulaca oleracea* L., and *Avena fatua* L. purchased from Herbiseed (Reading, UK) (year of collection 2017), which have been previously tested in a plant growth chamber EGCHS series from Equitec (Madrid, Spain) (30 ± 0.1 °C, 16 h light and 20 ± 0.1 °C, 8 h dark for *A. retroflexus* and *P. oleracea*; 23.0 ± 0.1 °C, 8 h light and 18.0 ± 0.1 °C 16 h dark for *A. fatua*) to assure their germination viability, were sown in pots (8 × 8 × 7 cm) filled with 2 cm of perlite and 5 cm of soil collected from a citrus orchard nontreated with herbicides. In Figure 1, the location (39°37′24.8″ N, 0°17′25.6″ W Puzol, Valencia province, Spain) and a view of the citrus orchard (0.4 ha) from which the soil was collected is reported. Table 1 shows the main physical characteristics of the soil used for the experiments.

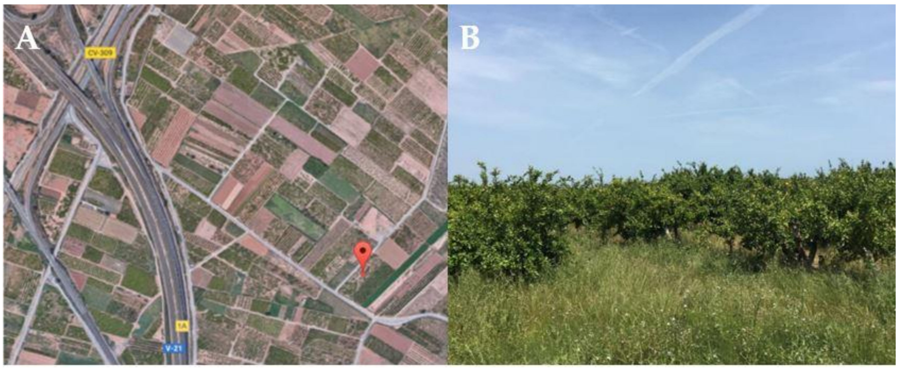


Figure 1. Location (**A**) and view (**B**) of the citrus orchard where the soil for the herbicidal tests was collected.

Table 1. Physical properties of the soil used for the experiments [59].

Soil Properties
Clay 21.85%
Silt 47.55%
Sand 30.60%

Erigeron bonariensis L. seeds were collected from an ecological weed management persimmon orchard located in Carlet (Valencia province, Spain) in July 2018. They were previously tested in the plant growth chamber described before (30 ± 0.1 °C, 16 h light and 20 ± 0.1 °C 8 h dark) to assure their germination capability and after that, sown in plastic pots filled with a mix of three-fourth peat and one-fourth perlite instead of soil because it was very difficult to germinate the seeds on the soil, as *E. bonariensis* germinates better in lighter soils [60] and, therefore, the properties of the soil collected from the citrus orchard (Table 1) did not fit the needs for their germination.

All weeds were irrigated by capillarity from trays (43 cm × 28 cm × 65 cm) placed under the pots and filled with water, until the plants were ready for the herbicidal experiments.

2.1.2. Treatments

Ten pots were prepared for each treatment, described in Table 2. The treatments were applied when plants reached the phenological stage of 2-3-true leaves, corresponding to stage 12-13 BBCH (Biologische Bundesanstalt, Bundessortenamt und Chemische Industrie) scale for the monocotyledonous *A. fatua*, and 3-4-true leaves, corresponding to stage 13-14 BBCH scale for the dicotyledonous *A. retroflexus* and *P. oleracea* and in rosette stage for *E. bonariensis*, stage 14-15 BBCH scale (Figure 2). Pelargonic acid, cinnamic aldehyde and carvacrol were provided formulated as emulsifiable concentrates (ECs) by the company Seipasa S.A. (L'Alcudia, Valencia province, Spain). Beloukha® was purchased from Ferlasa (Museros, Valencia province, Spain) and Roundup® Ultra Plus was purchased from Cooperativa Agrícola Nuestra Señora del Oreto (CANSO, L'Alcudia, Valencia province, Spain).

Table 2. Treatments tested.

	Treatments	Abbreviations
T1	Control treated with water	CW
T2	Pelargonic acid 5%	PA5
T3	Pelargonic acid 8%	PA8
T4	Pelargonic acid 10%	PA10
T5	Cinnamic aldehyde 6%	AC6
T6	Cinnamic aldehyde 12%	AC12
T7	Cinnamic aldehyde 24%	AC24
T8	Carvacrol 8%	CV8
T9	Carvacrol 16%	CV16
T10	Carvacrol 32%	CV32
T11	Bioherbicide reference: pelargonic acid (Beloukha® 8%)	BE
T12	Chemical reference: glyphosate (Roundup® Ultra Plus 10%)	GL

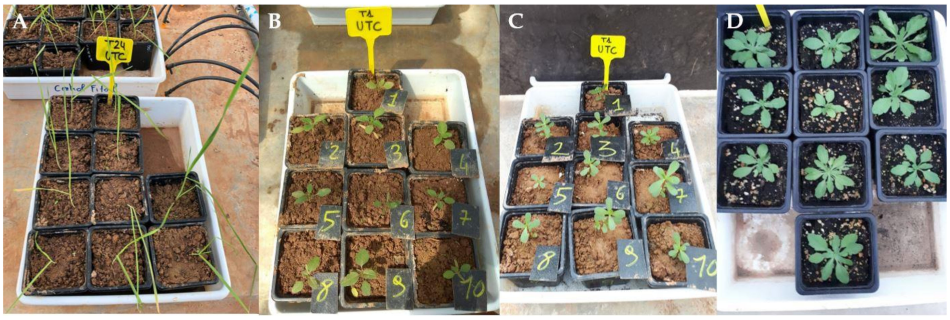


Figure 2. Pots ready for the postemergence treatments. (**A**) *A. fatua*, (**B**) *A. retroflexus*, (**C**) *P. oleracea*, and (**D**) *E. bonariensis.*

In Table 3, the dates of the herbicidal tests and the greenhouse conditions during the experimental periods are reported. Data were registered using a HOBO U23 Pro v2 data logger (Onset Computer Corporation, Bourne, MA, USA).

Table 3. Greenhouse conditions during the herbicidal tests.

Species	Starting-End Date	Temperature (°C)			Relative Humidity (%)		
		Mean	Max.	Min.	Mean	Max.	Min.
P. oleracea	August 9, 2018–September 9, 2018	28.03	38.39	22.87	68.04	87.03	37.18
A. retroflexus	September 2, 2018–October 2, 2018	26.38	35.42	19.82	70.91	85.88	31.14
A. fatua	December 3, 2018–January 3, 2019	18.57	25.72	12.75	57.87	75.56	29.84
E. bonariensis	February 15, 2019–March 15, 2019	22.62	27.16	17.99	45.88	50.26	40.40

2.2. *Evaluation of the Herbicidal Activity of Each Natural Product*

During the experiments, images from the plants were taken 24 h and 3, 7, 15, and 30 days after the treatments application to be processed with Digimizer v.4.6.1 software (MedCalc Software, Ostend, Belgium, 2005–2016).

To evaluate the herbicidal activity, two variables were measured for each plant: the efficacy, which was scored 0 if the plant was alive and 100 if the plant was dead, and the damage level, which was assessed between 0 and 4 as reported in Table 4 and Figure 3. The efficacy and damage level for each treatment were calculated as the mean of the 10 treated plants.

Table 4. Damage level assessment.

Level of Damage	
0	Undamaged plant
1	Plant with slight damage
2	Plant with severe damage
3	Dead plant
4	Regrown plant

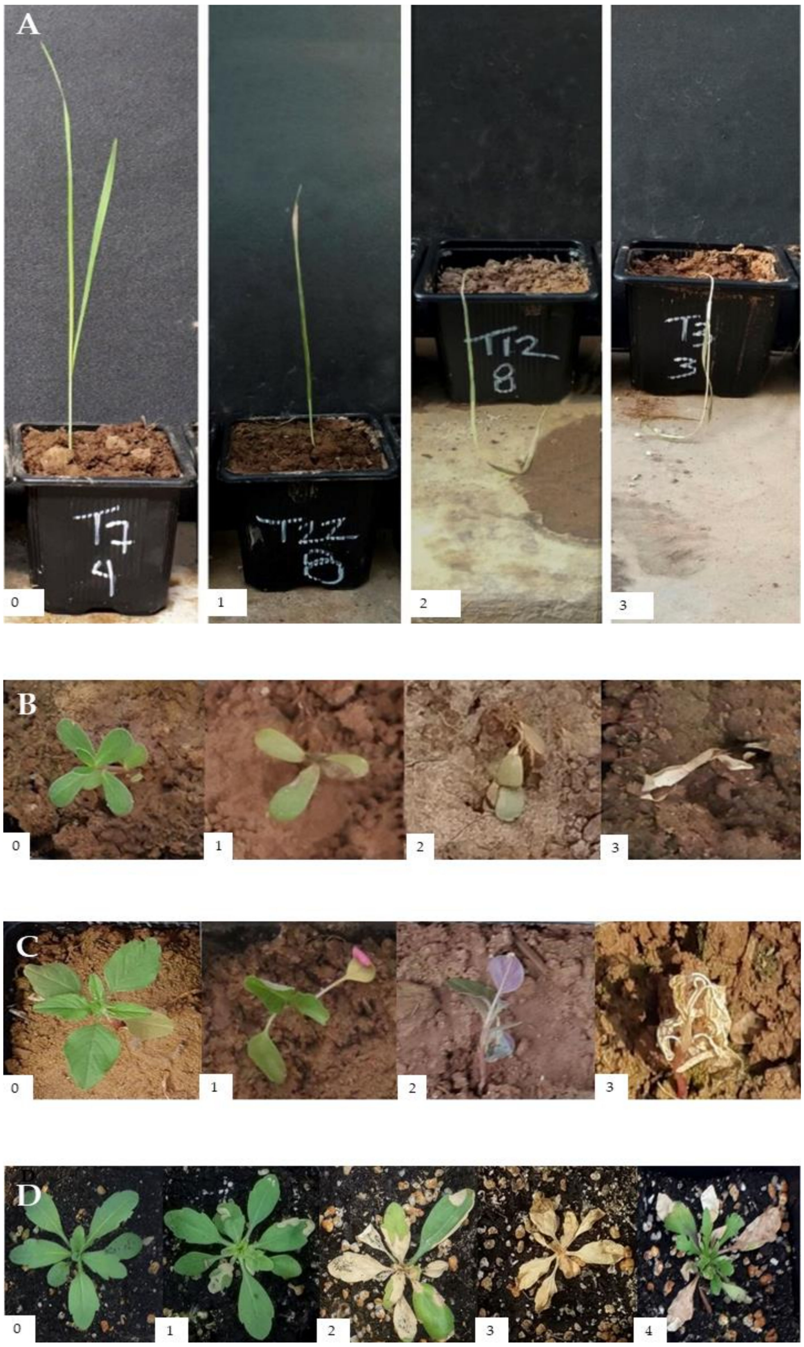


Figure 3. Damage scale for each species: (**A**) *A. fatua*, (**B**) *P. oleracea*, (**C**) *A. retroflexus*, and (**D**) *E. bonariensis*.

2.3. Statistical Analyses

Data were processed using Statgraphics® Centurion XVII (StatPoint Technologies Inc., Warrenton, VA, USA) software. A multifactor analysis of variance (ANOVA) was performed on efficacy and damage level including species, treatments, time after treatments application, and their double significant interactions as effects, followed by Fisher's multiple comparison test (LSD intervals, least significant difference, at $p \leq 0.05$) for the separation of the means.

3. Results and Discussion

3.1. Efficacy of Pelargonic Acid, Cinnamic Aldehyde, and Carvacrol against Target Weeds

A. retroflexus was the weed species most susceptible to the treatments tested, with 73.50 efficacy (Table 5). No significant differences were observed between the other species, which showed around 55 efficacies. The fact that all species tested were susceptible to all treatments with natural products assayed confirm that they could be a more sustainable alternative to synthetic herbicides, and they also offer new modes of action to control weeds that have developed resistant biotypes to many herbicides.

Table 5. Efficacy according to the species, time, and treatment.

Species	Efficacy
Portulaca oleracea	56.17 ± 1.11 b
Amaranthus retroflexus	73.50 ± 1.11 a
Avena fatua	54.83 ± 1.11 b
Erigeron bonariensis	55.67 ± 1.11 b
Time (Days after application)	**Efficacy**
1	41.67 ± 1.24 c
3	81.88 ± 1.24 b
7	87.08 ± 1.24 a
15	89.58 ± 1.24 a
Treatment	**Efficacy**
Control treated with water	4.00 ± 1.92 g
Pelargonic acid 5%	70.50 ± 1.92 b
Pelargonic acid 8%	73.50 ± 1.92 ab
Pelargonic acid 10%	74.50 ± 1.92 ab
Cinnamic aldehyde 6%	53.50 ± 1.92 e
Cinnamic aldehyde 12%	70.00 ± 1.92 bc
Cinnamic aldehyde 24%	70.00 ± 1.92 bc
Carvacrol 8%	60.50 ± 1.92 d
Carvacrol 16%	64.50 ± 1.92 d
Carvacrol 32%	65.00 ± 1.92 cd
Bioherbicide reference: pelargonic acid (Beloukha® 8%)	78.50 ± 1.92 a
Chemical reference: glyphosate (Roundup® Ultra Plus 10%)	36.00 ± 1.92 f

Values are efficacy ± standard error. Means followed by different letters in the same column differ significantly ($p \leq 0.05$).

Efficacy increased with time after treatments application, with values close to 90 between 7 and 15 days (Table 5). This happened because PA, at all doses applied, and the higher doses of CA and CV acted very quickly in the treated species, causing the death of all plants between 24 h and 3 days after application of treatment (Figures 4–7, Tables S1–S4). The same happened for the bioherbicide reference BE (as PA was also the active compound on it), while GL acted more slowly, depending on the species against which it was applied; it killed *A. retroflexus* plants after 3 days, *A. fatua* and *P. oleracea* after 15 days, and *E. bonariensis* after 30 days (Figures 4–7, Tables S1-S4). It has been reported that weed damage caused by PA can be observed visually few hours after application [61]. Thymol, *trans*-cinnamaldehyde, eugenol, farnesol, and nerolidol were tested in postemergence in *E. crus-galli* applied at two-leaf stage, and significantly reduced the shoot growth and the fresh and dry weight 2 days after the foliar treatments with 0.5%, 1.0%, and 2.0% concentrations. All treatments except thymol controlled the weed completely when applied at 1.0% and 2.0% [52]. The concentrations of CA used in this work were higher, and this could explain the quicker toxic effect observed on weeds. It is also remarkable that weed species displayed different sensitivity to low doses of CA; *E. bonariensis* and *P. oleracea* showed more resistance to this compound than the other weeds tested (Figures 4–7, Tables S1-S4), as the lowest concentration (6%) used took more time (15 days) to kill all the plants in *E. bonariensis* than in *A. retroflexus* (24 h) or *A. fatua* (3 days), whereas in *P. oleracea*, this dose reached 50 efficacy, i.e., only 50% of plants were dead at the end of the experiment (30 days). Previous studies also confirmed the rapid activity of carvacrol in plants; in a greenhouse experiment, a nanoemulsion (NE) of *Satureja hortensis* L. EO, rich in carvacrol (55.6%), was applied against *A. retroflexus* and *C. album*, and after 30 min, the weeds were exhibiting injury symptoms, reaching the maximum lethality within 24 h of treatment application. The lethality percentage was dependent on the doses applied and the species against which NE was applied [21]. As observed with CA, also weed species showed different sensibility to CV application, especially at the lower dose, which took more time to control the weeds (Figures 4–7, Tables S1–S4): *A. retroflexus* was the more sensitive species, being controlled by all doses 24 h after application of treatment (Figure 4, Table S1), whereas in *A. fatua* and *E. bonariensis*, the lowest dose took 7 and 15 days, respectively, to reach 100 efficacy (Figures 5 and 6, Tables S2 and S3), being again *P. oleracea* the most resistant weed species, 7 days after treatment application, all plants were killed in all CV treatments, although then some regrew 15 and 30 days after treatments application (Figure 7, Table S4).

All the treatments managed to control the weed species tested, and the results of the treatments were statistically significant compared to CW (Table 5). The most effective treatment was the PA formulation at 10%, achieving 74.50 efficacy. This treatment did not show significant differences compared to the results obtained by the commercial product used as biological reference, also containing PA as active ingredient, which obtained an efficacy of 78.50. Moreover, there were no significant statistical differences in the efficacy between the three doses of the PA-based formulations (5%, 8%, and 10%). The next most effective treatment was the CA-based formulation, which exhibited the same efficacy values for the two higher doses applied (12% and 24%), while the lowest dose (6%) had significant less efficacy. This can be explained by the different sensitivity of the weed species to low doses of CA, as commented above. Finally, the treatments with carvacrol did not show significant differences in efficacy between doses, but with the control, and were also very effective, reaching an efficacy between 60.50 and 65.00 (Table 5).

All treatments tested with natural products showed higher efficacy for the control of weeds than GL, which showed efficacy values of 36. This was because of its slower activity. Mechanism of action of GL is by affecting the enzyme 5-enolpyruvlyshikimate-3-phosphate synthase (EPSPS), and it is the only herbicide with this mode of action. The inhibition of EPSPS reduces levels of amino acids needed for the synthesis of proteins, cell walls, and secondary plant products. In addition, the inhibition of EPSPS causes deregulation of the shikimic acid pathway, promoting the disruption of plant carbon metabolism [62]. GL is translocated in plants and differential responses of weed species may be caused by differences in herbicide translocation, i.e., weeds capable to translocate GL more efficiently are more severely damaged [63]. In field experiments conducted for 2 years, it was verified that GL controlled more effectively *A. retroflexus* than other species [64], which supports our results. Decreased herbicide translocation to the meristem causes reduced glyphosate efficacy [65]. The necessity of being translocated explains the slow effect of GL compared with the natural compounds, as ^{14}C translocation throughout the plant demonstrated that glyphosate took 3 days to reach and accumulate in the meristematic tips of the roots and shoots [66].”

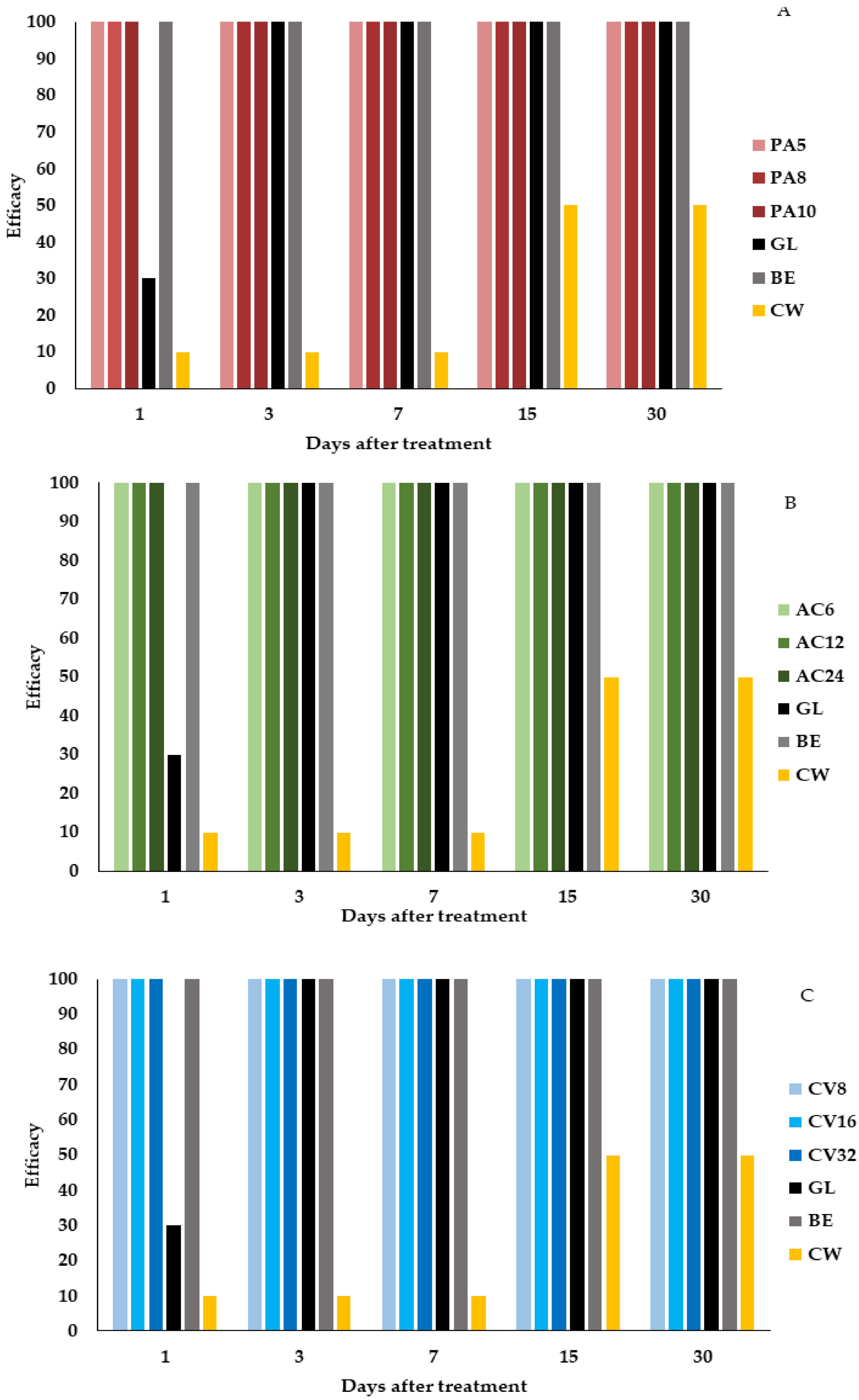
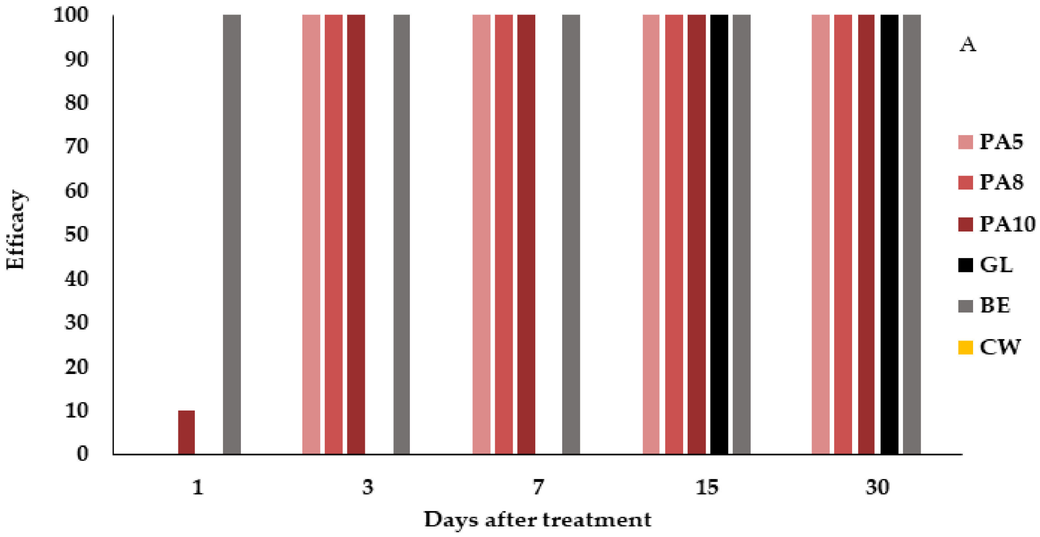
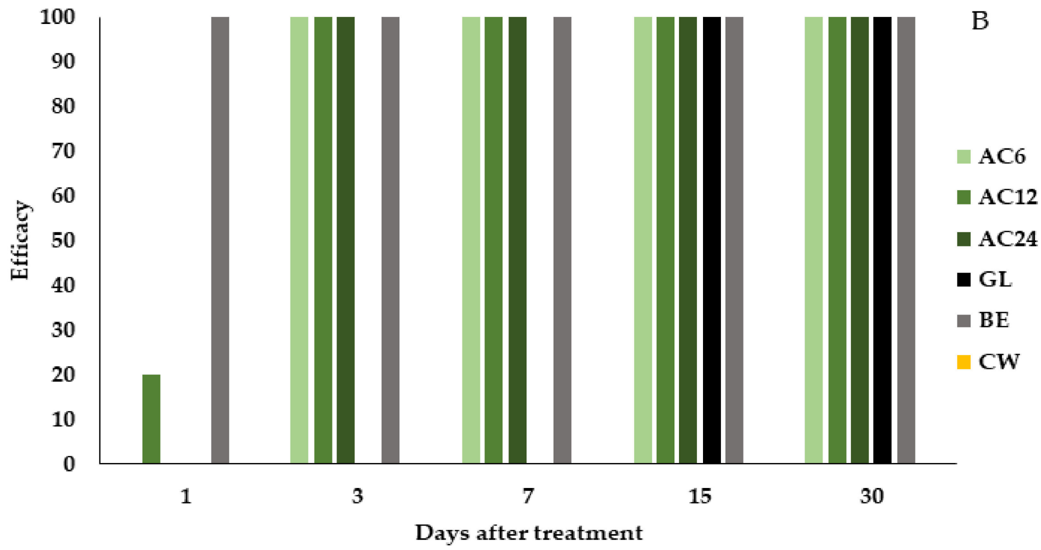


Figure 4. Evolution of efficacy of the tested treatments (**A**) pelargonic acid, (**B**) cinnamic aldehyde and (**C**) carvacrol in *A. retroflexus* during 30 days after application.





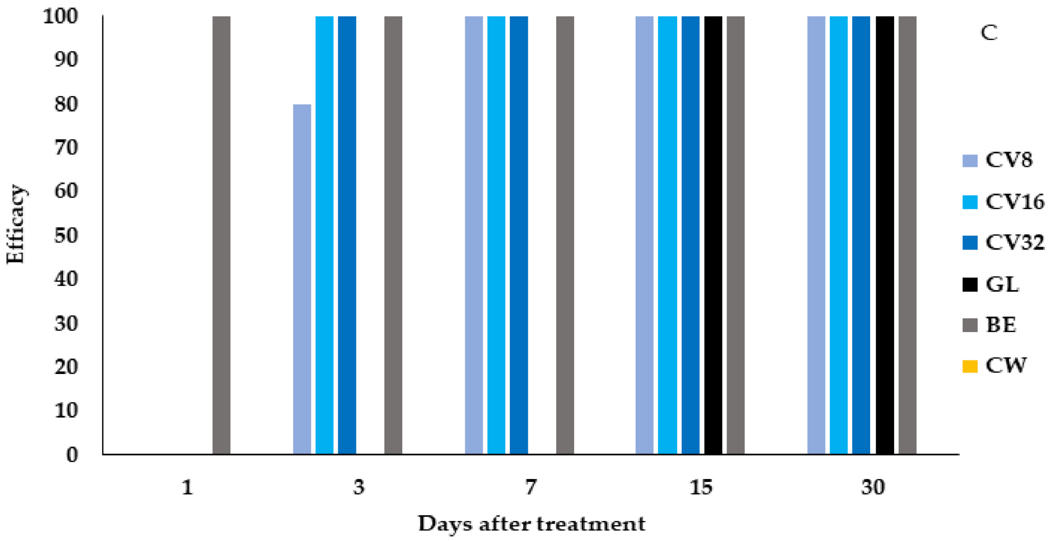


Figure 5. Evolution of efficacy of the tested treatments (**A**) pelargonic acid, (**B**) cinnamic aldehyde, and (**C**) carvacrol in *A. fatua* during 30 days after their application.

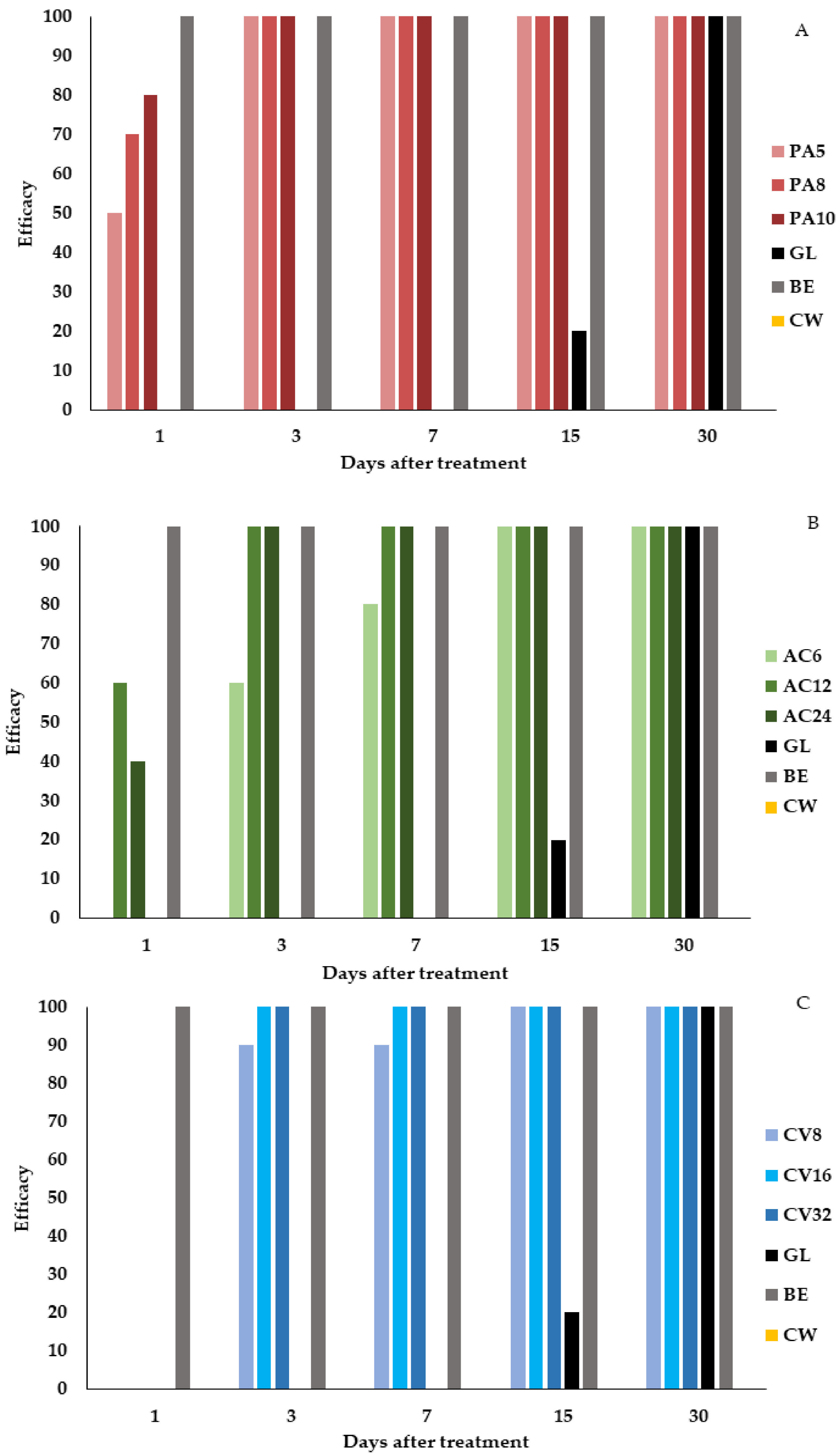


Figure 6. Evolution of efficacy of the tested treatments (**A**) pelargonic acid, (**B**) cinnamic aldehyde, and (**C**) carvacrol in *E. bonariensis* during 30 days after their application.

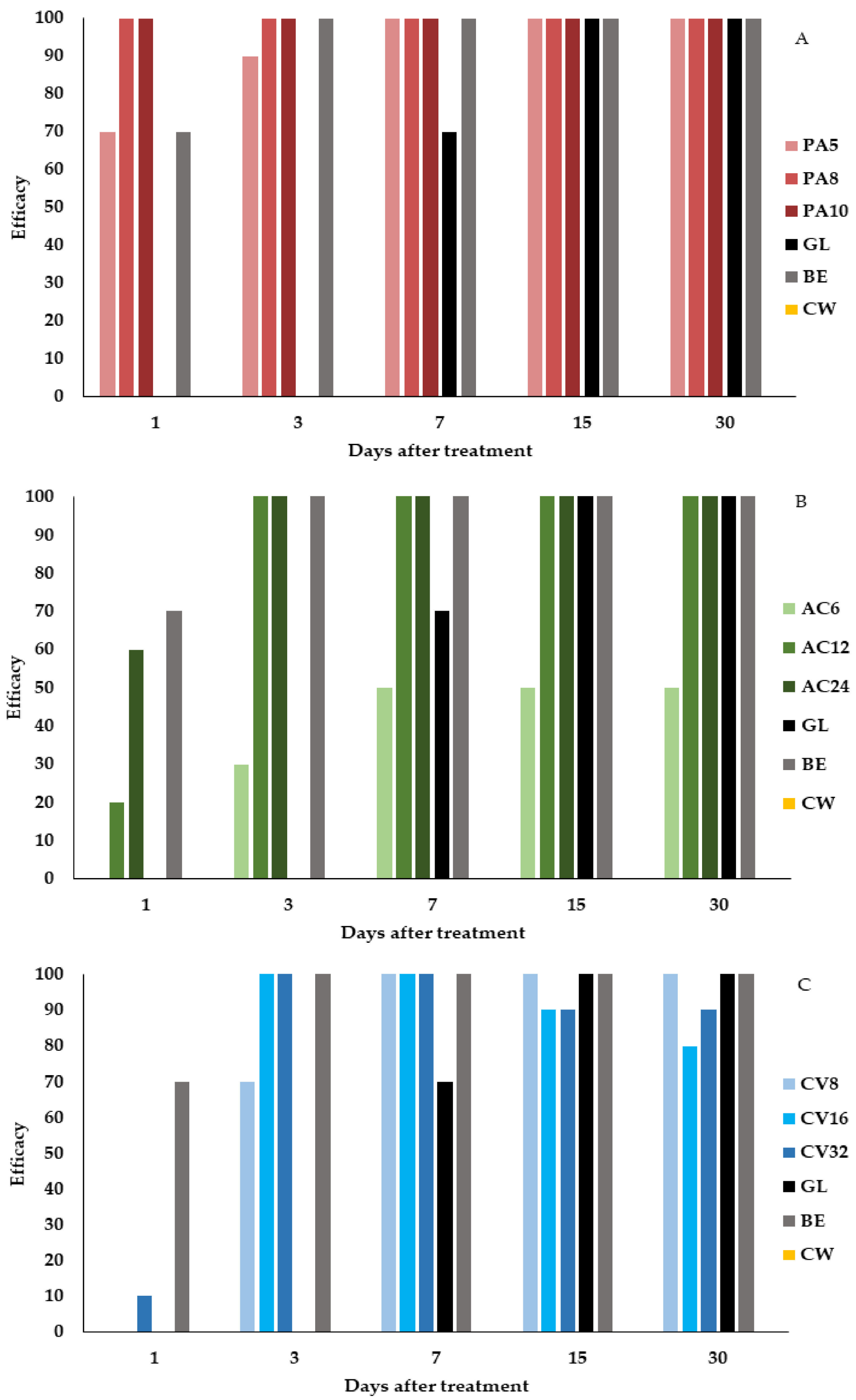


Figure 7. Evolution of efficacy of the tested treatments (**A**) pelargonic acid, (**B**) cinnamic aldehyde, and (**C**) carvacrol in *P. oleracea* during 30 days after their application.

3.1.1. Efficacy of Pelargonic Acid, Cinnamic Aldehyde, and Carvacrol on *A. retroflexus*

In the species *A. retroflexus* (Figure 4, Table S1) all the treatments tested obtained 100 efficacy (all treated plants were dead) one day after the application of the treatment, except for the chemical reference. The treatment with GL managed to control the species on the third day after its application. In this trial, there was a relevant percentage of mortality in the CW, especially at the end of the trial.

3.1.2. Efficacy of Pelargonic Acid, Cinnamic Aldehyde, and Carvacrol on *A. fatua*

All the tested treatments managed to control completely the species *A. fatua* from the third day after application (Figure 5, Table S2), except CV6, which achieved 100 efficacy after 7 days, and GL, which reached 100 efficacy 15 days after application. The treatments that showed phytotoxic effects more quickly were, starting from the first day after application, the bioherbicide reference (BE), AC12, and PA10.

3.1.3. Efficacy of Pelargonic Acid, Cinnamic Aldehyde, and Carvacrol on *E. bonariensis*

All treatments were able to control *E. bonariensis* (Figure 6, Table S3). The higher doses of the treatments performed with CA- and CV-based formulations achieved a total control of this species faster than their lower doses. It should be noted that despite this, all of them managed to control it completely 15 days after the application. The bioherbicide reference (BE) reached 100 efficacy 24 h after its application, instead GL took 30 days to reach 100 efficacy (death of all treated plants).

3.1.4. Efficacy of Pelargonic Acid, Cinnamic Aldehyde, and Carvacrol on *P. oleracea*

The most effective treatments to control *P. oleracea* were the three treatments carried out with the PA-based formulation (PA5, PA8, and PA10) (Figure 7, Table S4). A dose effect was observed in this species for the tested natural products, being higher doses more effective and showing phytotoxic effects faster than lower ones. The treatment AC6 reached 50 efficacy at the end of the experiment (30 days after application), while the higher doses of this compound (AC12 and AC24) killed all plants after 3 days of application. The treatments CV8, CV16, and CV32 decreased their efficacy from day 7, when some of the evaluated plants regrew. It should be noted that the treatment with the chemical reference, GL, exhibited a slower action than the rest of the treatments with natural products, showing phytotoxic effects on this species between 7 and 15 days after application.

When analyzing the effect of the interaction between species and time after treatments with respect to efficacy, the species that showed the highest sensitivity most rapidly was *A. retroflexus*. On the other hand, the species that took longer to show phytotoxic effects was *A. fatua*. However, at the end of the trials, all species showed high mortality rates, which were slightly higher in *A. retroflexus* and *A. fatua* than in *P. oleracea* and *E. bonariensis* (Figure 8).

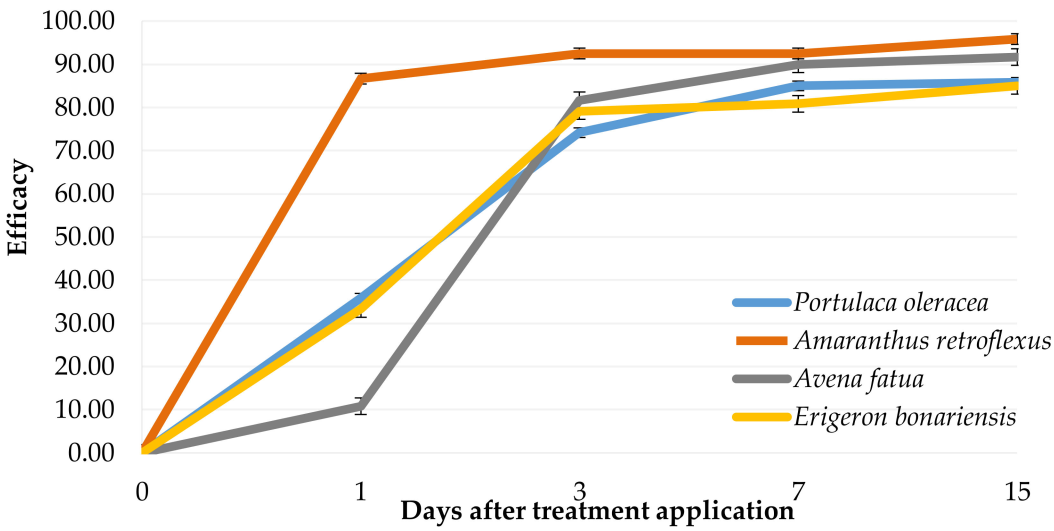


Figure 8. Effect of the interaction between treatment and days after treatment application in the efficacy per species.

3.2. Damage Level of Pelargonic Acid, Cinnamic Aldehyde, and Carvacrol against Target Weeds

A. retroflexus was the species which presented higher damage level, followed by *P. oleracea* and *A. fatua* (without significant differences between them), and finally *E. bonariensis* (Table 6). All species exhibited damage level near 2 or higher, which means severe damage (Table 4). It is important to consider the damage level caused by the treatments on the weed species in addition to their efficacy because it represents the state of the plants that were not killed. If the plants remaining alive were more damaged, it would mean that in field conditions, they would be less competitive with crops, causing less stress to them.

Table 6. Damage level depending on the species, time after application, and treatment.

Species	Level of Damage
Portulaca oleracea	1.98 ± 0.02 b
Amaranthus retroflexus	2.24 ± 0.02 a
Avena fatua	1.96 ± 0.02 bc
Erigeron bonariensis	1.92 ± 0.02 c
Time (Days after Application)	**Level of Damage**
0	0.00 ± 0.02 e
1	2.08 ± 0.02 d
3	2.59 ± 0.02 c
7	2.68 ± 0.02 b
15	2.78 ± 0.02 a
Treatment	**Damage level**
Control treated with water	0.16 ± 0.04 g
Pelargonic acid 5%	2.31 ± 0.04 abc
Pelargonic acid 8%	2.34 ± 0.04 ab
Pelargonic acid 10%	2.35 ± 0.04 ab
Cinnamic aldehyde 6%	2.13 ± 0.04 e
Cinnamic aldehyde 12%	2.30 ± 0.04 abc
Cinnamic aldehyde 24%	2.30 ± 0.04 abc
Carvacrol 8%	2.18 ± 0.04 de
Carvacrol 16%	2.23 ± 0.04 cd
Carvacrol 32%	2.25 ± 0.04 bcd
Bioherbicide reference: pelargonic acid (Beloukha 8%)	2.39 ± 0.04 a
Chemical reference: glyphosate (Roundup Ultra Plus 10%)	1.40 ± 0.03 f

Values are mean of damage level ± standard error (ten replicates). Different letters in the same column indicate significant differences ($p \leq 0.05$).

Throughout time, more severe levels of damage were reached as more days after treatment applications passed, with significant differences in the damage level assessment between different days after the applications (Table 6). All the treatments tested successfully controlled the weed species inducing a high level of damage compared with CW. The treatments that showed the strongest phytotoxicity on weeds were PA10 and BE, with no significant differences between them. PA10 showed no significant differences with the other two doses of PA-based formulations tested (PA5 and PA8), neither with the two highest doses of CA based formulations tested (CA12 and CA24) nor with the highest doses of CV tested (CV32) (Table 6).

The damage level increased in all species with time after treatments (Figure 9). *A. retroflexus* was confirmed as the most susceptible species to the treatments, as it showed a higher level of damage than the other species 24 h after the treatments were administrated. No differences between species were observed 15 days after treatment, as all showed similar levels of damage.

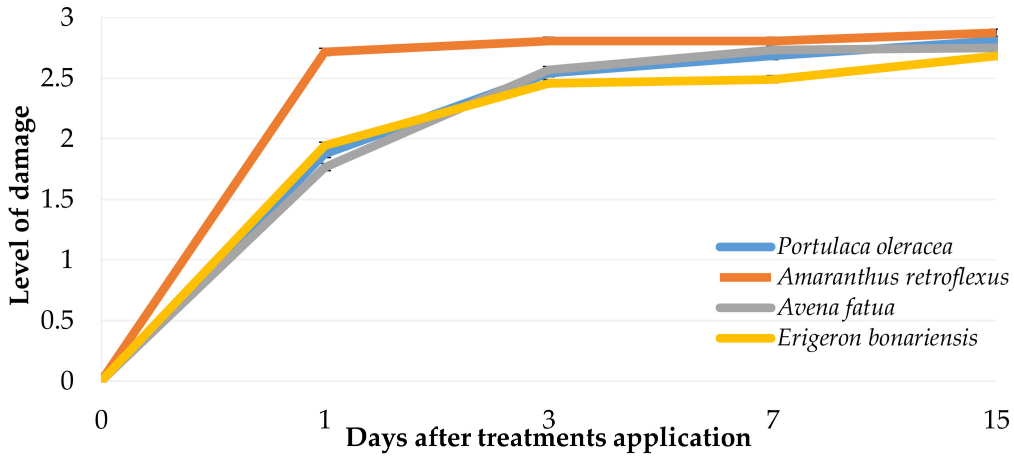


Figure 9. Effect of treatment and time after treatment interaction on damage level.

The effects induced by the different treatments on *E. bonariensis* 24 h after their administration are presented in Figure 10. This species is shown because of its intermediate response to all treatments as compared with *A. retroflexus* that was more sensitive or *P. oleracea*, which was more resistant and because phytotoxic effects can be better visualized in it than in *A. fatua*. The intermediate concentration tested for PA, CV, and CA is shown to be representative of the effects of the other concentrations tested. All the natural compounds tested caused more severe plant damage than the synthetic herbicide GL 1 day after treatment. The effects of 8% PA were very similar to those induced by the positive bioherbicide control Beloukha (also containing PA as active compound). Probably due to the effect of PA, the cuticles exhibited alteration on membrane permeability and peroxidation of thylakoid membranes [67] and leaves appeared desiccated, with reduced photosynthetic pigments but without punctual damages on the leaves, which resulted in a stoppage of growth and development of the whole plant. In contrast, CV-treated leaves showed signs of dehydration, resulting in curling and punctual damages on the leaves with increased necrotic spots related to application spots, which could be due to the disruption of cell membranes [68]. Finally, CA treatment resulted in growth reduction and loss of photosynthetic pigments, which could be related to oxidative damage induced by this compound. This oxidative damage has to be further investigated as no mode of action of CA has been reported in the literature up to now.

Bioherbicides are new products on the international markets and consequently, the processes for obtaining natural raw materials are not yet very efficient or the final cost of its extraction is elevated compared to synthetics. This fact affects the final cost of these formulated products, making them more expensive in some cases than conventional herbicides for farmers. Nevertheless, it is important to evaluate the cost–benefit factor of bioherbicides, including sustainability, reduction of soil and water contamination, or the absence of residues on crops. In line with legal framework, policies, and global sustainability objectives, the higher price of bioherbicides justifies the benefits that can be achieved with their implementation [69]. On the other hand, the rapid action, broad spectrum, and eco-friendly profile make bioherbicides molecules more attractive to the pesticide market, which is increasingly concerned with the sustainability of treatments applied in agriculture. Herbicide market is expected to reach a value of $37.99 billion by 2025 [38]. Improving the efficiency of raw material extraction, decreasing the applied doses per hectare using improved formulations, as well as combining active substances in search of synergies may be the future of new sustainable herbicides.

The natural products tested, PA, CV, and CA, performed strong herbicidal activity in all the treated weeds, causing high lethality and damage levels; hence, they demonstrated that they could be good candidates for bioherbicides formulations. Further investigations should focus on determining the dose–response of different weed species to these compounds in order to find the optimal doses, which is very important in the context of integrated weed management and sustainable agriculture.

Another key point is to find out the optimum phenological stage in which the products should be applied to weeds and crops, to achieve the maximum phytotoxic effect on weeds minimizing their phytotoxic effects and consequent stress on crops. A better understanding of their mode of action could lead to a more efficient administration. Finally, different combinations between these natural products could be a powerful tool for weed management. Their synergies and antagonisms must be also considered and studied.

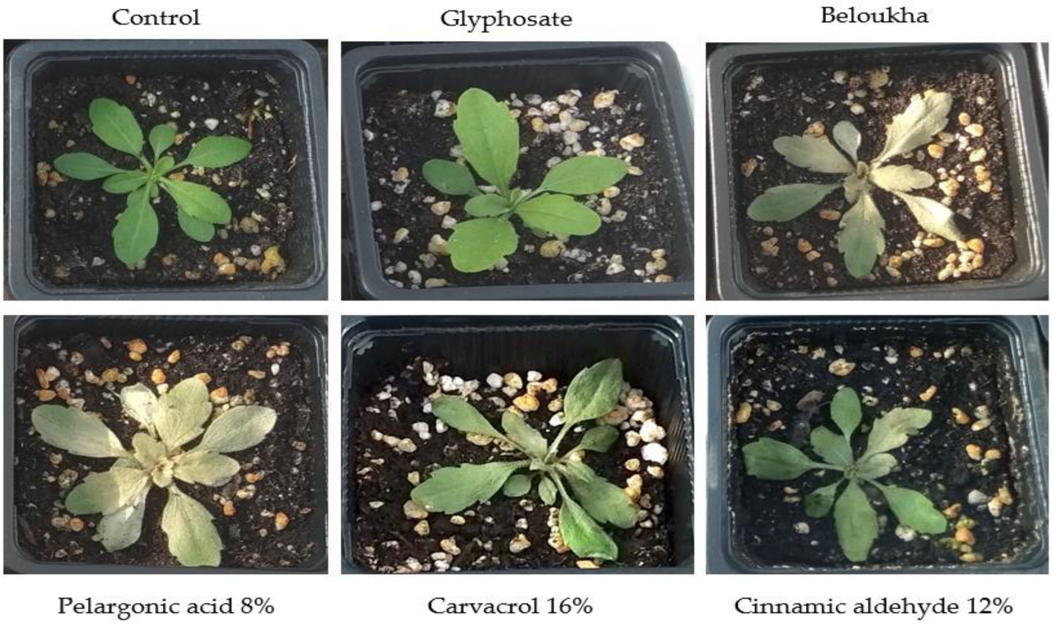


Figure 10. Images of *Erigeron bonariensis* plants 24 h after treatment applications.

4. Conclusions

The natural products PA, CV, and CA showed great herbicidal activity against the weeds *A. retroflexus*, *A. fatua*, *E. bonariensis*, and *P. oleracea* and could be good candidates for bioherbicides formulations. *A. retroflexus* was the most sensitive weed to all the applied treatments. For CV and CA, the higher doses applied exhibited greater and quicker phytotoxic effects than the lowest, with different responses in the weed species, while there were no significant differences in the herbicidal activity between the tested doses of PA. This study demonstrates that natural products could be sustainable as well as effective alternatives to synthetic herbicides, and they contribute to integrated weed management.

Supplementary Materials: The following are available online at http://www.mdpi.com/2073-4395/10/6/791/s1, Table S1. Efficacy of the tested treatments on *A. retroflexus* after 1, 3, 7, 15 and 30 days of application. Table S2. Efficacy of the tested treatments on *A. fatua* after 1, 3, 7, 15 and 30 days of application. Table S3. Efficacy of the tested treatments on *E. bonariensis* after 1, 3, 7, 15 and 30 days of application. Table S4. Efficacy of the tested treatments on *P. oleracea* after 1, 3, 7, 15 and 30 days of application.

Author Contributions: Conceptualization, M.V., M.M., and A.M.S.-M.; methodology M.V., M.M., N.T.-P., and R.G.; formal analysis, M.V., M.M., and N.T.-P.; investigation, M.V., M.M., A.M.S.-M., R.P., N.T.-P., and R.G.; resources, M.V., M.M., and R.G.; data curation, N.T., M.M., R.G. and R.P.; writing—original draft preparation, M.V., M.M., and N.T.-P.; writing—review and editing, M.V., A.M.S.-M., and R.P.; visualization, M.V., M.M., N.T.-P., A.M.S.-M., R.P., and R.G.; supervision, M.V., M.M., and A.M.S.-M.; project administration, M.V.; and funding acquisition, M.V. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by SEIPASA.

Acknowledgments: Thanks to Vicente Estornell Campos and the Library staff from Polytechnic University of Valencia that assisted us to get some helpful references.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Vos, R.; Bellù, L.G. Global trends and challenges to food and agriculture into the 21st century. In *Sustainable Food and Agriculture: An Integrated Approach*; Campanhola, C., Pandey, S., Eds.; Academic Press: London, UK, 2019; pp. 11–30. [CrossRef]
2. Oerke, E.C. Crop losses to pests. *J. Agric. Sci.* **2006**, *144*, 31–43. [CrossRef]
3. Vats, S. Herbicides: History, classification and genetic manipulation of plants for herbicide resistance. In *Sustainable Agriculture Reviews*; Lichtfouse, E., Ed.; Springer: Cham, Switzerland, 2015; Volume 15. [CrossRef]
4. Heap, I.M. Global perspective of herbicide-resistant weeds. *Pest Manag. Sci.* **2014**, *70*, 1306–1315. [CrossRef] [PubMed]
5. Bagavathiannan, M.; Singh, V.; Govindasamy, P.; Abugho, S.B.; Liu, R. Impact of concurrent weed or herbicide stress with other biotic and abiotic stressors on crop production. In *Plant Tolerance to Individual and Concurrent Stresses*; Senthil-Kumar, M., Ed.; Springer: New Delhi, India, 2017; pp. 33–45. [CrossRef]
6. Abbas, T.; Zahir, Z.A.; Naveed, M.; Kremer, R.J. Limitations of existing weed control practices necessitate development of alternative techniques based on biological approaches. In *Advances in Agronomy*; Sparks, D.L., Ed.; Academic Press: Cambridge, MA, USA, 2018; Volume 147, pp. 239–280. [CrossRef]
7. World Health Organization; Food and Agriculture Organization of the United Nations. The International Code of Conduct on Pesticide Management. Rome. 2014. Available online: http://www.fao.org/agriculture/crops/thematic-sitemap/theme/pests/code/en/ (accessed on 22 April 2020).
8. Villa, F.; Cappitelli, F.; Cortesi, P.; Kunova, A. Fungal biofilms: Targets for the development of novel strategies in plant disease management. *Front. Microbiol.* **2017**, *8*, 654–664. [CrossRef] [PubMed]
9. De Mastro, G.; Fracchiolla, M.; Verdini, L.; Montemurro, P. Oregano and its potential use as bioherbicide. *Acta Hortic.* **2006**, *723*, 335–346. [CrossRef]
10. Seiber, J.N.; Coats, J.; Duke, S.O.; Gross, A.D. Biopesticides: State of the art and future opportunities. *J. Agric. Food Chem.* **2014**, *62*, 11613–11619. [CrossRef] [PubMed]
11. Bailey, K.L. The bioherbicide approach to weed control using plant pathogens. In *Integrated Pest Management*; Abrol, D.P., Ed.; Academic Press, Elsevier: San Diego, CA, USA, 2014; pp. 245–266.
12. Dahiya, A.; Sharma, R.; Sindhu, S.; Sindhu, S.S. Resource partitioning in the rhizosphere by inoculated *Bacilluss* pp. towards growth stimulation of wheat and suppression of wild oat (*Avena fatua* L.) weed. *Physiol. Mol. Biol. Plants* **2019**, *25*, 1483–1495. [CrossRef]
13. Heap, I. The International Herbicide-Resistant Weed Database. Available online: www.weedscience.org (accessed on 25 April 2020).
14. Hazrati, H.; Saharkhiz, M.J.; Moein, M.; Khoshghalb, H. Phytotoxic effects of several essential oils on two weed species and tomato. *Biocatal. Agric. Biotechnol.* **2018**, *13*, 204–212. [CrossRef]
15. Bajwa, A.A.; Sadia, S.; Ali, H.H.; Jabran, K.; Peerzada, A.M.; Chauhan, B.B. Biology and management of two important Conyza weeds: A global review. *Environ. Sci. Pollut. Res.* **2016**, *23*, 24694–24710. [CrossRef]
16. Graziani, F.; Onofri, A.; Pannacci, E.; Tei, F.; Guiducci, M. Size and composition of weed seedbank in long-term organic and conventional low-input cropping systems. *Eur. J. Agron.* **2012**, *39*, 52–56. [CrossRef]
17. Benbrook, C.M. Trends in glyphosate herbicide use in the United States and globally. *Environ. Sci. Eur.* **2016**, *28*, 3–18. [CrossRef]
18. Önen, H.; Özer, Z.; Telci, I. Bioherbicidal effects of some plant essential oils on different weed species. *J. Plant Dis. Prot.* **2002**, *18*, 597–605.
19. Salamci, E.; Kordali, S.; Kotan, R.; Cakir, A.; Kaya, Y. Chemical compositions, antimicrobial and herbicidal effects of essential oils isolated from Turkish *Tanacetum aucheranum* and *Tanacetum chiliophyllum* var. *chiliophyllum*. *Biochem. Syst. Ecol.* **2007**, *35*, 569–581. [CrossRef]
20. Mutlu, S.; Atici, Ö.; Esim, N. Bioherbicidal effects of essential oils of *nepeta meyeri* benth. On weed spp. *Allelopath. J.* **2010**, *26*, 291–300.
21. Synowiec, A.; Kalemba, D.; Drozdek, E.; Bocianowski, J. Phytotoxic potential of essential oils from temperate climate plants against the germination of selected weeds and crops. *J. Pest Sci.* **2017**, *90*, 407–419. [CrossRef]
22. Hazrati, H.; Saharkhiz, M.J.; Niakousari, M.; Moein, M. Natural herbicide activity of *Satureja hortensis* L. essential oil nanoemulsion on the seed germination and morphophysiological features of two important weed species. *Ecotoxicol. Environ. Saf.* **2017**. [CrossRef]

23. Verdeguer, M.; Blazquez, M.A.; Boira, H. Phytotoxic effects of *Lantana camara*, Eucalyptus camaldulensis and *Eriocephalus africanus* essential oils in weeds of Mediterranean summer crops. *Biochem. Syst. Ecol.* **2009**, *37*, 362–369. [CrossRef]
24. Benarab, H.; Fenni, M.; Louadj, Y.; Boukhabti, H.; Ramdani, M. Allelopathic activity of essential oil extracts from *Artemisia herba-alba* Asso. on seed and seedling germination of weed and wheat crops. *Acta Sci. Nat.* **2020**, *7*, 86–97. [CrossRef]
25. Benchaa, S.; Hazzit, M.; Abdelkrim, H. Allelopathic Effect of *Eucalyptus citriodora* essential oil and its potential use as bioherbicide. *Chem. Biodivers.* **2018**, *15*, e1800202. [CrossRef]
26. Verdeguer, M.; Castañeda, L.G.; Torres-Pagan, N.; Llorens-Molina, J.A.; Carrubba, A. Control of Erigeron bonariensis with *Thymbra capitata*, *Mentha piperita*, *Eucalyptus camaldulensis*, and *Santolina chamaecyparissus* essential oils. *Molecules* **2020**, *25*, 562. [CrossRef]
27. Scavo, A.; Pandino, G.; Restuccia, A.; Mauromicale, G. Leaf extracts of cultivated cardoon as potential bioherbicide. *Sci. Hortic.* **2020**, 109024. [CrossRef]
28. Ma, S.; Fu, L.; He, S.; Lu, X.; Wu, Y.; Ma, Z.; Zhang, X. Potent herbicidal activity of *Sapindus mukorossi* Gaertn. against *Avena fatua* L. and *Amaranthus retroflexus* L. *Ind. Crops Prod.* **2018**, *122*, 1–6. [CrossRef]
29. Pacanoski, Z.; Mehmeti, A. Allelopathic effect of Siberian iris (*Iris sibirica*) on the early growth of wild oat (*Avena fatua*) and Canada thistle (*Cirsium arvense*). *J. Cent. Eur. Agric.* **2019**, *20*, 1179–1187. [CrossRef]
30. Bainard, L.D.; Isman, M.B.; Upadhyaya, M.K. Phytotoxicity of clove oil and its primary constituent eugenol and the role of leaf epicuticular wax in the susceptibility to these essential oils. *Weed Sci.* **2006**, *54*, 833–837. [CrossRef]
31. Ahuja, N.; Singh, H.P.; Batish, D.R.; Kohli, R.K. Eugenol-inhibited root growth in *Avena fatua* involves ROS-mediated oxidative damage. *Pestic. Biochem. Phys.* **2015**, *118*, 64–70. [CrossRef]
32. Vaughn, S.F.; Spencer, G.F. Volatile Monoterpenes as Potential Parent Structures for New Herbicides[1]. *Weed Sci.* **1993**, *41*, 114–119. [CrossRef]
33. Chaimovitsh, D.; Shachter, A.; Abu-Abied, M.; Rubin, B.; Sadot, E.; Dudai, N. Herbicidal Activity of Monoterpenes is associated with disruption of microtubule functionality and membrane integrity. *Weed Sci.* **2017**, *65*, 19–30. [CrossRef]
34. Amri, I.; Lamia, H.; Mohsen, H.; Bassem, J. Review on the phytotoxic effects of essential oils and their individual components: News approach for weed management. *Int. J. Appl. Biol. Pharm. Technol.* **2013**, *4*, 96–114.
35. Verdeguer, M.; García-Rellán, D.; Boira, H.; Pérez, E.; Gandolfo, S.; Blázquez, M.A. Herbicidal activity of Peumus boldus and Drimys winterii essential oils from Chile. *Molecules* **2011**, *16*, 403–411. [CrossRef]
36. Saad, M.M.G.; Abdelgaleil, S.A.M.; Suganuma, T. Herbicidal potential of pseudoguaninolide sesquiterpenes on wild oat, *Avena fatua* L. *Biochem. Syst. Ecol.* **2012**, *44*, 333–337. [CrossRef]
37. Araniti, F.; Sánchez-Moreiras, A.M.; Graña, E.; Reigosa, M.J.; Abenavoli, M.R. Terpenoid trans-caryophyllene inhibits weed germination and induces plant water status alteration and oxidative damage in adult Arabidopsis. *Plant Biol. (Stuttg)* **2017**, *19*, 79–89. [CrossRef]
38. Ciriminna, R.; Fidalgo, A.; Ilharco, L.M.; Pagliaro, M. Herbicides based on pelargonic acid: Herbicides of the bioeconomy. *Biofuels Bioprod. Biorefining* **2019**, *13*, 1476–1482. [CrossRef]
39. Coleman, R.; Penner, D. Organic acid enhancement of pelargonic acid. *Weed Technol.* **2008**, *22*, 38–41. [CrossRef]
40. Crmaric, I.; Keller, M.; Krauss, J.; Delabays, N. Efficacy of natural fatty acid based herbicides on mixed weed stands. *Jul. Kühn Arch.* **2018**, *458*, 327–332. [CrossRef]
41. Dayan, F.E.; Duke, S.O. Natural compounds as next-generation herbicides. *Plant Physiol.* **2014**, *166*, 1090–1105. [CrossRef]
42. Croteau, R.; Kutchan, T.M.; Lewis, N.G. Natural products (secondary metabolites). In *Biochemistry & Molecular Biology of Plants*, 2nd ed.; Buchanan, B.B., Gruissem, W., Jones, R.L., Eds.; Wiley: Rockville, MD, USA, 2000; pp. 1250–1318.
43. Lebecque, S.; Lins, L.; Dayan, F.E.; Fauconnier, M.L.; Deleu, M. Interactions between natural herbicides and lipid bilayers mimicking the plant plasma membrane. *Front. Plant Sci.* **2019**, *10*, 329–340. [CrossRef]
44. Cordeau, S.; Triolet, M.; Wayman, S.; Steinberg, C.; Guillemin, J.P. Bioherbicides: Dead in the water? A review of the existing products for integrated weed management. *Crop Prot.* **2016**, *87*, 44–49. [CrossRef]

45. Gruenwald, J.; Freder, J.; Armbruester, N. Cinnamon and health. *Crit. Rev. Food Sci. Nutr.* **2010**, *50*, 822–834. [CrossRef]
46. Ranasinghe, P.; Pigera, S.; Premakumara, G.S.; Galappaththy, P.; Constantine, G.R.; Katulanda, P. Medicinal properties of "true" cinnamon (*Cinnamomum zeylanicum*): A systematic review. *BMC Complement. Altern. Med.* **2013**, *13*, 275. [CrossRef]
47. Doyle, A.A.; Krämer, T.; Kavanagh, K.; Stephens, J.C. Cinnamaldehydes: Synthesis, antibacterial evaluation, and the effect of molecular structure on antibacterial activity. *Results Chem.* **2019**, *1*, 100013–100018. [CrossRef]
48. Chericoni, S.; Prieto, J.M.; Iacopini, P.; Cioni, P.; Morelli, I. In vitro activity of the essential oil of *Cinnamomum zeylanicum* and eugenol in peroxynitrite-induced oxidative processes. *J. Agric. Food Chem.* **2005**, *53*, 4762–4765. [CrossRef]
49. Viazis, S.; Akhtar, M.; Feirtag, J.; Diez-Gonzalez, F. Reduction of Escherichia coli O157:H7 viability on leafy green vegetables by treatment with a bacteriophage mixture and trans-cinnamaldehyde. *Food Microbiol.* **2011**, *28*, 149–157. [CrossRef]
50. Kwon, J.A.; Yu, C.B.; Park, H.D. Bacteriocidal effects and inhibition of cell separation of cinnamic aldehyde on *Bacillus cereus*. *Lett. Appl. Microbiol.* **2003**, *37*, 61–65. [CrossRef]
51. Friedman, M. Chemistry, antimicrobial mechanisms, and antibiotic activities of cinnamaldehyde against pathogenic bacteria in animal feeds and human foods. *J. Agric. Food. Chem.* **2017**, *65*, 10406–10423. [CrossRef]
52. Kim, H.K.; Kim, J.R.; Ahn, Y.J. Acaricidal activity of cinnamaldehyde and its congeners against *Tyrophagus putrescentiae* (Acari: Acaridae). *J. Stored Prod. Res.* **2004**, *40*, 55–63. [CrossRef]
53. Saad, M.M.G.; Gouda, N.A.A.; Abdelgaleil, S.A.M. Bioherbicidal activity of terpenes and phenylpropenes against *Echinochloa crus-galli*. *J. Environ. Sci. Health B* **2019**, *54*, 954–963. [CrossRef]
54. Roselló, J.; Sempere, F.; Sanz-Berzosa, I.; Chiralt, A.; Santamarina, M.P. Antifungal activity and potential use of essential oils against *Fusarium culmorum* and *Fusarium verticillioides*. *J. Essent. Oil Bear Plants* **2015**, *18*, 359–367. [CrossRef]
55. Santamarina, M.; Ibáñez, M.; Marqués, M.; Roselló, J.; Giménez, S.; Blázquez, M. Bioactivity of essential oils in phytopathogenic and post-harvest fungi control. *Nat. Prod. Res.* **2017**, *31*, 2675–2679. [CrossRef]
56. Krepker, M.; Shemesh, R.; Danin Poleg, Y.; Kashi, Y.; Vaxman, A.; Segal, E. Active food packaging films with synergistic antimicrobial activity. *Food Control* **2017**, *76*, 117–126. [CrossRef]
57. Ye, H.; Shen, S.; Xu, J.; Lin, S.; Yuan, Y.; Jones, G.S. Synergistic interactions of cinnamaldehyde in combination with carvacrol against food-borne bacteria. *Food Control* **2013**, *34*, 619–623. [CrossRef]
58. De Sousa, J.P.; de Azerêdo, G.A.; de Araújo Torres, R.; da Silva Vasconcelos, M.A.; da Conceição, M.L.; de Souza, E.L. Synergies of carvacrol and 1,8-cineole to inhibit bacteria associated with minimally processed vegetables. *Int. J. Food Microbiol.* **2012**, *154*, 145–151. [CrossRef]
59. Oddo, M. Effects of Different weed Control Practices on Soil Quality in Mediterranean Crops. Ph.D. Thesis, Universita' degli Studi di Palermo, Palermo, Italy, Polytechnic University of Valencia, Valencia, Spain, 2 October 2017.
60. Wu, H.; Walker, S.; Rollin, M.J.; Tan, D.K.Y.; Robinson, G.; Werth, J. Germination, persistence, and emergence of flaxleaf fleabane (*Conyza bonariensis* [L.] Cronquist). *Weed Biol. Manag.* **2007**, *7*, 192–199. [CrossRef]
61. Webber, C.L.; Shrefler, J.W. Pelargonic acid weed control parameters. *HortScience* **2006**, *41*, 1034. [CrossRef]
62. Velini, E.D.; Duke, S.O.; Trindade, M.B.; Meschede, D.K.; Carbonari, C.A. Modo de acao do Glyphosate (Mode of Action of Glyphosate in Portuguese). In *Glyphosate*; Velini, E.D., Meschede, D.K., Carbonari, C.A., Trindade, M.L.B., Eds.; Fundaçã de Estudos e Pesquisas Agricoloas e Florestais: Botucato-SP, Brazil, 2009; pp. 113–133.
63. Hoss, N.; Al-Khatib, K.; Peterson, D.; Loughin, T. Efficacy of glyphosate, glufosinate, and imazethapyr on selected weed species. *Weed Sci.* **2003**, *51*, 110–117. [CrossRef]
64. Jordan, D.; York, A.; Griffin, J.; Clay, P.; Vidrine, P.; Reynolds, D. Influence of Application Variables on Efficacy of Glyphosate. *Weed Technol.* **1997**, *11*, 354–362. [CrossRef]
65. Mithila, J.; Swanton, C.J.; Blackshaw, R.E.; Cathcart, R.J.; Hall, J.C. Physiological basis for reduced glyphosate efficacy on weeds grown under low soil nitrogen. *Weed Sci.* **2008**, *56*, 12–17. [CrossRef]
66. Sandberg, C.L.; Meggitt, W.F.; Penner, D. Absorption, translocation and metabolism of ^{14}C-glyphosate in several weed species. *Weed Res.* **1980**, *20*, 195–200. [CrossRef]
67. Lederer, B.; Fujimori, T.; Tsujino, Y.; Wakabayashi, K.; Bögera, P. Phytotoxic activity of middle-chain fatty acids II: Peroxidation and membrane effects. *Pestic. Biochem. Physiol.* **2004**, *80*, 151–156. [CrossRef]

68. Albuquerque, C.C.; Camara, T.R.; Sant'ana, A.E.G.; Ulisses, C.; Willadino, L.; Marcelino Júnior, C. Effects of the essential oil of *Lippia gracilis* Schauer on caulinary shoots of heliconia cultivated in vitro. *Rev. Bras. Plantas Med.* **2012**, *14*, 26–33. [CrossRef]
69. Hasanuzzaman, M.; Mohsin, S.M.; Borhannuddin Bhuyan, M.H.M.; Farha Bhuiyan, T.; Anee, T.I.; Awal, A.; Masud, C.; Nahar, K. Phytotoxicity, environmental and health hazards of herbicides: Challenges and ways forward. In *Agrochemicals Detection, Treatment and Remediation. Pesticides and Chemical Fertilizers*; Vara Prasad, M.N., Ed.; Butterworth Heinemann: Hyderabad, India, 2020; pp. 55–99. [CrossRef]