Research Article

Capped polyethylene glycol esters of fatty acids as novel active principles for weed control

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Abstract

BACKGROUND: Ever since the beginning of agriculture, yields have been threatened by weeds. Chemical weed control is far more effective and economical than other methods. The frequent use of herbicides has led to environmental and human health concerns, resulting in the banning of several herbicides and challenges for the future of important active compounds such as glyphosate.

RESULTS: The herbicidal activity of sustainable alternatives based on certain esters of fatty acids (FA), the action of which is unrelated to the free acid, on common weeds is assessed and reported. The 13 derivatives of FA showed better physicochemical properties than pelargonic acid-based herbicides. All the reported compounds have phytotoxic activity, the highest efficacy being displayed by the methyl end-capped polyethylene glycol (mPEG) ester of pelargonic acid having 6EO (ethylene oxide). This mPEG ester showed equal or better phytotoxicity than the pelargonic acid benchmark at reduced application rate and spray volume. The active compound is a liquid at ambient temperatures, has no bad smell and is not volatile, in contrast to pelargonic acid. Notably, this active compound can be the final product, can be sprayed without adjuvants and is relatively easy to co-formulate.

CONCLUSION: A new lead substance is presented that is a sustainable alternative to current contact herbicides. In particular, it has potential application on railways, in precision agriculture and as a harvest aid. Its good performance and technical properties suggest this mPEG ester group may also overcome the volatility-related problems of other organic acids such as auxins.
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Keywords: Pelargonic acid; fatty acid derivatives; natural herbicides; non-toxic herbicide; novel herbicide; contact herbicide

1 INTRODUCTION

Weeds are responsible for up to 40% yield loss globally and are the most harmful biological threat to agricultural production.[1] In 1977, Holm *et al.* reported more than 200 plant species that are major weeds.[2] Kraehmer and Baur described 32 of the most frequent terrestrial weeds, among them several grasses such as *Digitaria sanguinalis* L. Scop. (large crabgrass).[3] Inappropriate use of herbicides and changes in agricultural practices have led to modifications in weed flora, increasing the number of problematic weeds.[3] For example, *Solanum nigrum* L. (black nightshade) has become more difficult to control due to the development of herbicide-resistant biotypes (Harrington KC; https://resistance.nzpps.org). Weed control is of major importance in agricultural production and is a significant cost. To date, weeds have been managed mainly using synthetic herbicides rather that other methods such as cultural, biological or mechanical removal.[4] However, the use of herbicides has raised many concerns because of related problems such as weed resistance,[4,5] the lack of novel chemistry for weed control in dicot crops,[6] poor agricultural practices,[7,8] environmental impacts,[9] food residues[10] and regulatory concerns.[6]

In 2009, the European Union adopted Directive 2009/128/EC on the sustainable use of pesticides, which obligated professional users to implement the principles of integrated pest management by 2014.[11] Industry and research institutions have intensified their search for solutions that minimize the shortcomings of existing conventional herbicides.[12,13] In recent years, efforts have included research into natural products with herbicidal effects, such as plant extracts or secondary metabolites from plants or microorganisms.[12]

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Some new active compounds have been used directly in weed control or as leads for new herbicides, being degradable, non-toxic and produced by or aligned with nature.[12,13] Many substances derived from natural products like triketones or essentials oils have proven herbicidal potential although only a few have been commercialized.[13,14] Especially needed are fast-acting and resistance-breaking contact herbicides, particularly since the loss of previous products such as paraquat.

Currently, some of the most popular products for sustainable weed control are fatty acids (FA) with a carboxylic chain length of between eight and ten carbons, for example pelargonic (nonanoic) acid (PA) or a mixture of caprylic and capric acids.[12,15–17] For many years, the rancid odour of short-chain FA has restricted its use in gardens, industry or crop production greenhouses, despite its popularity as a natural herbicide.[15,18] Currently, PA is the main proposed alternative for natural weed control in agriculture, being the most studied FA herbicide.[15–18] Notwithstanding its lack of toxicity,[19] environmental advantages[18] and fast and good efficacy,[20] there are some features limiting the use and combination of FA-based compounds in agriculture. For example at Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL; https://www.bvl.bund.de), some PA herbicides need to be sprayed at very high rates in a large volume of water, which is not viable economically[16]; the newest PA formulation is applied at a lower spray volume, but gives a weaker weed control.[16,17] In addition, the rapid symptoms caused by PA are not favourable for co-formulation or tank mixing with other systemic compounds.[21,22] Also, FAs are not soluble in water, and the demands of the formulation are considerable and not trivial. There is also a loss of weed control efficacy due to non-stable and heterogenous spray preparations (oil droplet formation followed by phase separation). The literature describes basic formulation concepts for FA,[23–25] but all of these formulations have one or more issues, such as the need to handle concentrated alkaline substances like ammonia,[26] limited active ingredient content, use of solvents, limited biological efficacy due to a lack of suitable adjuvants that boost performance, and the requirement for eye and skin irritation labelling.[18,27,28] In addition, these formulations do not address the high volatility of PA, and consequently its unpleasant smell, and likely reduction in efficacy.[8] Thereby, several unmet needs in current FA herbicides remain unresolved if performance equivalent to that of conventional contact herbicides is to be achieved. However, FA herbicides are perfectly suitable for use as a cornerstone of research into new active substances[29] because they are recently discovered new compounds.[30]

In this study, we aimed to synthetize new substances based on short FAs, although not acting as a pre-drug, and evaluate their biological performance against noxious weeds in greenhouse experiments to identify promising non-toxic herbicides. The resulting molecules should offer similar or better biological performance than the best PA-based herbicide, when applied at lower rates and spray volumes. In addition, these active compounds should overcome the above-mentioned drawbacks such as the troublesome formulation and volatility, avoiding loss of efficacy and the unpleasant smell.
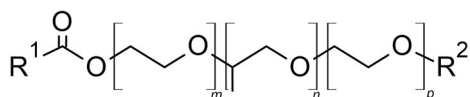
FIGURE 1. Simplified formula of fatty acid derivatives. Figure modified from Baur et al.[30]

2 MATERIALS AND METHODS

2.1 Chemicals
PA at 99% purity was acquired from Matrica. It was used for the synthesis of some test compounds as well as one of the two reference compounds in the biological assays. Other FAs were purchased from Sigma-Aldrich. Ethylene oxide (EO), propylene oxide (PO) and their respective mixtures produced by Clariant were used as gases or oligomeric glycols. The catalysts used for synthesizing the test compounds were purchased from Merck.

2.2 Synthesis of fatty acid derivatives
FA derivatives were prepared based on the literature.[30] They were provided by the Group Technology & Innovation of Clariant, following standard procedures.[31,32] A simplified formula is given in Figure 1, wherein R^1 is a linear aliphatic group and R^2 is a hydrogen, aliphatic or acyl group. Index values 'm', 'n' and 'p' have numbers from 0 to 8 (Table 1). The synthesis routes were esterification of open polyglycerin and/or polyethylene glycols (PEG) or with alkyl-end-capped PEG or ethoxylation insertion in methyl esters of FA.[30]

The obtained compounds were esters of certain FAs with alkylene glycol and/or glycerol mono-, oligo- or polymers.[30] Here, we report 13 of a large number of compounds, as shown in Table 1.

Test compounds A1–A3, A6–A9 and A11–A13 were prepared by reacting the particular FA and the respective alcohol alkoxylate in a bottle with a Dean-Stark head. To achieve a reaction between the two compounds, sulfuric acid was used as an acid catalyst at a reaction temperature of 200°C with constant agitation under a constant nitrogen flow to maintain an inert atmosphere. The reaction sub-products (water or methanol) were removed from the reactor until the final product was obtained.[31,32] A10 was synthetized using the same procedure, except that the reaction was carried out with a PA-alkoxylate and PA in a stoichiometric ratio of 1:1 to obtain the FA diester.[31]

For test compound A4, PA was reacted with potassium hydroxide in a 1-L stainless steel autoclave. The reaction process was dried at 100°C for 2 h while a vacuum was applied to evacuate water stream. The corresponding alkylene oxide was then added slowly to the reactor. This synthesis route resulted in a mixture of free PEG monoester, PEG diester and free PEG as described in the literature.[32] Test compound A5 was prepared by reacting PA ester with one or more alkylene oxides in the presence of a suitable calcium-based embedding catalyst at 170°C.

The structures of the synthesized products were confirmed by ^{1}H NMR spectroscopy. Spectral descriptions for the test compounds are provided in Figures S1–S13.

2.3 Formulation quality test
The quality of the formulation was first examined by testing the dilution stability of the test compounds at 10% v/v. Collaborative International Pesticides Analytical Council (CIPAC) guideline MT 41.1 (Dilution Stability of Aqueous Solutions) was followed.[33] Test compounds that did not form homogenous solution were formulated with castor oil ethoxylates (Emulsogen EL 400, -Clariant) or fatty alcohol alkoxylate (Emulsogen MTP 070, Clariant). The amount of emulsifier did not exceed 20% v/v in the test compound. After addition of emulsifier, an emulsion test was undertaken following CIPAC guideline MT 36.6 (Emulsion Characteristics and Re-emulsion Properties).[33] The pH value was also recorded for each test preparation as an indicator of stability.

TABLE 1. Fatty acid derivatives selected and synthesis route (see Fig. 1)

Test compound	Description	R^1	m	n	p	R^2	Synthesis
A1	Heptanoic acid 6EO ester methyl ether	C_6	6	0	0	CH_3	E[a]
A2	C_8/C_{10} fatty acid 6EO ester methyl ether	C_7/C_9	6	0	0	CH_3	E
A3	Pelargonic acid 6EO ester methyl ether	C_8	6	0	0	CH_3	E
A4	Pelargonic acid 6EO mono- / diester	C_8	6	0	0	CH_3 / $C_9H_{17}O$	DE[b]
A5	Pelargonic acid 6EO ester methyl ether	C_8	6	0	0	CH_3	IE[c]
A6	Dodecanoic acid 6EO ester methyl ether	C_{11}	6	0	0	CH_3	E
A7	Pelargonic acid 2 EO ester methyl ether	C_8	2	0	0	CH_3	E
A8	Pelargonic acid 8 EO ester methyl ether	C_8	8	0	0	CH_3	E
A9	Pelargonic acid 5 EO 1PO ester methyl ether	C_8	3	1	2	CH_3	E
A10	Pelargonic acid 6EO diester	C_8	6	0	0	$C_9H_{17}O$	E
A11	Pelargonic acid 5 EO ester hexyl ether	C_8	5	0	0	C_6H_{13}	E
A12	Pelargonic acid 6EO ester allyl ether	C_8	6	0	0	C_3H_5	E
A13	Pelargonic acid 6EO ester benzyl ether	C_8	6	0	0	C_6H_5	E

[a] Esterification.
[b] Direct ethoxylation.
[c] Insertion-Ethoxylation.

TABLE 2. Results of formulation quality and rate adjustment for greenhouse trials

		Emulsion results[b]	Greenhouse
Test compound	Straight dilution test results[a]	Rate (% v/v)	Application rate (L ha^{-1})
A1	Clear – Stable	n/a[c]	50
A2	Clear – Stable	n/a	50
A3	Clear – Stable	n/a	50
A4	Turbid – Not soluble	10[d]	55.5
A5	Clear – Stable	n/a	50
A6	Turbid - Phase separation	10[d]	55.5
A7	2 Phases - Phase separation	10[e]	55.5
A8	Clear – Stable	n/a	50
A9	Clear – Stable	n/a	50
A10	Cloudy – Phase separation	10[d]	55.5
A11	Cloudy – Not soluble	20[e]	62.5
A12	Turbid – Phase separation	10[e]	55.5
A13	Milky - Not soluble	10[d]	55.5
PA[f]	2 phases – Phase separation	10[d]	18
RV1[g]	Milky emulsion	n/a	130

[a] CIPAC MT 36.6.
[b] CIPAC MT 41.1.
[c] not applicable.
[d] Emulsogen EL 400.
[e] Emulsogen MTP 070.
[f] Straight pelargonic acid.
[g] Commercial pelargonic acid formulation.

2.4 Volatility measurement

A volatility test was performed by adding 10 µl of a spray solution of a known mass of active ingredient (a.i.) or the candidate to a weighed isolated cuticle of *Hedera helix* L. (ivy).[34] The droplet was exposed to controlled conditions of 25°C and 45% relative humidity (RH). The container was weighed again at 2, 24 and 48 h after droplet application to record the amount of evaporated product.[35] The result was calculated as the per cent mean weight recovery. Test compound (50 g L^{-1}) and straight PA (31 g a.i. L^{-1}) without emulsifiers were dissolved in a mixture of acetone/deionized water (1:1) and placed in an ultrasonic bath to obtain a homogenised solution suitable for application. The influence of pH adjustments on volatilization was also measured. To do this, different pH buffers were used for the preparations. A preparation at pH 5 was obtained by diluting acetone with a buffer solution of pH 4 (citric acid/sodium hydroxide/hydrogen chloride) at a 1:1 ratio. For pH 8, a 1:1 dilution of acetone was carried out using a buffer solution of potassium dihydrogen phosphate/disodium hydrogen phosphate (pH 7).

TABLE 3. Rating score used to interpretated weed control efficacy

Weed control efficacy (%)	Description
0–19	No control. Plants completely tolerant (weeds alive).
20–39	Poor control. Plants moderately tolerant. Transient desiccated symptoms.
40–59	Moderate control. Plants moderately susceptible. Desiccated tissues.
60–79	Good control. Plants susceptible. Necrotic tissues.
80–100	Excellent control. Plants Highly susceptible (weeds killed).

2.5 Greenhouse assays

A completely randomized design with four replications for each weed species was used to evaluate the effects of the test compounds in accordance with European and Mediterranean Plant Protection Organization (EPPO) guidelines. A commercial formulation of PA (RV1, Vorox Unkrautfrei Express, 237.59 g a.i. L^{-1}, EW, Compo) at the recommended rate, and straight PA (31 g a.i. L^{-1}) formulated with a castor oil ethoxylate (RPA) were used as positive controls.

D. sanguinalis and *S. nigrum* were used as representative monocotyledon and dicotyledon weed species, respectively. Seeds were planted in artificial substrate (Typ B Hawita Fruhstorfer. Hawita Gruppe) in 9 × 9 cm plastic pots. Seeds were grown in a greenhouse (phytotron) under a 16:8 h light/dark photoperiod with natural light, including UV, and supplemental sodium vapour lights to fulfil the plant's light requirements. The climate system was set up to give a daytime temperature of 23 ± 1°C and night-time temperature of 18 ± 1°C. RH was fixed at 55 ± 5%. Plants were watered from the bottom as needed to maintain adequate moisture until the end of the trial.

Test preparations and positive controls, as described in Table 2, were applied to medium sized (18 to 20 cm) plants of *D. sanguinalis* and *S. nigrum*. The plants were in development stage BBCH 22 and 16, respectively (Biologische Bundesanstalt, Bundessortenamt und Chemische Industrie). Treatments were applied at a spray volume of 500 L ha^{-1} at 300 kPa, using a spray chamber with a single flat fan nozzle (LU-120-06, Lechler). Visual estimates of per cent weed control were recorded 1, 2 and 7 days after application (DAA) on a scale of 0 to 100%, where 0% is no weed control and 100% is complete weed control. Desiccated and necrotic tissues were the main symptoms observed. Table 3 gives the rating scale for weed control. In case of regrowth, weed control values were decreased.

2.6 Statistical analysis

Data were subjected to analysis of variance (ANOVA) using ARM software (Gylling Data Management). Means were compared using Student–Newman–Keuls least significant difference (LSD) test ($P < 0.05$) for separation of the means. Prior to analysis, the normality and homoscedasticity of the data were verified using functionalities of the software, and corrective actions such as automatic arcsine square root percentage were undertaken if required.

## 3 RESULTS

3.1 Formulation quality test

Some of the test compounds were stable in the dilution assessment without formulation (Table 2). For compounds that were not stable, castor oil ethoxylation or fatty alcohol alkoxylation were needed to give a homogenous and stable spray solution. Adjustments were made in the application rate of the formulated test compounds in order to apply the same amount of product as shown in Table 2. There were no striking differences in pH values among the 13 preparations indicating a direct influence on herbicidal efficacy. The preparations were slightly acidic in comparison with the positive control spray liquids. pH values ranged between
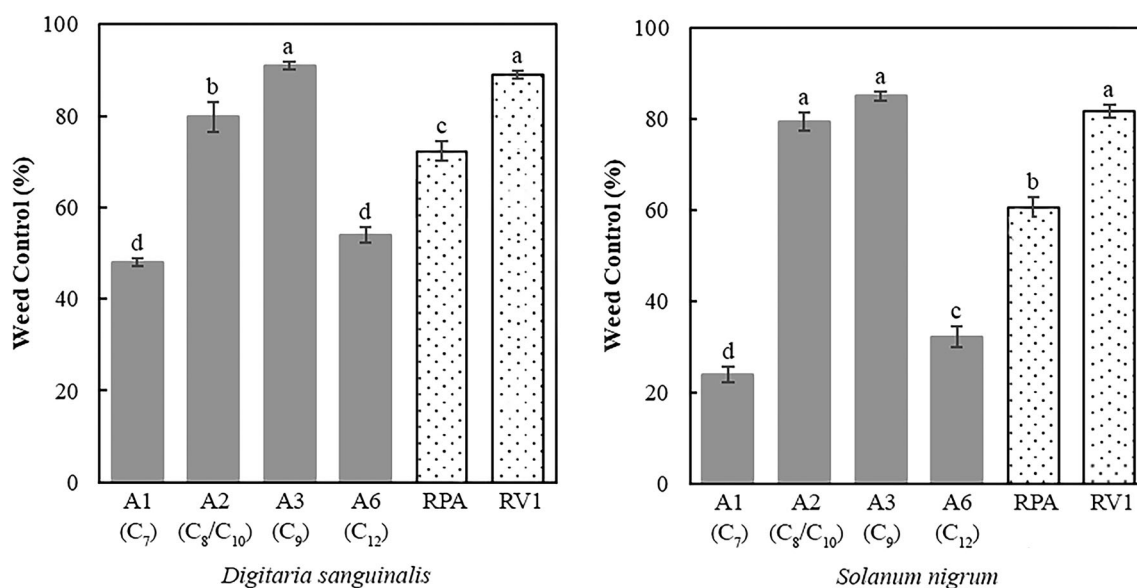
FIGURE 2. Effect of fatty acid chain length (C$_6$–C$_{12}$) in the fatty acid EO ester methyl ether on weed control at 2 days after application. A1–A3, A6: test compounds. RPA, RV1: Generic and commercial pelargonic acid formulation. Different letters above bars indicate significant differences ($P < 0.05$, Student–Newman–Keuls test).
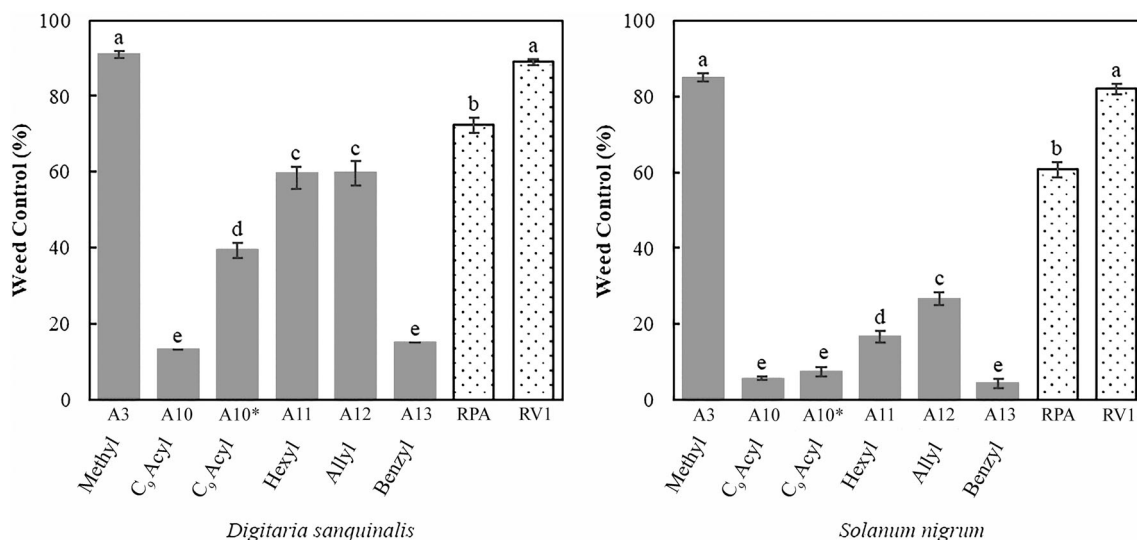
FIGURE 3. Influence of herbicidal activity of fatty acid diesters and type of end-capping of polyethylene glycols (PEG) monoesters on weed control at 2 days after application. A3, A10–A13: test compounds. RPA, RV1: generic and commercial pelargonic acid formulation. Different letters above bars indicate significant differences ($P < 0.05$, Student–Newman–Keuls test). The rate of A10* is the A10 rate increased four times.
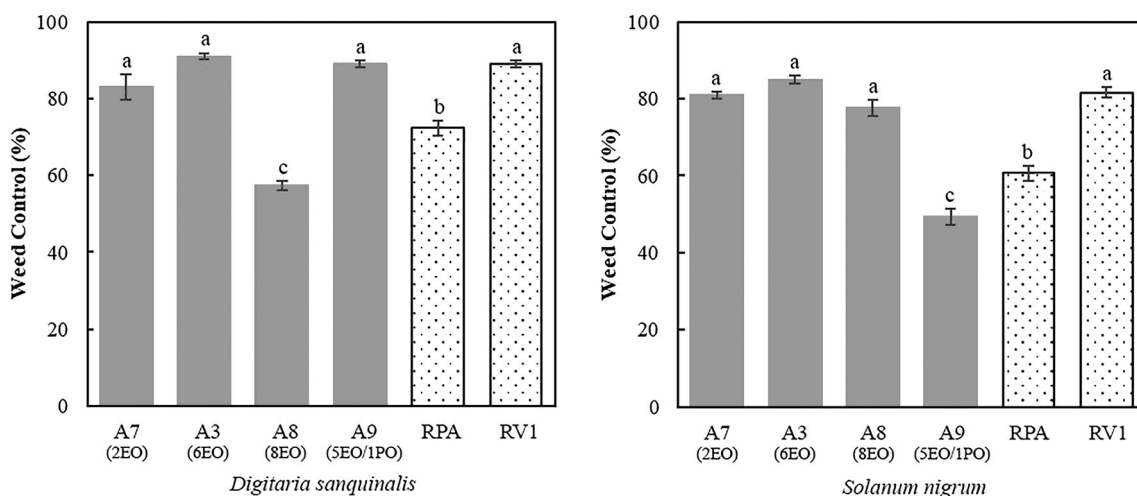
FIGURE 4. Effect of the ethoxylation degree of methyl-capped pelargonic acid ester ethoxylates on weed control at 2 days after application. A3, A7–A9: test compounds. RPA, RV1: generic and commercial pelargonic acid formulation. Different letters above bars indicate significant differences ($P < 0.05$, Student–Newman–Keuls test).

5.0 and 7.0, except for test preparation A12 which had the lowest pH value, 3.60.

3.2 Herbicidal activity in greenhouse assay

The weed control efficacy of the selected FA derivatives against benchmarks is shown in Figures 2–5. These are compared according to structural variations in the formula given in Figure 1 in each figure. Only performance at 2 DAA is shown because the maximum knockdown effect was reached by this point. Weed control at 7 DAA is shown only for A3 in Figures 6 and 7. Values are the mean of four replicates, and error bars represent standard errors.

3.2.1 Impact of fatty acid chain length on weed control

Maximum phytotoxicity was found with A3 (C_9 fatty acid), as shown in Figure 2. Both plant species were highly susceptible

to treatment with A2 (C_8/C_{10} fatty acid), which showed excellent control in *D. sanguinalis* and good control against *S. nigrum*. The other FA compounds had a lesser effect than A3 and A2. No significant differences were observed between A3 and RV1.

3.2.2 Herbicidal activity of FA diesters and type of end-capping of PEG monoesters

The most effective treatment in both weeds was the FA with methyl end-capping (A3). *D. sanguinalis* was moderately susceptible to A11 (-$C_6H_{13}O$) and A12 (-C_3H_5), whereas *S. nigrum* was tolerant to both. Other end-capping variations showed weaker weed control than RPA for both plant species, for example benzyl end-capping (A13), or even at higher rates like the FA diester (A10) as shown in Figure 3.

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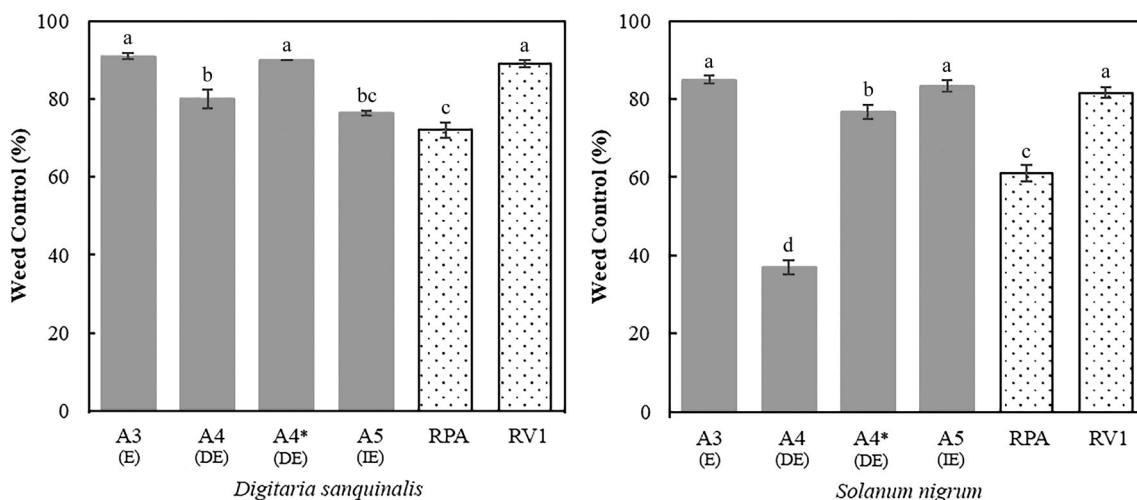
FIGURE 5. Impact of the synthesis route of pelargonic acid 6EO ester methyl ether on the weed control at 2 days after application. Synthesis: esterification (E), direct ethoxylation (DE), insertion ethoxylation (IE). A3–A5: test compounds. RPA, RV1: generic and commercial pelargonic acid formulation. Different letters above bars indicate significant differences ($P < 0.05$, Student–Newman–Keuls test). The rate of A4* is the A4 rate increased two times.
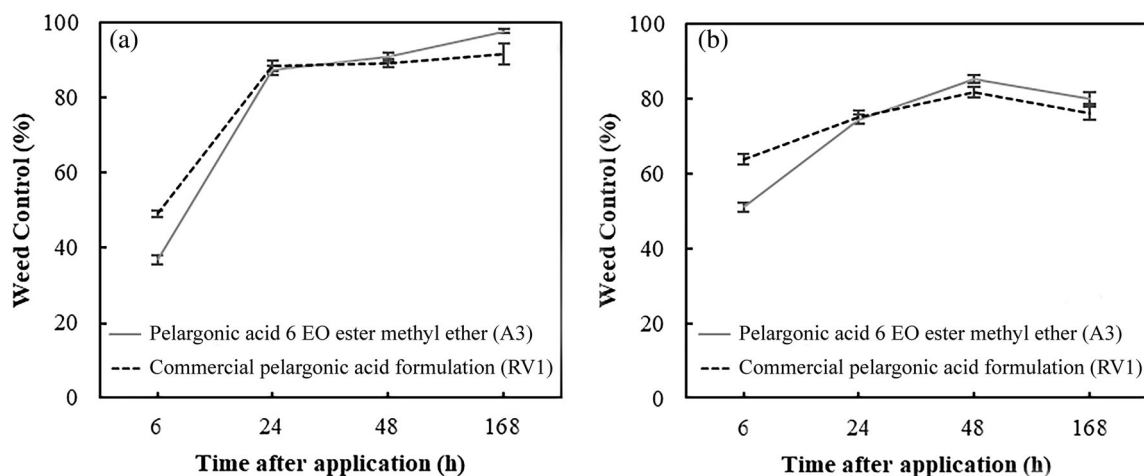
FIGURE 6. Time dependence of weed control of *Digitaria sanguinalis* (a) and *Solanum nigrum* (b).
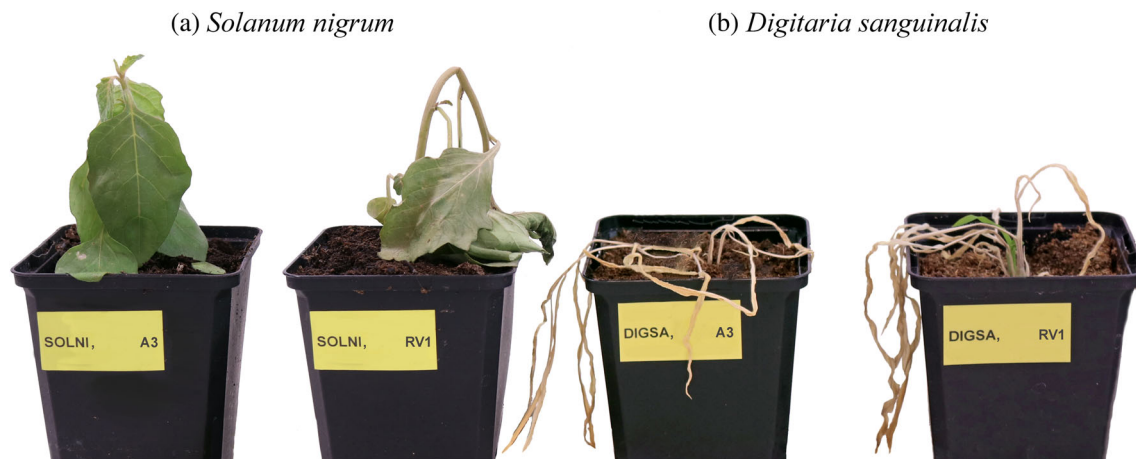
FIGURE 7. Example for differential weed control of pelargonic acid 6EO ester methyl ether (A3) and commercial pelargonic acid formulation (RV1). (Left) Weed treated with A3. (Right) Weed with RV1 applied. (a) Symptoms at 6 h after application. (b) Symptoms at 7 days after application.
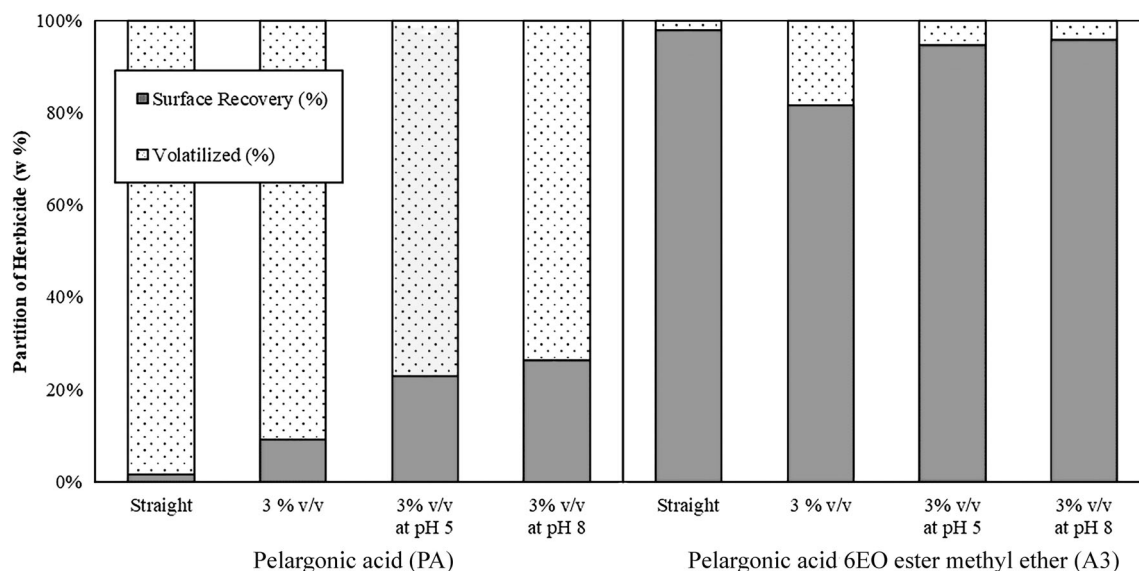
FIGURE 8. Fractions of surface recovery and volatilized product (weight %) after 2 days (mean of ten repetitions). Test conducted with low permeable cuticle of *Hedera helix* L.

3.2.3 Impact of ethoxylation of the test compound on weed control

A7 (2EO) was able to control *D. sanguinalis* and *S. nigrum*, as did A3 (6EO) and RV1. A8 (8EO) was less effective, but the level of control reached was acceptable for both weeds. Surprisingly, the copolymer A9 (5EO/1PO) did not show equal performance for the model plants, giving an excellent weed control for *D. sanguinalis*, but only fair control for *S. nigrum* (Figure 4).

3.2.4 Synthesis route on the herbicide efficacy

The products obtained using the different synthesis routes, direct esterification ethoxylation and ethoxylation insertion, were able to control *D. sanguinalis*, showing good to excellent efficacy. However, *S. nigrum* was highly susceptible only to A3 (esterification) and A5 (ethoxylation insertion). The efficacy of A4 (ethoxylation route) against *S. nigrum* was poor, increasing to good only at double application rates (Figure 5).

3.2.5 Detailed comparison between A3 and pelargonic acid (RV1)

Owing to its higher phytotoxicity, A3 was selected and subjected to further study to compare its activity against the commercial formulation RV1. In general, RV1 was slightly faster, but A3 achieved better results for both model plants. Significant differences were not found before the last assessment at 7 DAA. *D. sanguinalis* was more susceptible than *S. nigrum* to both products, with A3 giving an excellent level of control in *D. sanguinalis* and a good level of control in *S. nigrum* (Figure 6).

Weed control over a period of 7 days is shown in Figure 6, thereafter phytotoxicity symptoms did not develop further. Faster development of phytotoxicity was observed in weeds treated with RV1 after 6 h (Figures 6 and 7). However, at 1 DAA, both products achieved similar efficacy, with A3 giving the best weed control results at the end of the trial.

3.3 Volatility of test compound A3

The volatility study indicated zero volatility for the A3 derivative with the applied amount of straight A3 being recovered completely after 2 days. By contrast, straight PA was volatilized totally to ambient air after 2 days (Figure 8). The recovered amount of product was influenced by the pH conditions in the tested preparations, with buffered tap water giving less recovery than buffer systems. However, A3 still showed 80% or more recovery and much lower volatility from the leaf cuticle than RPA. A higher pH slightly reduced the volatility of both products, A3 and RPA.

4 DISCUSSION

FAs and FA derivatives have multiple applications in agriculture, for example as herbicides, fungistatic agents, insecticides, emulsifiers and wetting agents.[36–38] More than 50 derivatives of the formula shown in Figure 1 and others like amides have been synthesized and evaluated for their herbicidal activity.[30] In this work, new compounds based on short-chain FA esters and benchmarks were evaluated to identify a lead structure for new contact (bio)herbicides. In addition to their potential as contact herbicides, other benefits have been found that are not discussed here. For example, FA amides, alkyl and PEG esters with long chains are interesting for other applications, such as drift retardancy and solvent or carrier agent function without any herbicidal activity.[39,40]

The performance of PA herbicides depends on the concentration used and requires maximum coverage of the treated plant organs.[17,20] Climate conditions also interfere substantially their phytotoxic activity.[15–17] Thus, to prcevent external factors from affecting the efficacy of the test preparations, prior trials on climate conditions, weed size and application rate were performed (data not shown). Overall, the findings were consonant with published studies.[14–17] Accordingly, the trials were done under moderate climate conditions (approximately 23/18°C day/night), and on medium sized (18–20 cm) weeds. We confirm that *D. sanguinalis* and *S. nigrum* are representative monocot and dicot weeds for such contact products.[2,3] Rate application and spray volume were reduced to more appropriate agricultural levels, one of the requirements of this study, but also as a result of the

excellent performance of nearly all the test compounds when applied at the label recommendation of the commercial positive control (130 L ha^{-1} of product in a water volume of 870 L ha^{-1}).

All 13 FA PEG esters showed phytotoxic activity, with significant differences among them. Base materials (PEG) led to enhanced performance, but did not own herbicidal activity.[41] Furthermore, they are approved by the U.S. Environmental Protection Agency as inert ingredients in pesticide formulations[42] and are considered safe for humans in other industries such as personal care or pharmaceuticals, being used for example as purgatives.

A3 was the most effective of the obtained products, showing excellent control on the weeds tested. Comparing the effect of alkyl chain length (Figure 2) of the esters on a constant number of 6EO groups and methyl end-capping, optimum chain length was found to be C$_9$. This chain length is also reported in the literature as being superior to straight FA.[43,44] A2 with about 60% C$_8$ and 40% C$_{10}$ linear FA is slightly less effective, indicating that C$_9$ is better than C$_8$. By contrast, branched C$_8$, C$_9$ or C$_{10}$ is not effective (data not shown). The C$_{12}$ chain length (A6) performed distinctly less well than other derivatives of this chain length or longer (data not shown). The methyl substituent for end-capping was very beneficial for performance when compared with the open derivative with 6EO (A10) and other substituents such as benzyl, allyl or hexyl groups, all of which reduced efficacy significantly (Figure 3). At constant C$_9$ chain length and methyl end-capped, an EO number of 6 was superior to EO numbers of 2, and particularly 8 (Figure 4). Adding one propylene oxide group in the chain (A9) resulted in comparable good performance in *D. sanguinalis* control, but efficacy decreased significantly for the dicot, *S. nigrum* (Figure 4). It appears from these results that A3 is the most effective derivative and the highest active substance content in A3 was found when esterification was used for synthesis. Products with ethoxylation insertion contained some impurities or diesters,[45] which reduced efficacy at least in one of the two weeds studied (Figure 5). This is also known for polyglycerols in other applications.[45]

A new approach to the synthesis of molecules is presented. No literature is available on the action/effect of the substituents (Figure 1) on herbicidal outcome. Further studies are needed to discuss differences in herbicide efficacy. However, the foliar penetration hypothesis and penetration studies (data not shown) give some indication of the different effectiveness of these compounds. Foliar penetration across the cuticle depends on molar volume or molecular weight, and solutes above 450 g mol^{-1} penetrate very slowly if they do not swell the cuticle or have a linear structure, which increases penetration severalfold.[46] PA esters are interesting in this respect because they are almost linear with one ester group, and partly act as swelling agents.[34] The C$_{12}$ ethoxylate (A6), for example, has a molecular weight just above 480 g mol^{-1} and this is one of two unfavourable properties of this derivative. The other key property is lipophilicity, which impacts both movement of actives or solutes to the site of action and binding there. Passive translocation in the aqueous phase of cell walls and xylem is best at octanol/water partition coefficients or log$P$ values of 1.5 to 3.5.[47] For PA, log$P$ is 3.4 and together with a pK_a of approximately 5 this is within the suitable range.[18] The calculated log$P$ for A3 is 2.2, which also fits well. By contrast, the C$_{12}$ derivative (A6) has an estimated log$P$ of 3.7 with incremental 0.5 lipophilicity added to log$P$ per methylene group. This further limits its translocation to the limitation of movement due to higher molecular weight. Higher degrees of ethoxylation lower log$P$, and for both pure and technically polydisperse alcohol

ethoxylates 4.5EO reduces log$P$ by one unit with a corresponding impact on cuticle absorption and efficacy.[46,48] Other derivatives than A3 apparently deviate too much from the ideal combination of molecular weight and lipophilicity.

All derivatives, A1–13, are liquid at ambient temperatures. Many are water soluble or form reasonably stable micellar solutions, addressing PA formulation issues without addition of any non-ionic emulsifier (Table 2). For others, simple addition of an emulsifier is sufficient to achieve stable and homogenous dilutions, which are microemulsions or emulsions in contrast to commercial products like RV1, where PA is formulated in a tedious and expensive adjuvant system. No biological influence of the emulsifiers selected for the test compound was observed here, but both castor oil ethoxylate emulsifiers and fatty alcohol alkoxylates are able to increase the efficacy of systemic agrochemicals.[34] The presence of EO in the molecules adds more hydrophilic character,[49] which makes the new compounds self-emulsifiers or readily emulsifiers, unlike the straight PA. The number of 6EO appears to be optimum compared with lower numbers of EO for example A2 (2EO). A higher amount of EO like A8 (8EO) or an average of 6EO like the copolymer in A9 (5EO/1PO) leads to stable test preparations, although biological performance is affected (Figure 4). As mentioned above, the synthesis route is important and ethoxylation insertion causes a mixture of PEG monoester, PEG diesters and free PEG, all of which are inactive or even antagonistic, leading to higher rates of application for the same efficacy (Figure 5).[45] Gas chromatography–mass spectrometry confirmed that A3 contains some percentage of free acid but no meaningful non-active impurities. In addition to previous findings, the test compounds can act as wetting agents at the high used concentration with values for the dynamic surface tension below 45 mN m^{-1} and thus are excellent for spray adherence.[50] As a result, the active substances are often also the final product (Table 2), which can be applied straight away using drones or autonomous robots for precision agriculture.

A3 clearly stands out among the other test compounds. It showed the best weed control (Figures 2–5) and does not need any formulation (Table 2), being relatively easy to co-formulate with other herbicidal substances.[51] Co-formulation should be further studied, for example A3 and the triketone leptospermone, which showed good efficacy in combination with PA in the spray tank.[14] The biological outcome for A3 is equal, or even superior, to the PA herbicide applied (Figure 6), but this outstanding efficacy was achieved with 50 L of product and a water volume of 450 L ha^{-1}, a reduction of 80 L ha^{-1} of product and 420 L ha^{-1} of water in comparison with the benchmark label recommendations. Thus, it appears that A3 could represent a substantial reduction in cost for farmers due to the reduced amount of product and water used in its application, and the absence of formulation.

Injuries on treated weeds suggest that A3 acts in the same way as the positive controls by destroying meristematic and differentiating cells.[43,44,52] Because PA constitutes the core of A3, they share many characteristics such as rapid wilting in treated plants, followed by necrotic tissues. Although the mode of action of PA is not fully understood, the consensus is that both active compounds (PA and A3) suppress the weed through membrane degradation, as claimed for PA in previous studies. The other major effect suggested was increased cuticular transpiration, thereby causing rapid wilting of plants.[15] Despite having similar modes of action, the herbicidal activity of A3 showed a reduced effect at 6 hours after application (Figures 6 and 7), offering some advantages, such as possible greater control of larger plants or the

possibility of co-formulation with other systemic actives, like sulfonylureas,[51] which could be better translocated in the first hours after application.[22]

A peculiar feature of PA is its strong malodour combined with high volatility (vapour pressure at 20°C of 1.0×10^5 mPA).[18] The rancid aroma of PA, which is released after a few hours and lasts for days, limits its use in homes and gardens, as well as on plantations or in railway applications. In addition, the high volatility of PA results in some loss of biological activity and problems known from other volatile herbicides like dicamba or clomazone.[9] A3 is practically not volatile (Figure 8) and has no bad odour, giving it a further advantage over PA products.

Looking at the results (Figures 2–6), it is striking that control of *D. sanguinalis* was better than control of *S. nigrum* throughout. Although it is tempting to conclude a difference in biological sensitivity to PA esters, this is unlikely. *D. sanguinalis*, like most weed grasses, is difficult to wet due to the high density of crystalline waxes on both leaf surfaces, whereas *S. nigrum* does not have wax crystals and is easy to wet.[3] The wettability with water is therefore dramatically different, with *D. sanguinalis* retaining no water, whereas *S. nigrum* is completely wetted by spray droplets, even with plain water. The situation changes completely with surfactants. A dynamic surface tension below 45 mN m^{-1} at 200 ms and a static (equilibrium) surface tension just below 40 mN m^{-1} cause spray droplets to be captured almost quantitatively, and also spread over the whole leaf surface due to capillary wetting.[50] By contrast, on a wettable dicot like *S. nigrum*, droplets stick well but do not spread and the coverage is much lower than on monocot leaves. For contact herbicides that are not distributed within the plant and only slightly in the contacted tissue, maximum coverage affects herbicide action directly. Therefore, good dynamic wetting will ensure control with contact herbicides, particularly of monocots and difficult to wet dicots like *Chenopodium album* L. (Lamb's quarters). For others, maximum coverage is typically achieved by using high water volumes, because oil spreaders like mineral oils, typically also used in high concentrations, often counteract the penetration of lipophilic actives.

The two precursors, PA and PEG, used in the chemical reaction for the test substances are non-toxic,[18,19,42,53] and as far as is currently known, A3 and its analogues are accordingly putative candidates to be generally recognized as safe substances. For this reason and because A3 can be synthesized easily from a renewable resource like PA and obtained on a large scale, this compound could be a good and sustainable alternative for weed control.

5 CONCLUSION

Methyl-capped pelargonic acid 6EO ester demonstrated equal or better herbicidal contact activity than commercial benchmarks of PA at a lower spray volume and without the negative properties that limit wider use of such FA. This new substance provides a slightly slower (yet still fast) contact action after application, which may offer better synergism in co-formulations or tank mixtures with systemic herbicides that need adequate translocation. Formulation of the solo product is easy and the liquid active compound is both self-dispersing and a wetting agent on its own. This contrasts with PA, where the formulation effort for effectiveness is high. Application in precision agriculture to control site-resistant weeds seems particularly interesting, either pure or in small quantities. Furthermore, the 6EO ester has no unpleasant smell and is practically non-volatile. Although

the aforementioned drawbacks of FA products have been addressed, further research is needed to resolve other problems with contact herbicides like regrowth or increasing efficacy at lower spray volumes, which could be improved with suitable growth-regulator herbicides. Additional research to enhance the product is ongoing, for example through as yet unidentified adjuvants or synergists.

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CONFLICTS OF INTEREST

SUPPORTING INFORMATION

Supporting information may be found in the online version of this article.

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