Benzofuran-2-acetic esters as a new class of natural-like herbicides

Research Article

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Benzofuran-2-acetic esters as a new class of natural-like herbicides

Fabrizio Araniti,[a] Raffaella Mancuso,[b] Antonio Lupini,[a] Francesco Sunseri,[a] Maria Rosa Abenavoli[a*] and Bartolo Gabriele[b*]

Abstract

BACKGROUND: In recent decades, the use of synthetic herbicides has been increasing, mainly in emerging countries. However, their intensive and indiscriminate application is a major cause of environmental pollution and human health injury. Therefore, there is an increasing need to develop new herbicides with safer toxicological and environmental profiles. A promising strategy is to synthesize new molecules containing the core of natural products as a template for the production of 'bio-inspired' or 'natural-like' herbicides.

RESULTS: The potential herbicidal activity of some benzofuran-2-acetic esters was assessed *in vitro* on *Arabidopsis thaliana*, a model species. All five molecules (M1-M5) showed significant phytotoxic activity, reducing both shoot and root system at low concentrations. In particular, methyl 2-(5-methoxybenzofuran-2-yl)hexanoate (M3) exhibited the highest phytotoxicity displayed against two crops and weeds, monocots (*Zea mays* L. and *E. crus-galli*) and dicots (*Lactuca sativa* L. and *Amaranthus retroflexus* L.). The M3 activity was also compared with glyphosate, a common herbicide, showing a lower but similar activity. Moreover, the results evidenced that M3 was more effective in post-emergency.

CONCLUSION: Readily synthesizable benzofuran-2-acetic esters possessing the benzofuran ring as 'bio-inspired' core, show significant herbicidal activity making them very efficient even at low concentrations. They can be sprayed in liquid form, and the addition of adjuvants can improve penetration through the leaf cuticle. These results confirm the importance of these molecules as models for the development of new natural-like herbicides.

Keywords: benzofurans; crop protection; herbicides; natural-like herbicides

1 INTRODUCTION

Weeds have the largest negative impact on crop productivity[1,2] since they compete for soil, water and nutrients, causing significant economic losses.[3,4] Cultural, mechanical, chemical and biological methods are the most prominent approaches used for weed management. Among these, synthetic herbicides, whose use is increasing in recent decades, mainly in emerging countries, remain to date the most effective method for their ease of application and greater accessibility for farmers.[5] However, the intensive and indiscriminate application of these chemicals, very persistent in agricultural end-products and not easily biodegradable, is a major cause of environmental pollution and human health injury. In addition, their poor selectivity along with the rapid evolution of weed resistance determine huge damage to crops and negative consequences in agriculture.[6] Therefore, there is an increasing search to develop new herbicides with safer toxicological and environmental profiles and new mechanisms of action (MOA). A very promising strategy is to synthesize new molecules containing the core of natural products as a template for the production of 'bio-inspired' or 'natural-like' herbicides. They could be characterized by high biological activity, novel target sites and alternative MOA, low or no toxicity, high biodegradability compared to the commercial herbicides, and consequently an increased environmental and health safety.[7] Until now, natural products have not played an important role in herbicide development compared to other pesticides,[8,9] although some natural-like compounds with herbicidal activity have been developed.[10–17]

In this paper, benzofuran-2-acetic esters are presented as a new class of 'bio-inspired' potential herbicides.[19] The benzofuran motif constitutes the core of many pharmacologically active substances, with biological activities that include anti-inflammatory, anticancer, cytotoxic, antimicrobial, antioxidant, insecticidal and antiplasmodial effects.[20–25] However, the herbicidal activity of benzofuran-2-acetic esters has not been reported so far.[19] In this work, the phytotoxic activity of these compounds, readily synthesizable by a catalytic carbonylation process, was evaluated on the model plant *Arabidopsis*, crops and weeds, and was also compared to glyphosate, a common commercial herbicide.

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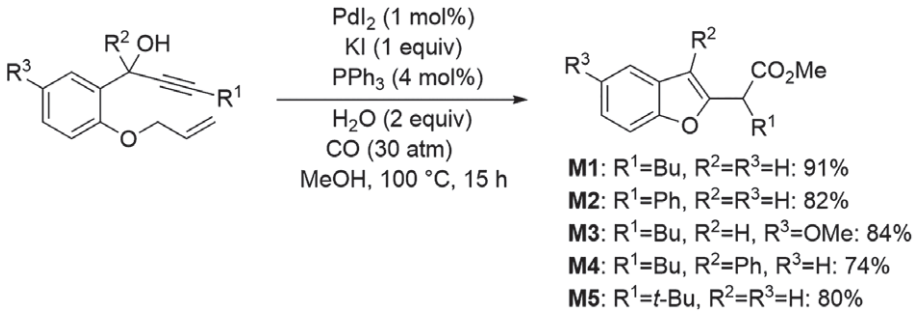


Figure 1. Synthesis of benzofuran-2-acetic esters **M1**-**M5**.[26]

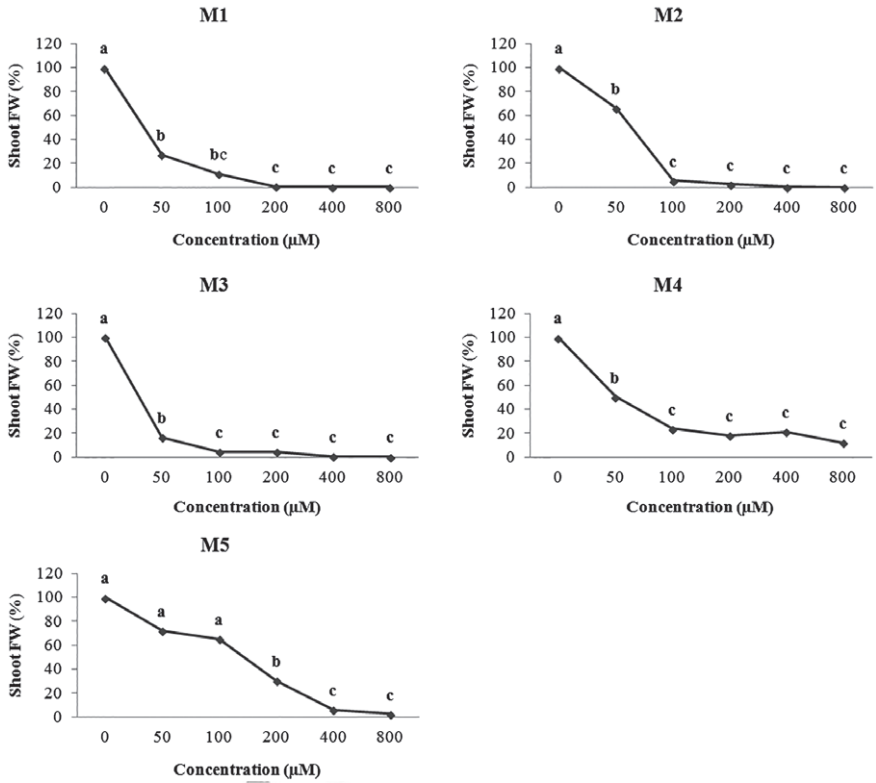


Figure 2. Dose–response curve of shoot fresh weight (SFW) of *A. thaliana* seedlings treated with benzofurans **M1-M5** for 14 days. Data are expressed as percentage compared to the control. Different letters along the curves indicate significant differences at $P \leq 0.05$ (Tukey's test, $n = 4$).

2 MATERIALS AND METHODS

2.1 Synthesis of benzofuran-2-acetic esters

Benzofuran-2-acetic esters **M1-M5** were prepared by palladium-catalyzed carbonylation of (2-allyloxyphenyl)-2-yn-1-ols, as we already reported.[26] Briefly, a 250 mL stainless steel autoclave was charged with PdI_2 (7.2 mg, $2.0 \cdot 10^{-2}$ mmol), KI (332.0 mg, 2.0 mmol), PPh_3 (21.0 mg, $8.0 \cdot 10^{-2}$ mmol) and a solution of the substrate (2.0 mmol) in anhydrous MeOH (9.1 mL). Water (72 µL, 4.0 mmol) was then added, and the autoclave was sealed, purged at room temperature several times with CO with stirring (10 atm) and eventually pressurized to 30 atm. After stirring at 100 °C for 15 h, the autoclave was cooled and degassed. The solvent was eliminated by rotary evaporation, and products were purified by column chromatography on silica gel using 1:1 hexane-CH_2Cl_2 (**M1**), 8:2 hexane-acetone (**M2**), 8:2 hexane-AcOEt (**M3**, **M5**), and 95:5 hexane-AcOEt (**M4**). The yields obtained are shown in Figure 1. Characterization data for all products can be found in the above-mentioned paper.[26]

2.2 *In vitro* bioassays on *Arabidopsis thaliana*

The *in-vitro* bioassays were carried out as previously reported by Araniti *et al.* with some modifications.[27] *Arabidopsis thaliana* (L.) Heynh. seeds ecotype Columbia (Col-0) were surface sterilized in 50% EtOH (3 min), 0.5% NaOCl with 0.01% Triton X-100 (3 min), and then rinsed three times in distilled water.

Seeds were maintained in 0.1% agar at 4 °C for 72 h to promote the synchronization of germination. Then, 25 seeds were sown in Petri dishes (100 × 150 mm) containing agar medium (0,8% w/v) enriched with micro- and macronutrients (Murashige-Skoog, Sigma-Aldrich) and sucrose (1%). Plates were placed vertically in the growth chamber (22 ± 2 °C temperature, 55% HR, and 90 $mol \cdot m^{-2} \cdot s^{-1}$ light intensity) to promote geotropic root growth. Four days after sowing, six seedlings (7 days old) were transferred to a single plate and grown in the same medium containing 0, 50, 100, 200, 400, 800 µM of synthetic benzofuran derivatives (**M1-M5**), for 14 days (see section 2.1 for benzofuran derivatives preparation). All the molecules were previously dissolved in 0.1%

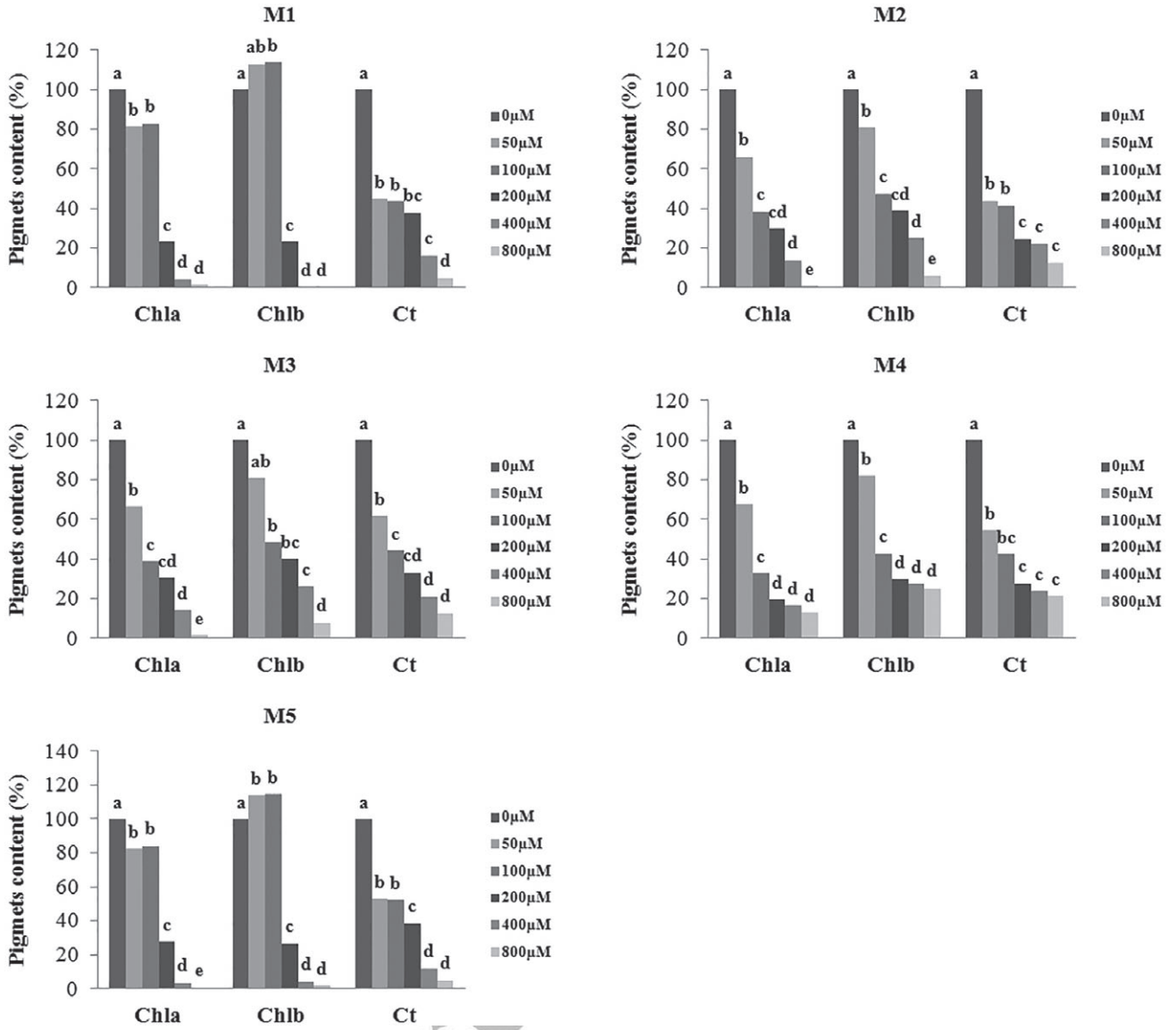


Figure 3. Pigment content [Chlorophyll a (Chla), chlorophyll b (Chlb) and carotenoids (Ct)] in young *Arabidopsis* plants treated with **M1-M5** for 14 days. Data are expressed as percentage compared to the control. Different letters along the bars indicate significant differences at $P \leq 0.05$ (Tukey's test, n = 4).

EtOH (*v*/*v*), and then autoclaved. The same amount of EtOH was added to the control plates. After treatment, seedlings were collected and separated into shoot and root. Shoot Fresh Weight (SFW), Leaf Number (LN), Total (TRL) and Lateral Root Length (LRL) were evaluated. The root system was imaged by scanning (STD 1600, Régent Instruments Inc., Quebec, QC, Canada) and analyzed by WinRhizo Pro System v. 2002a (Instruments Règent Inc., Quebec, Canada). Root hair density (RHD) was evaluated with an Olympus microscope (SZX9).

2.3 Pigments content

Chlorophyll a (Chla), chlorophyll b (Chlb), and carotenoid (Ct) content was quantified on *Arabidopsis* seedlings treated with each molecule (**M1-M5**) for 14 days. One hundred milligrams of leaf tissue, for each replicate and treatment, were ground in liquid nitrogen and extracted with 1.5 mL methanol. The extract was then centrifuged at 170 *g* for 5 min, and afterwards, 500 µL of supernatant was mixed with 500 µL methanol. The absorbance of the extracts was determined at 470, 653, 666 and 750 nm. The pigment content (mg g^{-1} of SFW) was evaluated according to the following equations proposed by Wellburn[28]:

$$\text{Chla (µg)} = [15.65\,(DO_{666} - DO_{750}) - 7.34\,(DO_{653} - DO_{750})] \times V$$

$$\text{Chlb (µg)} = [27.05\,(DO_{653} - DO_{750}) - 11.21\,(DO_{666} - DO_{750})] \times V$$

$$\text{Carotenoids (X + C) (µg)} = [1000\,(DO_{470} - DO_{750}) - 2.86\,\text{Chla} - 129.2\,\text{Chlb})/221] \times V$$

where DO is the optical density, V is the volume of methanol used (mL) and (X + C) the sum of carotenoids and xanthophylls.

2.4 Benzofuran M3 *vs* glyphosate

The potential herbicidal activity of the most bioactive benzofuran **M3** was compared to glyphosate, a common commercial herbicide. The preparation of the commercial herbicide (Roundup®)

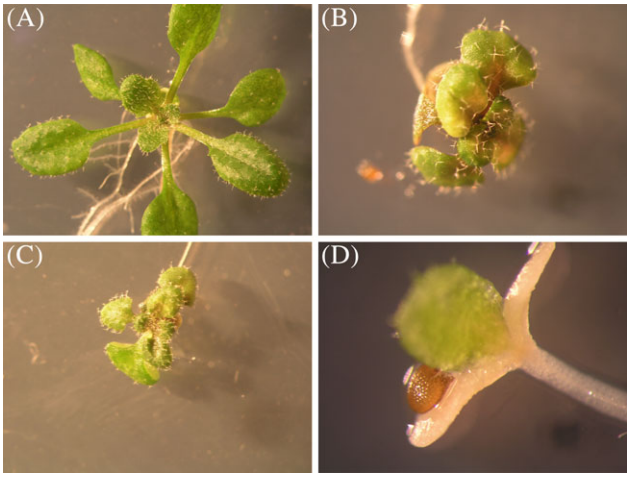


Figure 4. *Arabidopsis thaliana* seedlings grown in agarized medium and treated with benzofuran **M1** for 15 days. (A) Control; (B) 50 μM; (C) 100 μM; (D) 200 μM.

was carried out following package instructions to simulate an open field application. **M3** was solubilized in 96% ethanol (1:5 w/w), and then diluted with deionized water to reach 0 (control), 3.6 and 7.2 mM concentrations. Further, the **M3** solubility was increased by adding in the solution few drops of 0.001 mM NaOH, as emulsifying agent together with a surfactant and a wetting product [Etravon Pro (1 L/200 L/ha), Syngenta, Italy] that increased its penetration and efficacy during foliar treatment. Foliar-applied distribution was carried out by spraying, calculating an equal amount of active principle to be diluted in 200–300 L, the amount of solution distributed in a hectare.

2.5 *In vivo* bioassays on crops and weeds and pigment content

The phytotoxic activity of benzofuran **M3** and glyphosate were assayed *in vivo* on two crops and their respective weeds: *Zea mays* L. (monocot) and *Echinochloa crus-galli* (monocot), *Lactuca sativa* L. (dicot) and *Amaranthus retroflexus* (dicot). These species are commonly used in phytotoxic experiments, but, above all, this choice allowed us to evaluate the potential selectivity of **M3** against monocot and dicot.[29,30] Seeds of each species were surface sterilized in 15% NaClO solution (*v/v*) for 15 min and then rinsed three times with deionized water. Then, seeds (a seed/hole) were placed in a tray (0.2 m^2) with hole (5 × 5 cm) corresponding to a total volume of about 250 cm^3, containing potting soil. After sowing, trays were placed in a growth chamber (26 °C, 65% humidity, 12 h photoperiod with a light intensity of 350 mol m^{-2} s^{-1}) and watered with Hoagland nutrient solution (Hoagland and Arnon, 1950) every 2 days. Twenty-one days after sowing, young plantlets of each species were sprayed with a solution containing 0 (control), 3.6 and 7.2 mM **M3** or glyphosate concentrations. After 7 days of treatment, shoots were collected for measuring fresh weight (g), stem length (cm) and pigment content (%). Stem length was measured by the WinRHIZO system pro STD 1600 (Instruments Régent Inc. Canada) after scanner acquisition (Epson Expression 800). Shoot dry weight (g) was determined after keeping seedlings at 72° C until constant weight was reached. The determination of pigments content was carried out as seen in Section 2.3.

2.6 Statistical analysis

A completely random design with four replications was adopted to evaluate the effects of the benzofuran derivatives in the *in-vitro Arabidopsis* bioassay. Data were evaluated for normality (Kolmogorov–Smirnov test) and tested for the homogeneity of variances (Levene's test). Shoot fresh weight (SFW), TRL, LRL of seedlings in response to different doses of benzofuran derivatives were evaluated by a nonlinear regression model using a log-logistic function that allowed to estimate the ED_{50} parameter, the dose required to reduce 50% of measured parameter compared to control. The phytotoxicity comparison among molecules was performed by one-way ANOVA using the ED_{50} as a variable and the molecule as main factor. The ED_{50} data were first checked for deviations from normality (Kolmogorov–Smirnov test) and tested for homogeneity (Levene's test). The statistical significance of differences among means was estimated by analysis of variance and Tukey test ($P \leq 0.05$). The statistical significance of pigments

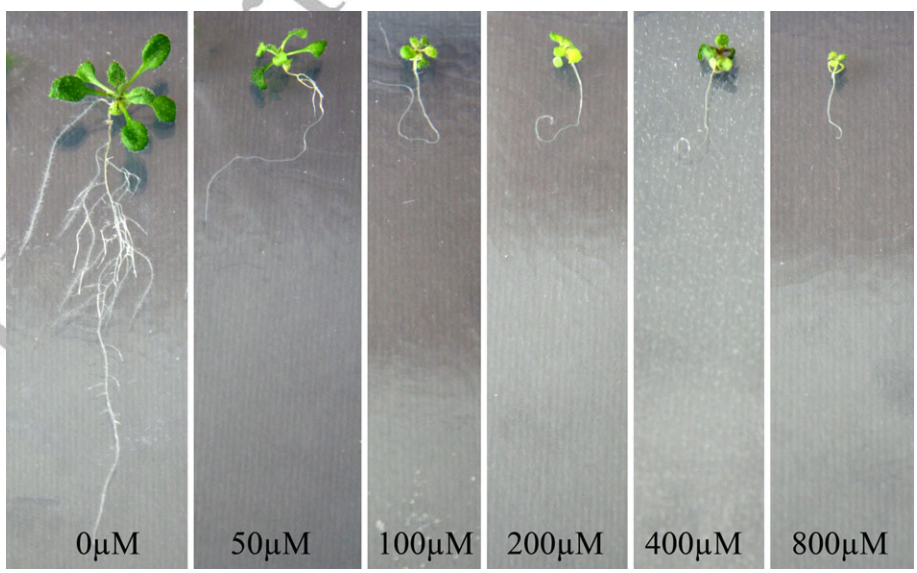
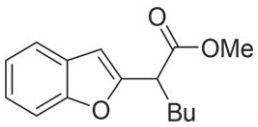
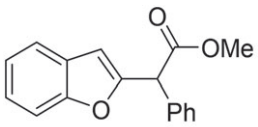
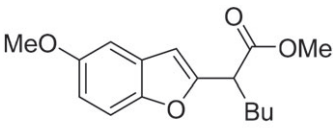
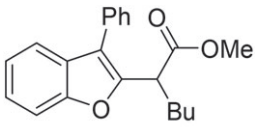
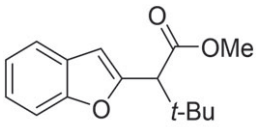


Figure 5. *Arabidopsis thaliana* seedlings grown in agarized medium and treated with benzofuran **M3** (0–800 μM) for 15 days.

Table 1. ED_{50} (μM) values related to shoot fresh weight (SFW), total root length (TRL) and number of lateral root (NLR) of *A. thaliana* treated with different **M1-M5** concentrations

ED_{50} (μM)			
Benzofuran derivative	SFW	TRL	NLR
 **M1**	29.13 (±8.01)[a]	102.17 (±9.92)[b]	42.15 (±9.46)[b]
 **M2**	57.25 (±0.78)[a]	45.51 (±6.05)[ab]	30 (±1.64)[b]
 **M3**	17.22 (±5.68)[a]	12.18 (±1.02)[a]	10 (±0.05)[a]
 **M4**	36.16 (±12.55)[a]	284.5 (±87.14)[d]	144.68 (±36.67)[d]
 **M5**	123.46 (±23.96)[b]	466.75 (±51.59)[e]	96.11 (±16.94)[c]

Statistical differences among ED_{50} values were evaluated through one-way ANOVA using Tukey's test as post-hoc. Different letters along the columns indicate statistical differences with $P \leq 0.05$. N = 4.

content was estimated by analysis of variance (one-way ANOVA) and the data was processed as previously described.

A completely random design with 10 replications was adopted to evaluate the effects of **M3** and glyphosate in the *in vivo*-bioassays with crops and weeds. All the data were evaluated for normality (Kolmogorov–Smirnov test) and tested for homogeneity of variances (Levene's test). The statistical significance of differences among means was estimated by analysis of variance (two-way ANOVA) where the experimental factors were molecule/herbicide and concentration followed by Tukey's test ($P \leq 0.05$). All the analyses were performed by using SPSS ver. 6.1 software (Insightful Corporation, Seattle, WA, USA).

3 RESULTS

3.1 *In vitro* bioassays on *Arabidopsis thaliana*

All the benzofuran derivatives **M1-M5** caused a strong inhibitory effect on *Arabidopsis* seedlings. Except for **M5**, all molecules caused a significant SFW reduction already at the lowest concentration (50 μM), with inhibition values ranging from 44% (**M2**) to 83% (**M3**). As the concentration increased (≥ 100 μM), all molecules showed a SFW inhibition higher than 76% (Fig. 2). On the contrary, **M5** induced a significant SFW reduction only at concentrations higher than 100 μM, with inhibition values ranging from 70% (200 μM) to 97% (800 μM) (Fig. 2). These effects were sometimes accompanied by a failure of leaf development, as shown for **M1** and **M3** (Figs. 4 and 5, respectively), whose treated seedlings failed to develop the first true leaves. In **M1** treated plants, the cotyledons appeared to be depigmented (Figs. 3 and 4(d)).

All molecules significantly affected pigment content at a different extent (Fig. 3). Among them, **M2**, **M3** and **M4** were the most effective, causing a high reduction of all the pigments already at the lowest concentration. In particular, they induced a chlorophyll a reduction about 32% at the lowest concentration (50 μM), reaching inhibition values higher than 87% at 800 μM (Fig. 3). A similar trend was observed in chlorophyll b content, which was reduced by 20% at the lowest concentration, reaching an inhibition value higher than 75% at the highest concentration (800 μM) (Fig. 3). Finally, the carotenoid content was the most affected parameter in seedlings treated with 50 μM, pointing out inhibition values ranging from 38% (**M3**) to 57% (**M4**). At the highest concentration (800 μM), an inhibition higher than 79% was observed (Fig. 3).

Moreover, root system showed a significant reduction in TRL, NLR and root hair density (data not shown). To compare the potential phytotoxicity of the benzofuran derivatives on root system, the ED_{50}, which defines the dose required to reduce 50% of the

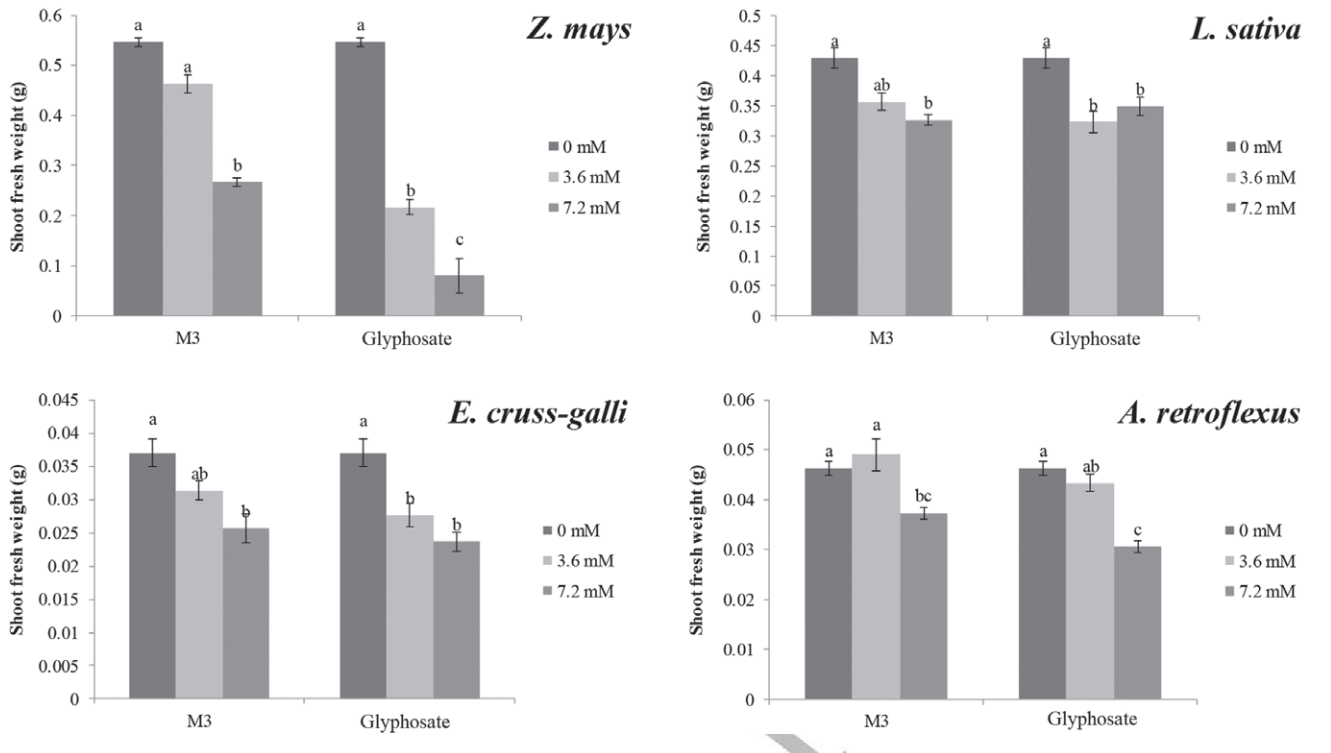


Figure 6. Shoot fresh weight (g) of *Z. mays*, *L. sativa*, *E. cruss-galli* and *A. retroflexus* exposed to 0, 3.6 or 7.2 mM **M3** or glyphosate for 7 days. Different letters within species indicate significant differences at $P < 0.05$ (Tukey's test, $n = 10$).

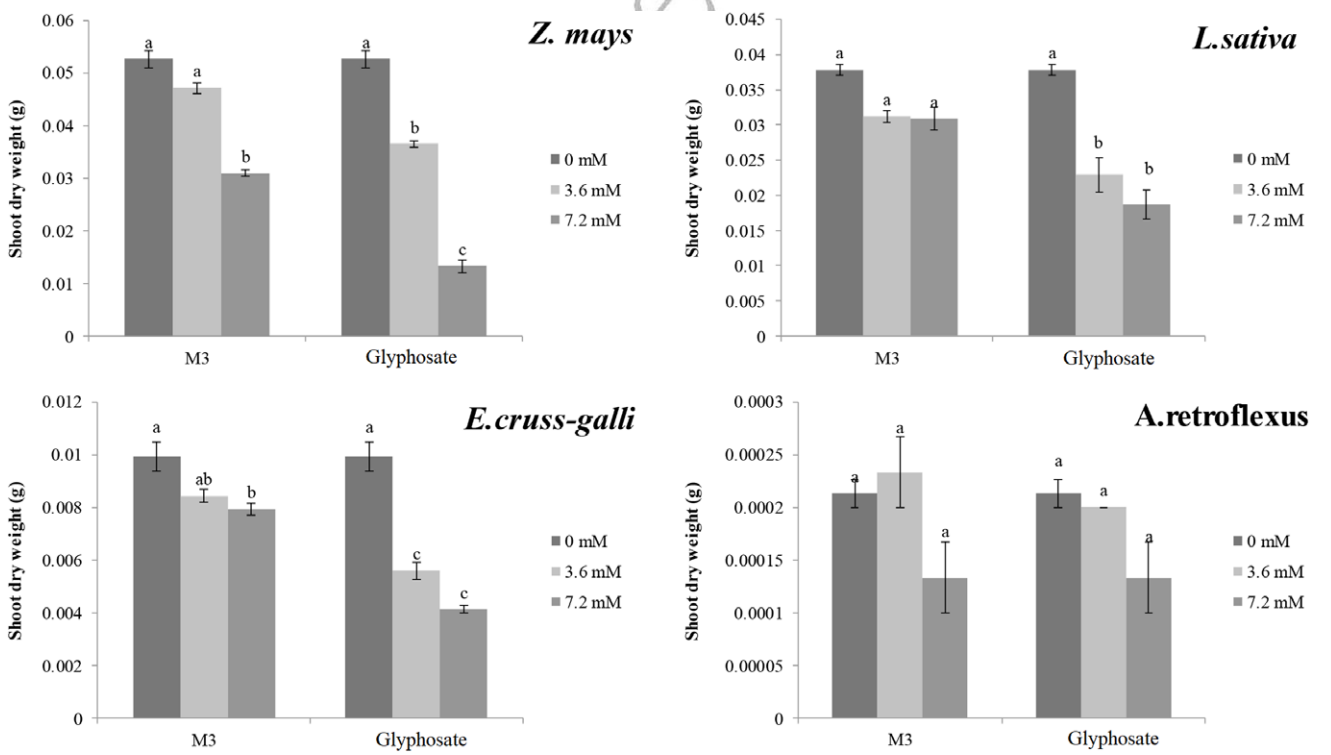


Figure 7. Dry weight (g) of *Z. mays*, *L. sativa*, *E. cruss-galli* and *A. retroflexus* exposed to 0, 3.6 or 7.2 mM **M3** or glyphosate for 7 days. Different letters within species indicate significant differences at $P < 0.05$ (Tukey's test, $n = 10$).

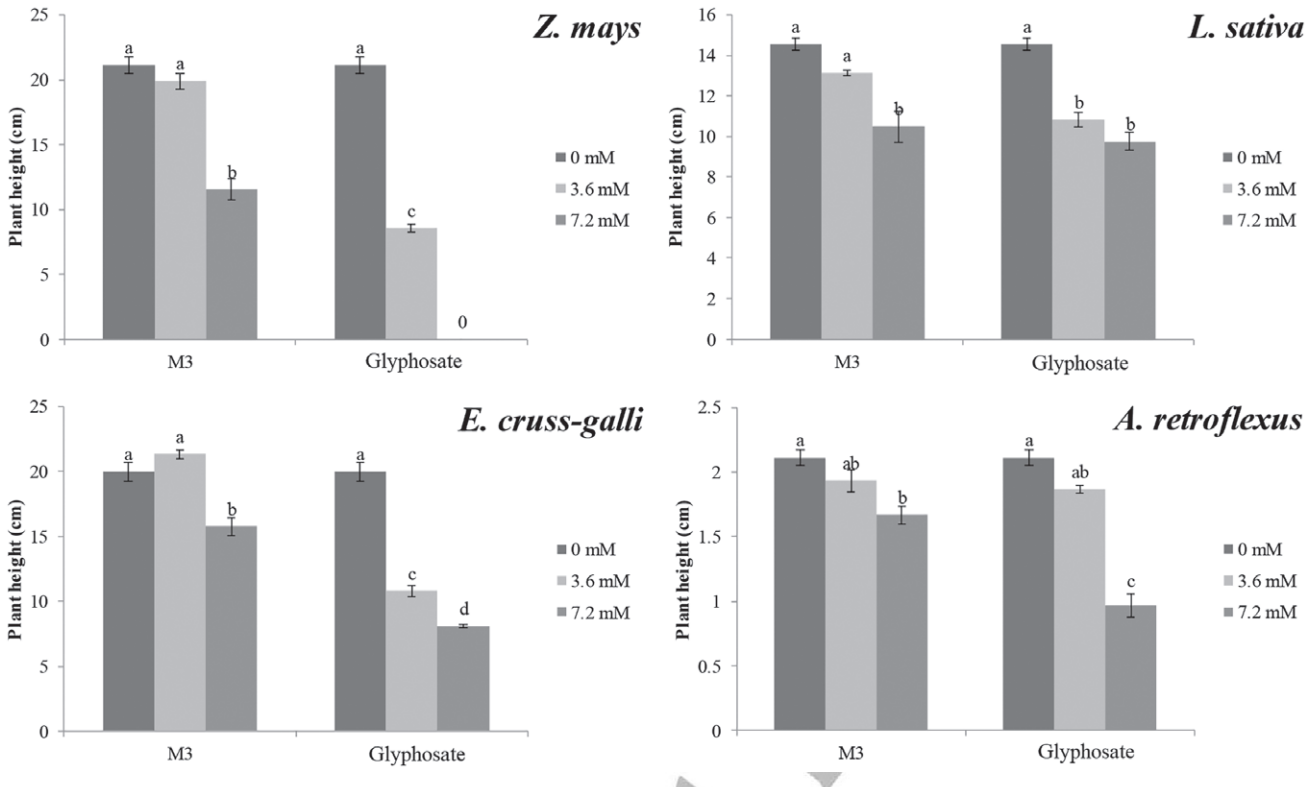


Figure 8. Plant height (cm) of *Z. mays*, *L. sativa*, *E. cruss-galli* and *A. retroflexus* exposed to 0, 3.6 or 7.2 mM **M3** or glyphosate for 7 days. Different letters within species indicate significant differences at $P < 0.05$ (Tukey's test, $n = 10$).

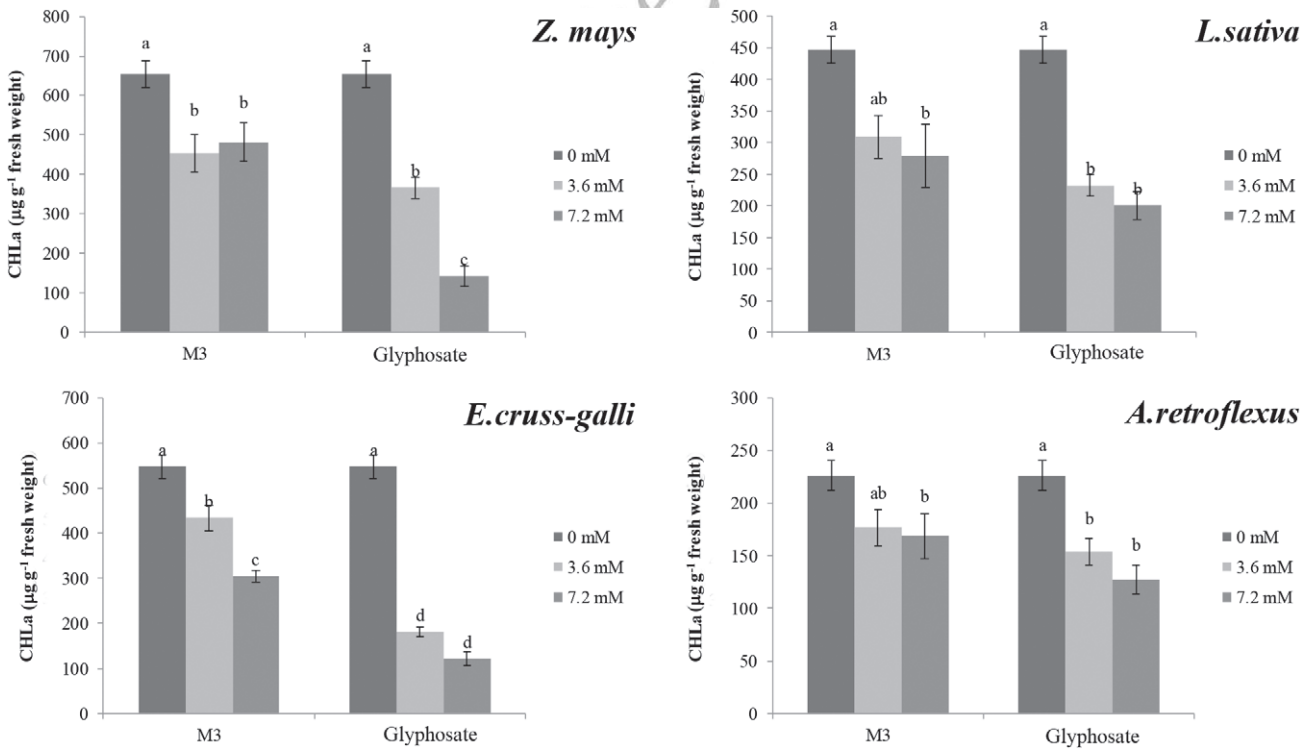


Figure 9. Chlorophyll a content (µg g^{-1} shoot fresh) of *Z. mays*, *L. sativa*, *E. cruss-galli* and *A. retroflexus* exposed to 0, 3.6 or 7.2 mM **M3** or glyphosate for 7 days. Different letters within species indicate significant differences at $P < 0.05$ (Tukey's test, $n = 10$).

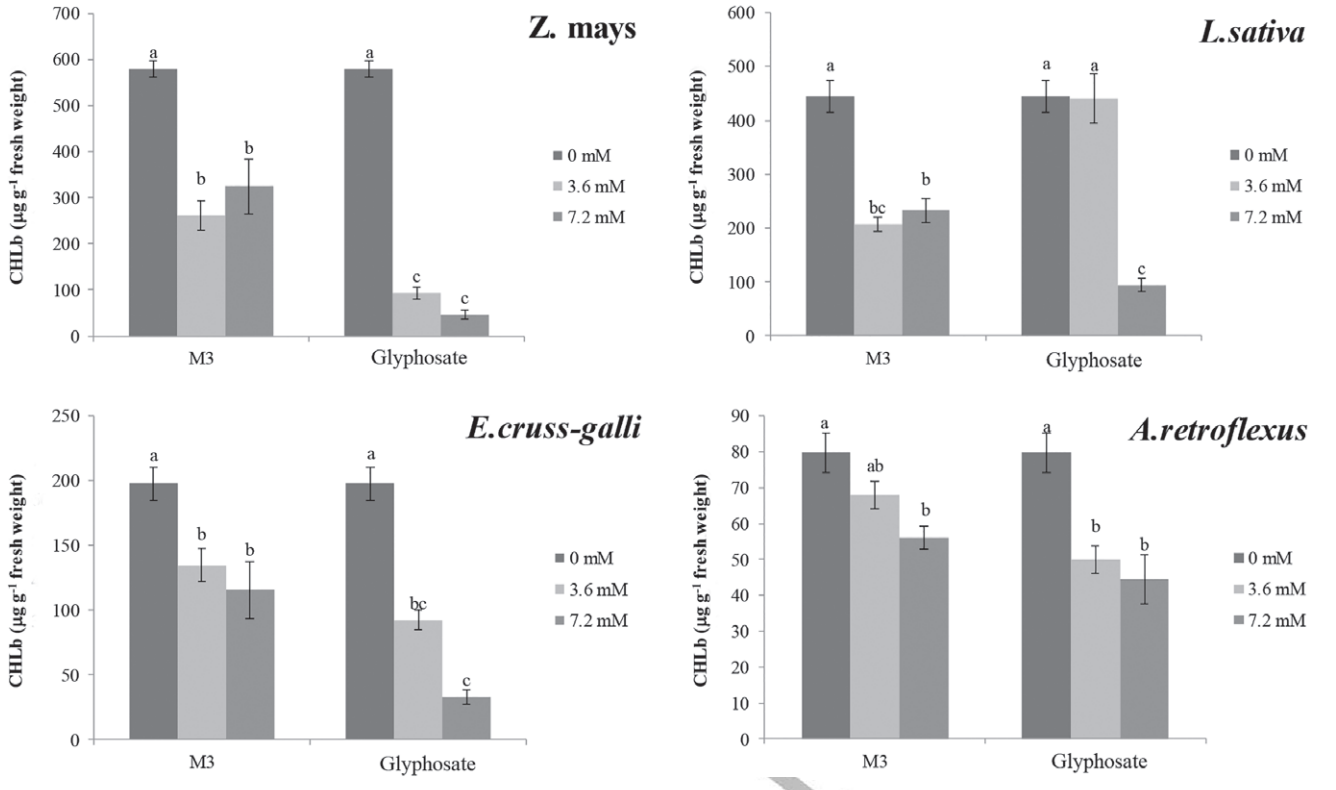


Figure 10. Chlorophyll b content (µg g^{-1} shoot fresh) of *Z. mays*, *L. sativa*, *E. cruss-galli* and *A. retroflexus* exposed to 0, 3.6 or 7.2 mM **M3** or glyphosate for 7 days. Different letters within species indicate significant differences at $P < 0.05$ (Tukey's test, $n = 10$).

total response, was calculated. The results showed that all these molecules exhibited a high phytotoxicity at <466 µM concentrations. In particular, TRL was strongly reduced at concentrations ranged from 12 to 466 µM, while lower concentrations, ranging from 10 to 145 µM, were able to cause the SFW and NRL reduction (Table 1). Among the benzofuran derivatives, **M3** appeared the most effective, showing ED_{50} values for SFW, TRL and NLR at <20 µM concentration (Fig. 5 and Table 1). By contrast, **M5** resulted the less effective, while the other molecules showed different effects based on the parameter taken into account (Table 1).

3.2 *In vivo* bioassays on crops and weeds: M3 *vs* glyphosate

Due to its higher phytotoxicity, **M3** was chosen for the *in vivo* assays on two crops (maize and lettuce, monocot and dicot, respectively) and two weeds (*E. crus-galli* and *A. retroflexus*, monocot and dicot, respectively). The **M3** effectiveness was compared with that of glyphosate based on biomass production (shoot fresh and dry weights, SFW and SDW) and photosynthetic pigments (chlorophyll a and b, carotenoids content). All showed a significant reduction after treatment with both the molecules in both crops and weeds. In particular, a significant SFW reduction (52%) was observed in maize at the highest **M3** concentration (7.2 mM), even though lower compared to that caused by commercial herbicide (85%). This inhibitory effect on fresh weight was also evident, at lower extent, in the other species, resulting in a reduction of 20, 24, and 30% compared to the control in *A. retroflexus, L. sativa*, and *E. cruss-galli*, respectively. By comparison, the glyphosate was able to reduce significantly SFW also at the lowest concentration (3.6 mM) (Fig. 6). Shoot dry weight (g) was less affected by **M3** at the lowest concentration, while glyphosate confirmed greater efficacy being able to reduce SDW already at 3.6 µM in all the species except for *A. retroflexus*, which did not appear to be affected by both molecules (Fig. 7). At the highest concentration, **M3** was able to reduce SDW in maize and *E. crus-galli* (41 and 21% compared to the control, respectively) but not lettuce (Fig. 7).

After 7 days of treatment, a significant decrease in stem length was observed (Fig. 8). In particular, **M3** caused a reduction of 45, 28, 22, and 21% in maize, lettuce, *E. crus-galli* and *A. retroflexus*, respectively, at the highest concentration with no significant effects observed at the lowest one (Fig. 8). By contrast, the commercial herbicide showed a high phytotoxicity on maize and *E. crus-galli* at the lowest concentration (3.2 mM), causing plant death in maize at the highest concentration (Fig. 8). Finally, in all the treated plants, both **M3** and glyphosate treatment significantly reduced all the pigments content (chlorophyll a and b, carotenoids) at all the concentrations (Figs. 9–11).

4 DISCUSSION

Benzofuran derivatives constitute a major group of biologically active heterocyclic compounds among natural and synthetic products.[31] The benzofuran core is present in many biologically active compounds, characterized by antifungal, insecticidal, antioxidant, antiviral and anticancer activities.[32,33] For this reason, benzofuran has also been introduced as the core to develop new herbicides as reported in recent literature.[19,34,35] Recently, the investigation of methods for developing novel benzofuran derivatives with herbicidal activity has become an important goal to develop new natural-inspired herbicides.

In this paper, we have assessed the potential herbicidal activity of some synthetic benzofuran-2-acetic esters **M1-M5**, synthesized according to Figure 1. All five benzofuran derivatives showed

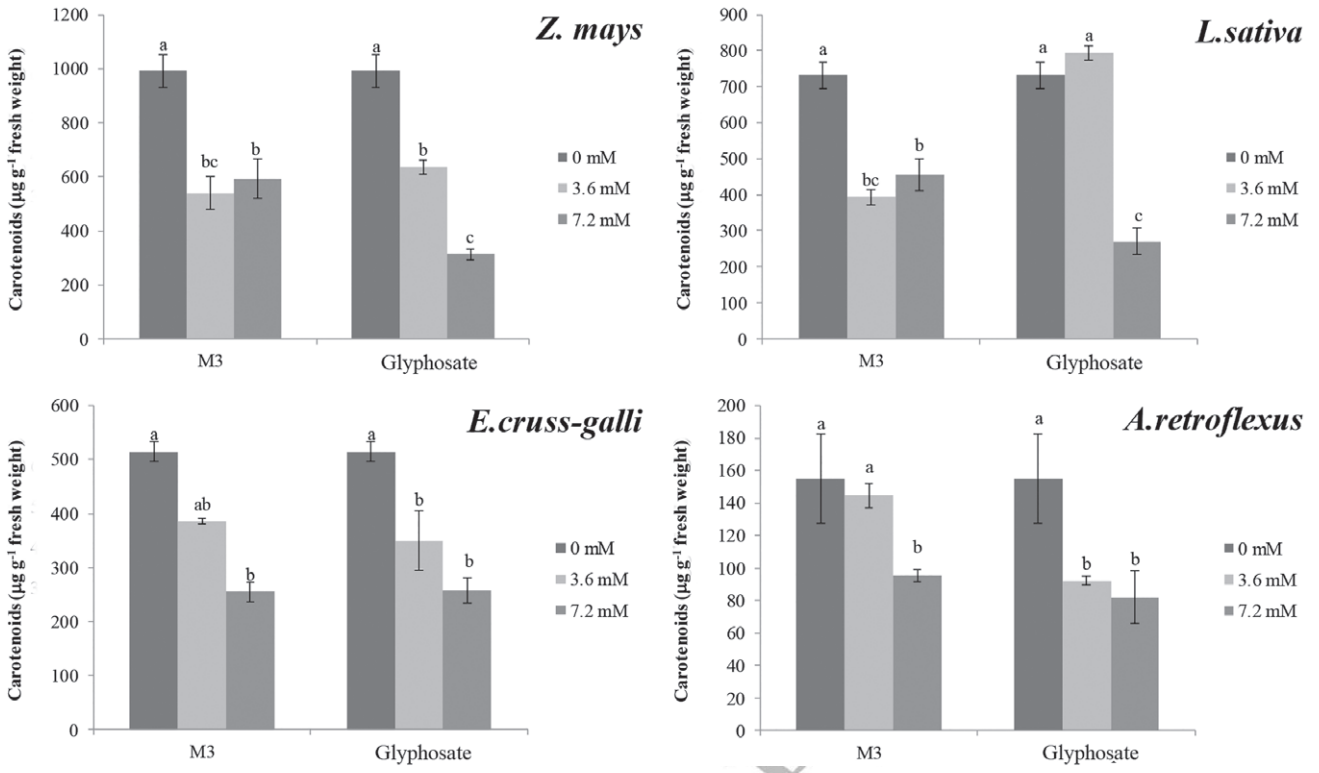


Figure 11. Carotenoid content (μg g^{-1} shoot fresh) of *Z. mays*, *L. sativa*, *E. cruss-galli* and *A. retroflexus* exposed to 0, 3.6 or 7.2 mM **M3** or glyphosate for 7 days. Different letters within species indicate significant differences at $P < 0.05$ (Tukey's test, $n = 10$).

a high phytotoxic potential, inhibiting biomass production (SFW) and reducing shoot pigment content in *Arabidopsis*. These effects suggested that these compounds could limit photosynthesis causing subsequent plant growth inhibition. Interestingly, pigments have often been used as biomarkers for new molecules with herbicidal activity in crops and model plants.[36,37] Fai *et al.* demonstrated that some herbicides caused chlorophyll inhibition blocking its synthesis.[38] However, this may not be the only cause because pigment content reduction could be determined by a chemically-induced degradation or an oxidative stress induced by benzofuran derivatives. The effects induced by benzofurans were dose- and molecule-dependent for all the pigments. Carotenoids appeared to be more sensitive than both Chla and Chlb. As known, carotenoids play an important role to overcome oxidative stress,[39] quenching reactive oxygen species (ROS) and stabilizing photosynthetic complexes.[40–42] Furthermore, carotenoids act as 'energy reducing agents' for capturing excess energy during photosynthesis, which in turn destroys membranes of cells and organelles such as chloroplasts. Therefore, carotenoid reduction and ROS production could be the cause of chlorophyll biosynthesis inhibition and, consequently, of chlorotic and less developed leaves as observed in *Arabidopsis* seedlings treated with all benzofurans **M1-M5**. Similar effects on plant biomass and pigment content were previously observed with other compound classes.[17,18]

To understand the different effectiveness of these chemicals, the ED_{50} of SFW, TRL and NLR were compared. These values confirmed the strong inhibitory activity of all the molecules underlying also their significant different efficacy. Among them, **M3** was the most effective, showing the lowest ED_{50} values for each parameter taken into account. It is well known that the presence of substituents in the aromatic ring may affect phytotoxicity. For example, the hydroxylation of *trans*-cinnamic acid decreased ion uptake ability,[39] and the position and/or the isomerization of the substitution group made *cis*-cinnamic acid 10 times more active than *trans*-cinnamic acid in *Arabidopsis* root growth inhibition.[40] Furthermore, lactonization increased the effect of coumarin making it a stronger inhibitor than *trans*-cinnamic acid in the germination process.[41] Comparing the chemical structure of the five benzofurans, **M3** shows a methoxy substituent at the C-5 position, which might be responsible for its higher phytotoxicity. For this reason, **M3** was chosen to be compared with glyphosate, the most common herbicide used in agriculture on several crop and weed species.

The *in vivo* bioassay results indicate that **M3** possesses a moderate/good herbicidal efficacy, highlighting also a certain selectivity against monocots, as reported for other compounds containing the benzofuran moiety.[35] Despite the higher effectiveness of glyphosate, **M3** caused a significant plant growth inhibition mainly at the highest concentration (7.2 mM). Moreover, the results show a strong effect on the photosynthetic pigments as already observed in *Arabidopsis*, suggesting that the **M3** target could be the shoots, and consequently, it was more effective in post-emergency (spray treatment on sprout).

5 CONCLUSIONS

In conclusion, we have found that readily available benzofuran-2-acetic esters possess a high herbicidal activity even at low doses. In particular, all the molecules assayed *in vitro* strongly affected the growth and development of the model species *Arabidopsis thaliana* affecting both shoot and root growth and development. The results obtained suggest that these natural-like molecules represent a promising pharmacophore for the development of new agrochemicals.

For future applications, in order to improve the efficacy of these molecules, benzofuran-2-acetic esters could be formulated using adjuvants to reduce the surface tension between the spray droplet and the leaf surface and to improve their penetration through leaf cuticle.

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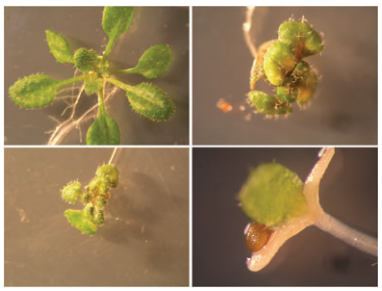
Research Article

There is an increasing need to develop new 'bio-inspired' herbicides. This article shows how readily available benzofuran-2-acetic esters constitute a new class of synthetic compounds with significant herbicidal activity.



Benzofuran-2-acetic esters as a new class of natural-like herbicides

Fabrizio Araniti, Raffaella Mancuso, Antonio Lupini, Francesco Sunseri, Maria Rosa Abenavoli and Bartolo Gabriele

