NJC

PAPER

Cite this: *New J. Chem.*, 2021, **45**, 6344

# Glycine betaine-based ionic liquids and their influence on bacteria, fungi, insects and plants†

Damian Krystian Kaczmarek, *[a] Daniela Gwiazdowska,[b] Krzysztof Juś,[b]
Tomasz Klejdysz,[c] Marta Wojcieszak,[a] Katarzyna Materna [a] and Juliusz Pernak [a]

Received 30th January 2021,
Accepted 16th March 2021

DOI: 10.1039/d1nj00498k

rsc.li/njc

A new group of bioinspired ionic liquids (ILs) based on glycine betaine and natural or synthetic anions was synthesized. The developed synthesis methods enabled the preparation of designed salts with high yields. The melting points for 17 of the 21 betaine-based salts were below 100 °C, allowing them to be classified as ionic liquids. Moreover, the solubilities of the novel salts in water and organic solvents of different polarities were examined, and their surface activity was determined. In the greenhouse experiment, all ILs were used as pesticide adjuvants, and their impact on the herbicidal activity of iodosulfuron-methyl was determined. Additionally, the effects of the obtained salts on the deterrent properties towards pests as well as on toxicity to microorganisms and plants were determined. It turned out that most of the ILs were weak feeding deterrents; however, their toxicity to the examined organisms was relatively low. The conclusion is that some of the presented salts are high-quality pesticide adjuvants that are safe for the environment and exhibit potential weak activity towards storage pests. An essential aspect of this work was also the correlation of herbicidal activity with the wettability of hydrophobic surfaces.

## Introduction

Since crop cultivation started on an industrial scale, various substances have been used to increase yields. The application of many active substances simultaneously and their inappropriate usage has resulted in negative effects on the environment. Inappropriate application of plant protection products increases their accumulation in the soil, leads to contamination of groundwater, rivers and lakes, and increases the resistance of weeds and insects to herbicides, insecticides or antifeedants.[1] Therefore, in recent years, large-scale research has been conducted to resolve these problems. Currently, challenges have been addressed by the use of natural compounds to obtain new products that will reduce the pollution of our planet.[2,3]

The latest studies indicate a significant increase in interest in natural compounds in agrotechnical treatments. The main focus is on glycine betaine, which is an inexpensive compound used for the synthesis of many new biosubstances that have a reduced impact on living organisms and the environment.[4] Currently, glycine betaine is applied in medicine,[5,6] cosmetics,[7] livestock breeding[8,9] or scientific research.[10] Due to both the structure and properties of glycine betaine, glycine betaine has become an essential source of cations in the synthesis of biobased quaternary ammonium salts (QASs) and ionic liquids (ILs).[11] Furthermore, ILs containing betainium cations or their derivatives enable novel products to be obtained that exhibit rationally designed physicochemical properties and biological activity.[12] Betaine-based ionic liquids belong to the third generation of ILs,[13] which are very important chemical compounds due to their biological activity. This property has been used to obtain potential substitutes for active substances in pharmaceuticals (drugs or active substance carriers),[14] medicines (used in cancer therapy or dentistry),[15] and agrochemicals (herbicides, fungicides, feeding deterrents, or adjuvants).[16,17] Unfortunately, in 2018 and 2020, alarming reports have reported that glycine betaine reacting with pelargonic acid or indole-3-butyric acid did not lead to the production of ILs but resulted in binary mixtures.[18,19] However, Pernak and coworkers noted a different reaction character when replacing a methyl substituent at a quaternary nitrogen atom with a dodecyl substituent.[20] This modification of the structure of glycine betaine

---

[a] *Department of Chemical Technology, Poznan University of Technology, ul. Berdychowo 4, Poznan 60-965, Poland. E-mail: damian.rom.kaczmarek@doctorate.put.poznan.pl*

[b] *Department of Natural Science and Quality Assurance, Poznan University of Economics and Business, Al. Niepodległości 10, Poznan 61-875, Poland*

[c] *Institute of Plant Protection – National Research Institute, ul. W. Węgorka 20 Poznan 60-318, Poland*

† Electronic supplementary information (ESI) available: Experimental section; Elemental analysis (Table S1); NMR and IR spectra of salts (Fig. S1–S63); surface tension of the aqueous solutions of the obtained salts (Fig. S64–S66); deterrent activity (Table S2); germination test (Tables S3 and S4); microbial toxicity assay (Table S5–S7). See DOI: 10.1039/d1nj00498k

resulted in a change in the reaction path and yielded suitable ILs. Therefore, it is essential to carry out detailed analyses of the products obtained with betaine derivatives.

This study focused on QASs and ILs containing glycine betaine and its derivatives (butylbetaine and dodecylbetaine) as cations and natural (glycolate, D-gluconate, L-pyroglutamate, cholate, and α-ketoglutarate) or synthetic (dioctyl sulfosuccinate, docusate; bis(2-ethylhexyl)phosphate, DEHPA) anions. The combination of the abovementioned ions resulted in new products that increase the effectiveness of biologically active substances. Furthermore, they perfectly fit into the current trend for natural origin compounds that have a negligible impact on the environment. Moreover, the previous studies have already indicated the significant influence of functional groups and anion structure on the application potential of adjuvant ILs. However, this is the first publication where the effect of alkyl substituent length in the cation of pesticide adjuvant ILs on improving weed control efficacy was demonstrated. We also highlighted that additives to tank mixes, apart from improving surface activity, can further contribute to pest control. This innovative solution potentially eliminates the need for using additional active ingredients.

The first stage of the study included a description of the efficient synthesis and purification methods for new QASs and ILs. Then, the influence of alkyl substituents in the cation and anion structure on the surface activity, thermal stability, phase transformations, and solubility were determined. Additional studies were conducted to define the effect of the obtained QASs and ILs on biological activity (use of synthesized compounds as adjuvants for herbicides or feeding deterrents) as well as to determine the toxicity to plants, fungi, bacteria, and warehouse insects. The results of these studies ultimately present the best combination of cations and anions, resulting in a new pesticide additive that will be environmentally friendly.

## Results and discussion

### Synthesis

The main challenge during the design of a series of QASs or ILs with varying anion structures is to develop an efficient synthesis method for the entire group. The optimal solution would be to select a unified method that enables the production of all salts in the same installation. Moreover, this solution seems to be crucial for the urgent global economic changes observed worldwide and the rising demand for certain products. Such a solution would allow, among other things, the launching an additional production line and the prevention of supply shortages. Therefore, we have developed a method of synthesizing salts with glycolate (**a**), D-gluconate (**b**), α-ketoglutarate (**c**), L-pyroglutamate (**d**), cholate (**e**), docusate (**f**) and DEHPA (**g**) anions and betainium (**1**), butylbetainium (**2**) and dodecylbetainium (**3**) cations to ensure that both synthesis methods result in all products described (Fig. 1). However, QASs with cholate anions cannot be obtained by a metathesis reaction because of the difficulties in removing the byproduct.[21]

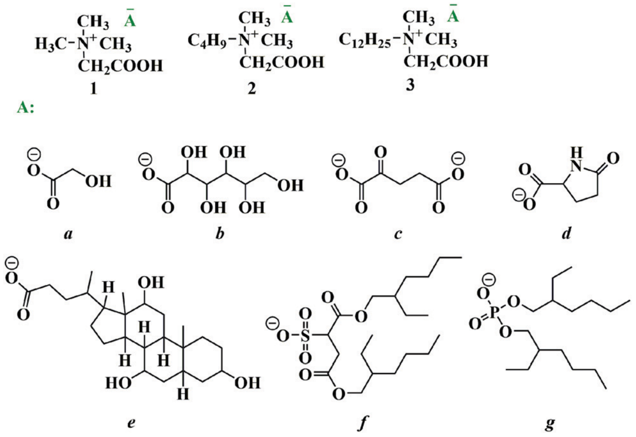
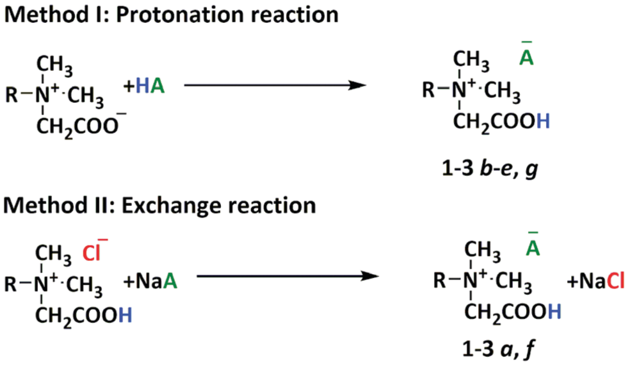


Fig. 1 Structure of ILs with the anion structures.

The most economical method was to use the zwitterion form of glycine betaine, butylbetaine, and dodecylbetaine, where no byproducts were produced and the only residue in the process was the solvent ethanol (Scheme 1 – Method I). After the synthesis process, the remaining ethanol did not contain any hazardous impurities and could be recovered in a simple process and reused without any treatment. This operation may reduce the generation of pollutants and represents part of the recent trend in the development of closed-loop technology. One of the major disadvantages of this method is the necessity of precisely adding both substrates in an equal ratio during the reaction to avoid the purification step when unreacted substrates are present. By contrast, the method based on an exchange reaction did not require precision, although an appropriate method of purification of the product from unreacted substrates and byproducts had to be defined (Scheme 1 – Method II). Therefore, taking into account the above information, we recommend using method I.

The developed and described methods of synthesis in the experimental part in the ESI,† resulted in products with high yields exceeding 82%, as shown in Table 1. Twenty-one salts were obtained as a result of the reactions (see structures in Fig. 1); only salts **1c** and **e** were described in patents, and **1f** was described in publications.[22–24] The water content in all products was assayed by Karl Fischer measurements, and the



Scheme 1 Methods of synthesizing ILs.

Table 1 Salts synthesized with alkylbetainium cations

| No. | –R | Anion | Yield [%] | State at 25 °C | No. | –R | Anion | Yield [%] | State at 25 °C |
|---|---|---|---|---|---|---|---|---|---|
| **1a** | $-CH_3$ | Glycolate | 91 | Wax | **1e** | $-CH_3$ | Cholate | 97 | Solid |
| **2a** | $-C_4H_9$ | | 90 | Wax | **2e** | $-C_4H_9$ | | 89 | Solid |
| **3a** | $-C_{12}H_{25}$ | | 93 | Solid | **3e** | $-C_{12}H_{25}$ | | 95 | Solid |
| **1b** | $-CH_3$ | D-Gluconate | 97 | Wax | **1f** | $-CH_3$ | Docusate | 99 | Solid |
| **2b** | $-C_4H_9$ | | 91 | Wax | **2f** | $-C_4H_9$ | | 83 | Wax |
| **3b** | $-C_{12}H_{25}$ | | 92 | Solid | **3f** | $-C_{12}H_{25}$ | | 92 | Wax |
| **1c** | $-CH_3$ | α-Ketoglutarate | 93 | Wax | **1g** | $-CH_3$ | DEHPA[a] | 94 | Wax |
| **2c** | $-C_4H_9$ | | 70 | Wax | **2g** | $-C_4H_9$ | | 92 | Wax |
| **3c** | $-C_{12}H_{25}$ | | 82 | Wax | **3g** | $-C_{12}H_{25}$ | | 98 | Wax |
| **1d** | $-CH_3$ | L-Pyroglutamate | 95 | Wax | | | | | |
| **2d** | $-C_4H_9$ | | 90 | Wax | | | | | |
| **3d** | $-C_{12}H_{25}$ | | 98 | Solid | | | | | |

[a] Bis(2-ethylhexyl)phosphate anion.

value was less than 500 ppm. At 25 °C, the obtained salts appeared in the form of wax (**1–2a**, **1–2b**, **1–3c**, **1–2d**, **2–3f**, **1–3g**) or solid (**3a**, **3b**, **3d**, **1–3e**, **1f**).

The resulting IR, $^1$H NMR and $^{13}$C NMR spectra and elementary analysis allowed us to confirm the structures of the obtained salts, as described in the ESI† (Fig. S1–S63 and Table S1 in the ESI†). In the $^1$H and $^{13}$C NMR spectra, the expected signals from methylene groups in the cation were present in the following chemical shift ranges: 3.28–3.37 ppm ($^1$H NMR) and 52.0–54.3 ppm ($^{13}$C NMR). Moreover, characteristic signals from each anion were observed in the respective $^1$H NMR spectra with correct integration: 4.09 ppm (glycolate anion – **a**, $-CH_2$ group), 4.57 ppm (D-gluconate anion – **b**, –CH group), 2.61–2.63 ppm (α-ketoglutarate anion – **c**, $-CH_2$ group), 4.25–4.27 ppm (L-pyroglutamate anion – **d**, –CH group), 2.26 ppm (cholate anion – **e**, $-CH_2$ group), 4.05 ppm (docusate anion – **f**, –CH group), and 3.82–3.87 ppm (DEHPA anion – **g**, $-CH_2$ group). The spectrum analysis also showed no signs of decomposition of the analyzed products. Additionally, the analysis of the IR spectra allowed us to further verify the structure of the obtained salts. A characteristically significant increase in the intensity of bands at 2800–3000 cm$^{-1}$ was observed, which corresponded to the length of the alkyl substituent in the cation. More importantly, however, was the identification of the characteristic band at 1602–1739 cm$^{-1}$, which indicated the presence of the acid form (–COOH) and the salt form ($-COO^-$) of the carboxylic groups. Two signals were observed for salts **1–3a–c** and **e**, whereas a single broad signal was observed for **1–3d**, **f** and **g**. The reason for the discrepancy was the more complex structures that contributed to the overlap of signals.[25] A combination of NMR and IR spectroscopic studies was used to elucidate the structure and confirm that the hydrogen atom is attached to the carboxyl group of alkylbetainium cations. This is indicated by a significant change in the chemical shifts of the products relative to the initial substrates and the above-mentioned presence of bands at the appropriate wavelength on the analysed spectra.

Table 2 Thermal properties of salts with alkylbetainium cations

| No. | $T_g$ [°C] | $T_c$ [°C] | $T_m$ [°C] | $T_{0.05}$ [°C] | $T_{0.5}$ [°C] | No. | $T_g$ [°C] | $T_c$ [°C] | $T_m$ [°C] | $T_{0.05}$ [°C] | $T_{0.5}$ [°C] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **1a** | −28 | — | — | 194 | 253 | **1e** | — | — | — | 250[c] | 374[c] |
| **2a** | −40 | — | — | 182 | 234 | **2e** | 39 | — | — | 211[d] | 369[d] |
| **3a** | — | 108[a] | 117[b] | 184 | 228 | **3e** | 40 | 107[b] | 118[b] | 210[e] | 352[e] |
| **1b** | −8 | — | — | 204 | 247 | **1f** | −61 | 36[b] | 73[b] | 265 | 314 |
| **2b** | −14 | — | — | 201 | 246 | **2f** | −68 | — | — | 242 | 299 |
| **3b** | — | 70[a] | 96[b] | 207 | 246 | **3f** | — | −23[b]/ 57[b] | −10[b]/ 65[b] | 250 | 295 |
| **1c** | 14 | — | — | 178 | 249 | **1g** | — | — | — | 196 | 262 |
| **2c** | −18 | — | — | 169 | 229 | **2g** | — | — | — | 186 | 259 |
| **3c** | −16 | — | — | 181 | 236 | **3g** | — | 107[b] | 118[b] | 184 | 255 |
| **1d** | 3 | — | — | 218 | 257 | | | | | | |
| **2d** | −12 | — | — | 183 | 251 | | | | | | |
| **3d** | — | 108[a] | 103[b] | 197 | 244 | | | | | | |

$T_g$ – glass transition temperature; $T_c$ – temperature of crystallization; $T_m$ – melting point; $T_{0.05}$ – decomposition temperature of 5%; $T_{0.5}$ – decomposition temperature of 50%. [a] During the cycle of cooling. [b] During the cycle of heating. [c] Two steps of decomposition: 1st – 186.96–299.37 °C (19.93%); 2nd – 300.01–469.91 °C (70.28%). [d] Two steps of decomposition: 1st – 155.40–291.77 °C (24.96%); 2nd – 291.77–467.49 °C (69.28%). [e] Two steps of decomposition: 1st – 141.23–294.86 °C (36.14%); 2nd – 295.50–461.70 °C (61.50%).

## Thermal properties

Thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC) data for the salts are presented in Table 2 (the methodology is described in the ESI†). The melting point of the four products obtained (**3a**, **d** and **e**) exceeded 100 °C; therefore, they were considered QASs. Furthermore, salts **1–2e** were solid over the whole range of measurements and therefore were classified as quaternary ammonium salts, whereas the other salts with a melting point below 100 °C were classified as ILs. Three salts (**1e**, **1g**, and **2g**) had no phase transitions within the analyzed temperature range, and ten of the synthesized salts (**1–2a–b**, **1–3c**, **1–2d** and **2e**) had only a glass transition temperature ($T_g$).

Further analysis indicated that for salts **3a**, **b** and **d**, only common phase transitions occurred ($T_c$ = 108 °C and $T_m$ = 117 °C, $T_c$ = 70 °C and $T_m$ = 96 °C, and $T_c$ = 108 °C and $T_m$ = 103 °C, respectively). Salts **3f** and **g** exhibited a melting point and crystallization temperature only in the heating cycle. In the case of **3e**, during the heating cycle, a glass transition followed by cold crystallization and a melting point was observed. The appearance of this unexpected cold crystallization is the result of salt supercooling behavior.[26] Moreover, compounds with differences in one substituent in the cation, namely, hydroxyl (–OH) or carboxyl (–COOH) group, present a large change in the measured parameters of phase transitions, which may be related to the higher hygroscopicity.[21] Additionally, information is available about the influence of intermolecular hydrogen bonds on the aberration of the normal phase transitions, which may explain the occurrence of cold crystallization or two phase transitions in one cycle.[27]

The thermogravimetric analysis results showed that all obtained salts exhibited simple thermal decomposition in one stage except for QASs **1–3e** (Table 2). Therefore, only the salts with cholate anions were characterized by two-step decomposition, regardless of the alkyl chain length. In addition, the results presented in Table 2 show that the lowest decomposition temperature of $T_{0.05}$ was observed for salts with butyl groups (**2**) and that the highest was observed for salts with methyl substitutions (**1**). The collected data showed that this parameter appears to be poorly correlated with the length of the alkyl substituent. However, a stronger tendency may occur at decomposition temperatures ($T_{0.5}$), which appear to decrease gradually with alkyl chain elongation. Natural origin anions (**a–d**) and the DEHPA anion (**g**) exhibited significantly lower thermal stability than cholate anions (**e**) and docusate anions (**f**), as confirmed by previous reports (except for salts **1–3g**).

### Solubility

An essential aspect of the analysis of all novel compounds during characterization is to determine their solubility. Providing information about this parameter leads to the selection of a suitable solvent for the synthesis, purification or preparation of a useful formulation. Considering the solubility of the obtained salts, including the influence of their structure, information about the solvent polarity was important.[28,29] The analysis also included information about the dielectric constant and its impact on the solvent's ability to dissolve a selected class of compounds.[30,31]

Our research clearly showed that the solubility in water and the selected organic solvents was strongly dependent on both the anions and cations. The elongation of one of the substituents in the cation caused minor changes in solubility, which was linked to an increase in the size of cations and effective charge density, thus reducing the polarity of the tested ILs.[32] Such a result was obtained in the case of salts **1–3a–d**, where alkyl chain elongation decreased the solubility in water. However, a reversed effect was observed in ethyl acetate, which is a weakly polar solvent, for ILs **1–3f**, where the solubility increased with increasing cation size (Table 3).

Moreover, the solubility test pointed out a significant effect of the anion on the solubility in solvents of varied polarity. The structures of anions did not have an influence on the solubility in acetonitrile, acetone, 2-propanol, toluene or hexane. However, D-gluconate (**b**) and cholate (**e**) anions had increased solubility in DMSO, and this behavior was associated with the presence of hydroxyl (–OH) groups in the structure of those anions, which contributed to a strong interaction between this solvent and the anion by forming hydrogen bonds and generating an appropriate dipole moment.[33] Furthermore, an increased solubility in chloroform has been observed for salts **1–3c**, **f** and **g**. The differences observed in the solubility of those salts correspond well with the theory that QASs are mostly immiscible with liquids characterized by low dielectric constants. Therefore, none of the obtained compounds were soluble in hexane or toluene. In contrast, chloroform, as the solvent with the highest dielectric constant, increased the solubility of these products.[30]

Note that salts with cholate (**e**), docusate (**f**) and DEHPA (**g**) anions did not dissolve in water owing to their hydrophobicity,

Table 3 Solubilities of the synthesized salts **1–3a–g** at 25 °C

| No. | Water | Methanol | DMSO | Acetonitrile | Acetone | 2-propanol | Ethyl acetate | Chloroform | Toluene | Hexane |
|---|---|---|---|---|---|---|---|---|---|---|
| **1a** | + | + | − | − | − | − | − | − | − | − |
| **2a** | + | + | − | − | − | − | − | − | − | − |
| **3a** | ± | + | − | − | − | − | − | − | − | − |
| **1b** | + | ± | ± | − | − | − | − | − | − | − |
| **2b** | ± | ± | ± | − | − | − | − | − | − | − |
| **3b** | ± | ± | ± | − | − | − | − | − | − | − |
| **1c** | + | + | − | − | − | − | − | ± | − | − |
| **2c** | + | + | − | − | − | − | − | ± | − | − |
| **3c** | ± | + | − | − | − | − | − | ± | − | − |
| **1d** | + | + | − | − | − | − | − | − | − | − |
| **2d** | + | + | − | − | − | − | − | − | − | − |
| **3d** | ± | + | − | − | − | − | − | − | − | − |
| **1e** | − | ± | + | − | − | − | − | − | − | − |
| **2e** | − | ± | + | − | − | − | − | − | − | − |
| **3e** | − | ± | ± | − | − | − | − | − | − | − |
| **1f** | − | + | − | − | − | − | − | + | − | − |
| **2f** | − | + | − | − | − | − | ± | + | − | − |
| **3f** | ± | + | − | − | − | − | + | + | − | − |
| **1g** | − | + | − | − | − | − | − | ± | − | − |
| **2g** | − | + | − | − | − | − | − | ± | − | − |
| **3g** | − | + | − | − | − | − | − | ± | − | − |

+: Good solubility. ±: limited solubility. −: poor solubility.

and supplementary studies had to be conducted to determine the form of application of these salts in biological experiments. Studies confirmed that 0.1 g of salts **1–3f–g** and **3e** could be dissolved in 100 mL of water, while salts **1–2e** were insoluble. Therefore, in further studies with aqueous solutions, salts **1–2e** were used as suspensions.

### Surface properties

Aqueous solutions of the obtained salts were analyzed to determine the effect of the structure on selected surface activity parameters: critical micelle concentration (CMC), surface tension at the CMC point ($\gamma_{\mathrm{CMC}}$) and contact angle at the CMC point ($\mathrm{CA_{CMC}}$) (the methodology is described in the ESI†). The salts with a–d anions and betainium (**1**) or butylbetainium (**2**) cations were nonamphiphilic compounds with no CMC. Therefore, the surface tension ($\gamma$) and contact angle (CA) were determined for salts **1–2a–d** at the highest concentration, where the compounds were fully dissolved in water. The obtained results are presented in Table 4 and Fig. S64–S66 (ESI†).

The CMC values indicated that this parameter decreased with the elongation of the alkyl substituent in the cation[34] and with the increase in anion hydrophobicity.[35,36] This correlation is well known and has been described in the literature. Moreover, there was a decrease in the concentration of aqueous solutions of salts **1–2a–d** with elongation of the alkyl substituent in the cation at the maximum content. Note also that the combination of an amphiphilic cation and amphiphilic anion had a CMC of 0.33–0.54 mmol L$^{-1}$, where salts with one surface-active ion had a CMC of 0.80–7.12 mmol L$^{-1}$.

Similarly, a trend analogous to the CMC of IL aqueous solutions was observed for surface tension at the CMC. The influence of the substituent on the surface tension was noticed for series **1–3e** and **g**, where the elongation of the alkyl substituent resulted in a decrease in the surface tension from 40–47 mN m$^{-1}$ for the methyl substituent to 28–33 mN m$^{-1}$ for the dodecyl substituent. This effect is associated with the formation of increasingly stable micelles with the elongation of the alkyl substituent, which leads to a longer relaxation time of the micelles.[37] Moreover, the structure of the anions had a significant impact on the change in surface tension. Salts with only an amphiphilic cation in their structure had a surface tension at 34–36 mN m$^{-1}$ for 0.81–3.01 mmol L$^{-1}$ (CMC), whereas two amphiphilic ions had a surface tension at 26–33 mN m$^{-1}$ for 0.33–0.54 mmol L$^{-1}$ (CMC). This is a well-known phenomenon described in the literature as a synergic effect of both ions, which results in a decreased surface tension.

Table 4 Surface activity parameters of the prepared salts

| No. | CMC [mmol L$^{-1}$] | $\gamma_{\mathrm{CMC}}$ [mN m$^{-1}$] | $\mathrm{CA_{CMC}}$ [°] | No. | CMC [mmol L$^{-1}$] | $\gamma_{\mathrm{CMC}}$ [mN m$^{-1}$] | $\mathrm{CA_{CMC}}$ [°] |
|---|---|---|---|---|---|---|---|
| **1a** | —[a] | —[a] | —[a] | **1e** | 7.12 | 46.64 | 84 ± 1 |
| **2a** | —[b] | —[b] | —[b] | **2e** | 6.75 | 39.65 | 85 ± 1 |
| **3a** | 1.62 | 35.24 | 69 ± 1 | **3e** | 0.54 | 33.00 | 51 ± 2 |
| **1b** | —[c] | —[c] | —[c] | **1f** | 1.26 | 27.31 | 35 ± 1 |
| **2b** | —[d] | —[d] | —[d] | **2f** | 0.80 | 25.91 | 36 ± 3 |
| **3b** | 3.01 | 33.77 | 61 ± 3 | **3f** | 0.33 | 25.58 | 36 ± 2 |
| **1c** | —[e] | —[e] | —[e] | **1g** | 1.71 | 40.12 | 69 ± 1 |
| **2c** | —[f] | —[f] | —[f] | **2g** | 1.59 | 37.86 | 63 ± 2 |
| **3c** | 0.81 | 35.81 | 65 ± 2 | **3g** | 0.38 | 28.39 | 48 ± 1 |
| **1d** | —[g] | —[g] | —[g] | | | | |
| **2d** | —[h] | —[h] | —[h] | | | | |
| **3d** | 1.68 | 34.74 | 69 ± 2 | | | | |

[a] $\gamma$ = 59.94 mN m$^{-1}$ and CA = 94° in maximum water concentration (626.10 mmol L$^{-1}$). [b] $\gamma$ = 46.15 mN m$^{-1}$ and CA = 69° in maximum water concentration (582.29 mmol L$^{-1}$). [c] $\gamma$ = 61.34 mN m$^{-1}$ and CA = 92° in maximum water concentration (408.71 mmol L$^{-1}$). [d] $\gamma$ = 35.35 mN m$^{-1}$ and CA = 64° in maximum water concentration (244.70 mmol L$^{-1}$). [e] $\gamma$ = 31.79 mN m$^{-1}$ and CA = 45° in maximum water concentration (593.60 mmol L$^{-1}$). [f] $\gamma$ = 35.71 mN m$^{-1}$ and CA = 64° in maximum water concentration (392.20 mmol L$^{-1}$). [g] $\gamma$ = 43.47 mN m$^{-1}$ and CA = 97° in maximum water concentration (617.20 mmol L$^{-1}$). [h] $\gamma$ = 42.54 mN m$^{-1}$ and CA = 71° in maximum water concentration (345.50 mmol L$^{-1}$).

Especially important is the surface tension values for ILs **1–3f**, where the influence of the anion on this parameter was so significant that the impact of cation structure was irrelevant to the value of this parameter; the docusate anion caused the surface tension to remain at the constant level irrespective of the length of the alkyl substituent (approximately 25 mN m$^{-1}$). Moreover, the docusate anion with some other cations (including nonamphiphilic cations) had a surface tension of 25 mN m$^{-1}$ at the CMC.[22,38] Therefore, it can be assumed that the structure of the anion reduced the surface tension to this low value and that counterions only promoted the lowering of the concentration at which this value was achieved.

Since salts **1–2a–d** had no CMC, it was not possible to compare them with salts **3a–d** and **1–2e–g**. The analysis of surface tension at the maximum concentration was only determined to assess the potential of these compounds to reduce the surface tension of water. Salts **1–2a–d** as well as salt **1b** reduce the water surface tension by approximately 10–30 mN m$^{-1}$, which is not satisfactory in relation to other salts.

Another important issue was to determine the wettability of water solutions on the hydrophobic surface of paraffin. An analysis of the contact angle results is essential if we are considering compounds that will be applied in agriculture and should remain on the plant or seed surface. Increased wettability allows for better contact and reduces the drop slippage from these surfaces.[39–41] The analysis of the results had to be divided into two parts as above: wettability analysis at the CMC for salts **3a–d** and **1–2e–g** and at the maximum concentration for ILs **1–2a–d**. In the case of salts with a CMC, the wettability of paraffin ranged from 36 to 85°, where the best wettability was recorded for ILs with docusate anions (**1–3f**). Moreover, a well-known correlation was observed for salts **1–3e** and **g**, where the contact angle of the hydrophobic surface decreased with elongation of the alkyl substituent. In contrast, the salts whose wetting angles were measured at the maximum concentration did not exhibit satisfactory parameters.

Based on the surface activity data for ILs with dodecylbetainium cations (**3a–g**) and a comparison with previously described salts with identical anions and dodecyl(2-hydroxy-ethyl)dimethylammonium cations, intriguing differences were observed between 2-carboxymethyl and 2-hydroxyethyl substituents.[21] The most notable difference was observed in the case of a–d anions, where the surface activity parameters declined and were more favorable for salts with dodecylbetainium cations (**3**). The CMC, $\gamma$ and CA values decreased by 14–27 mmol $L^{-1}$, 10–13 mN $m^{-1}$ and 12–25° (except for salts with $\alpha$-ketoglutarate anion (**c**), where no change was observed), respectively. This effect was due to the formation of stronger hydrogen bonds in molecules in which a carboxylic group was present, thus resulting in improved molecular orientation and packing at the phase boundary.[42] Moreover, the presence of a surface-active anion in the structure contributed to the limited effect of hydrogen bonding with substituents in the cation, excluding ILs with bis(2-ethylhexyl)phosphate anions. However, it will be necessary to use molecular modeling to determine these effects in further studies.

### Application in agriculture

**Adjuvant activity in pesticide formulations.** The effect of the pesticide adjuvants obtained on herbicide activity was determined by a greenhouse experiment on cornflower (*Centaurea cyanus*). Following the methodology described in the Experimental section in the ESI,† plants were sprayed with aqueous solutions of iodosulfuron-methyl sodium (ISM-Na) with adjuvant salts **1–3a–g**. Spray solutions without adjuvant (ref. 1) or with a commercially available adjuvant (Biopower, ref. 2) were used as a reference.

The results of the greenhouse experiments are presented in Fig. 2. We confirmed that the addition of an appropriately selected adjuvant was necessary to ensure high biological activity of ISM-Na. Moreover, the results showed that the compound with low surface activity (**1–2a**, **b** and **d**, as well as **1c** and **d**) resulted in a relatively low herbicidal activity (from 22 to 46% reduction in fresh weight compared to the control). The results were disappointing when comparing the 33% effectiveness of ISM-Na (without adjuvant, ref. 1) and 88% reference (Biopower, ref. 2). IL adjuvants containing one amphiphilic ion (**3a**, **b** and **d**, **2c** and **1–2g**) improved the biological activity of ISM-Na but were less successful than commercially available additives. The application of IL adjuvants composed of both amphiphilic ions (**3e–g**) ensured high effectiveness of the herbicide applied, which resulted in a reduction of cornflower fresh mass by 70–88%. Note that results similar to those for both surface-active ions were obtained by applying dianionic ionic liquid, which contains two amphiphilic cations (**3c**), and the tank mix with this IL reduced the fresh mass by 75%. Curiously, the effect of alkyl substituent length for ionic liquids with docusate anions was the lowest, which was associated with reducing the effect of the cation on the surface activity. This result leads to the conclusion that the use of IL adjuvants **3c** and **e**, which consist of both anions and cations of natural origin, is a favorable solution for achieving good herbicidal results without negative environmental impacts.

Nevertheless, favorable additives for tank mixes were ILs with the docusate anion (**f**), exhibiting excellent surface activity and low toxicity with simultaneous very high biological activity. However, Biopower was more efficient than the IL adjuvants in terms of the accelerating effect of the active substance, and it was the only adjuvant to cause plant necrobiosis approximately 3–4 days earlier.

Furthermore, a similar trend was observed when comparing the data obtained from the literature results on the influence of IL adjuvants on biological activity. Amphiphilic anions (**e–g**) together with a cation with no less than twelve carbon atoms in the alkyl chain were good additives to spray solutions used for weed control. In addition, the essential issue was that these results were achieved for various species of invasive plants, which implies that they will be useful adjuvants for application in the agricultural sector.[21,22] Another noteworthy fact is that a recent study presented ionic liquids with ISM anions and betaine-based cations. These compounds were suggested to be good herbicidal ionic liquids for oilseed rape. However, it is important to consider that this plant is sensitive to ISM; therefore, further studies need to be carried out on cornflowers or other more resistant weeds to verify whether these compounds are as efficient as our IL adjuvants.[43]

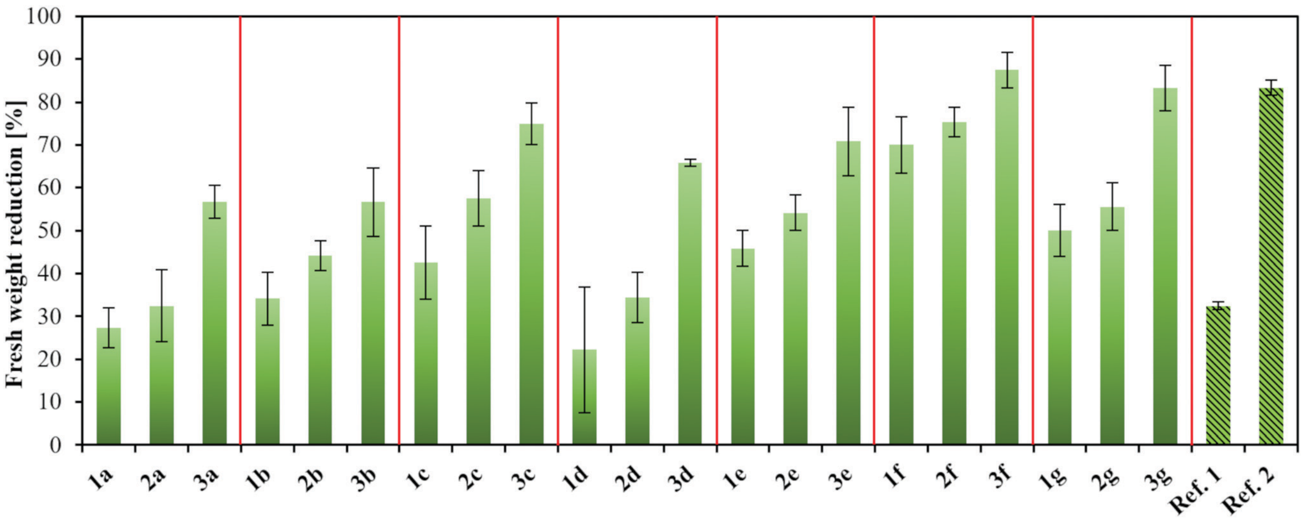


Fig. 2 Fresh weight reduction of cornflower treated with ISM-Na with and without adjuvants at 3 weeks after application; ref. 1 – without adjuvants; ref. 2 – Biopower.

**Antifeedant properties.** The deterrent activity of the synthesized salts **1–3a–g** was determined by the standard method described in the literature.[44] The control substance was azadirachtin, which is a chemical compound of natural origin with very good biological activity. The studies were carried out on beetles and larvae of common storage pests: beetles of granary weevil (*Sitophilus granarius*) and larvae of the khapra beetle (*Trogoderma granarium*). The antifeedant activity results are presented in Fig. 3. Detailed values with statistical analyses and the methodology are available in the ESI,† in Table S2.

The biological activity results with the tested storage pests indicated that ILs consisting of glycolate (**a**) or bis(2-ethylhexyl) phosphate (**g**) anions, regardless of the length of the alkyl substituent in the cation, showed very good or good deterrent activity. In contrast, the lowest repellent activity was observed for all other anions with betainium cations (**1**), exhibiting weak or hardly any effect on the feeding of both tested storage pests. Most likely, the reason for this phenomenon is the lack of betaine deterrent activity. Betaine is commonly detected in both plants and animals (in the largest amounts in sugar beets) that can be attacked by various insect species. Therefore, betaine and its derivatives may be an inert factor for insects that does not impact their receptors.[45]

On the other hand, it is worth pointing out that the reported values for salts **2–3b–f** indicated average activity (from 71 to 114). In addition to the good or very good activity of ILs **1–3a** and **g** (128–198), salts **2b–f** were statistically good feeding deterrents (115–124). The low biological activity of the salts with betaine cation was explained above, however, the lower deterrent activity of the salts with dodecylbetainium cation (**3**) compared to the products with butylbetainium cation (**2**) requires explanation. Generally, with increasing hydrophobicity and elongation of the alkyl chain, biological activity towards storage pests increases. Only a study by Niemczak *et al.* observed that excessive hydrophobicity contributed to a decrease in deterrent activity.[30] Thus, this is most probably contributing to the decrease in deterrent activity for salts with the longest alkyl substituent.

Interestingly, anions have shown a crucial function in deterrent activity for the salts studied, and it is related to the abovementioned neutral character of some compounds towards storage pests. To the best of our knowledge, only glycolic acid[46] and bis(2-ethylhexyl)phosphate[47] are used in pure form or are derivatives of compounds applied to eliminate or repel storage pests. Hence, perhaps the other anions did not contribute to improving deterrent activity. Therefore, it can be concluded that the obtained salts used as an adjuvant for herbicides may also support plant protection against pests feeding, but it must be noted that this may not be sufficient protection. By contrast, only ILs with bis(2-ethylhexyl)-phosphate (**g**) anions can be used as potential substitutes for antifeedants. Nevertheless, the fact that no insects died during the experiment was significant, which may indicate the lack of toxicity of the tested compounds to these organisms.

**Surface activity properties of the tank mixes used in the greenhouse experiments.** Our previous studies have shown that surface activity analyses for tank mixes represent an essential assay for pesticide adjuvants. These measurements allow us to determine the correlation between herbicidal activity and contact angle, namely, the linear relationship between these parameters.

Since we used 0.1% aqueous solutions of adjuvants in the greenhouse experiments, only concentrations of the salts **1–2f** and **g** and **3a–f** were above the CMC, whereas the other tank mixes of examined ILs were below the CMC or the highest possible concentration. The addition of a proper adjuvant into ISM-Na solutions resulted in a significant decrease in both the surface tension and contact angle compared to those tank

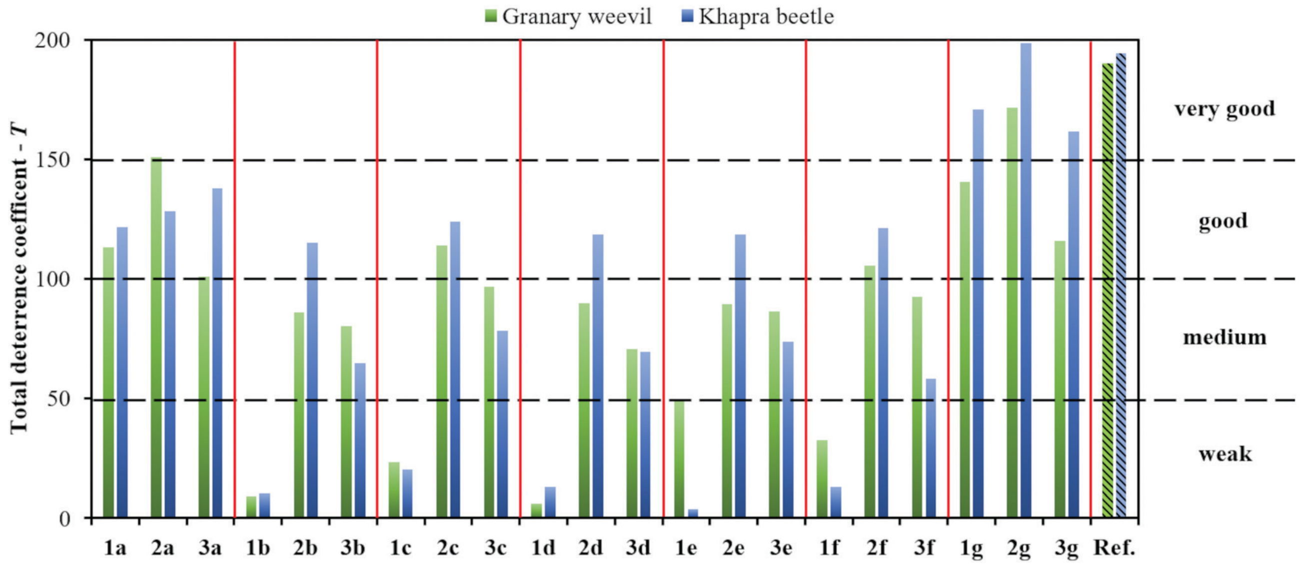


Fig. 3 Deterrent activity of salts (**1–3a–g**) towards the adult granary weevil and larvae of the khapra beetle compared to that of azadirachtin (Ref.). Deterrence criteria based on total coefficient *T* – left side of the graph.

Table 5 Surface activity of the tank mixes

| No. | $\gamma$ [mN m$^{-1}$] | CA [°] | No. | $\gamma$ [mN m$^{-1}$] | CA [°] |
|---|---|---|---|---|---|
| **1a** | 76.62 | 109 ± 1 | **1e** | 46.64 | 84 ± 1 |
| **2a** | 76.59 | 108 ± 1 | **2e** | 39.65 | 85 ± 1 |
| **3a** | 35.64 | 69 ± 2 | **3e** | 33.00 | 51 ± 2 |
| **1b** | 75.42 | 101 ± 2 | **1f** | 27.31 | 35 ± 1 |
| **2b** | 75.28 | 99 ± 1 | **2f** | 25.91 | 36 ± 3 |
| **3b** | 35.96 | 70 ± 1 | **3f** | 25.58 | 36 ± 2 |
| **1c** | 76.99 | 104 ± 2 | **1g** | 40.12 | 69 ± 1 |
| **2c** | 63.72 | 92 ± 1 | **2g** | 37.86 | 63 ± 2 |
| **3c** | 35.84 | 55 ± 1 | **3g** | 28.39 | 48 ± 1 |
| **1d** | 76.23 | 110 ± 2 | Herbicide[a] | 75.35 | 113 ± 1 |
| **2d** | 74.80 | 108 ± 1 | Herbicide + Biopower[b] | 34.99 | 55 ± 2 |
| **3d** | 36.42 | 67 ± 3 | | | |

[a] Iodosulfuron-methyl sodium. [b] Commercial agricultural adjuvant.

mixes without an adjuvant (Table 5). Moreover, the spray solutions containing salts **1–3f** and **3g** had $\gamma$ values that were approximately 6–10 mN m$^{-1}$ lower than those of the ISM-Na + Biopower system. However, in the case of CA, only salts **3e**, **1–3f** and **3g** had lower CAs, by 4, 19–20 and 7°, respectively. Unfortunately, compared to Biopower, the other synthesized ILs did not improve the surface activity parameters. Moreover, tank mixes with ILs **1–2a–d** and ISM-Na had surface parameters at the level of ISM-Na without adjuvant addition. The data confirmed previous reports, where the surface activity of the tank mixes was influenced by the adjuvant structure.[21,22,48]

Based on our previous studies on additives to herbicides, we decided to correlate the biological activity and surface properties of the spraying solutions.[21,22,49] The relationship between CA and fresh weight reduction is shown in Fig. 4. The analysis indicated that the correlation of these parameters was at the same level ($R^2$ = 0.86) as in previous reports ($R^2$ = 0.95 and 0.86). Moreover, it is worth mentioning that the previous studies were based on various types of weeds and different active substances, which implied that the herbicidal activity can be determined by simply and quickly examining the wettability of the tank mixes.

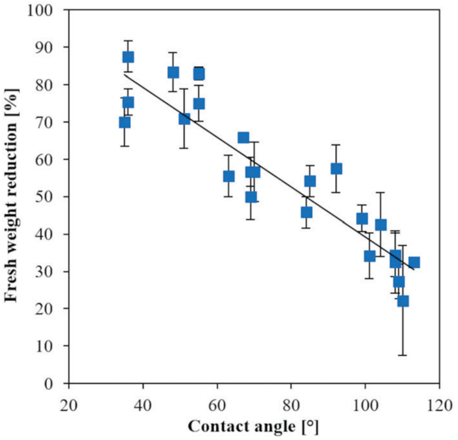


Fig. 4 Relationship between the contact angle of the tank mix solution and its herbicidal activity.

## Influence on the environment

**Phytotoxicity.** The effect of the obtained salts on germination, as well as the length and weight of shoots or the root length of white mustard at a concentration of 0.1%, were tested using the commercially available Phytotoxikit test (the methodology is described in the ESI†).[50] The results are presented in Fig. 5 and 6 and Tables S3 and S4 in the ESI.† The obtained salts and commercial adjuvant (Biopower, Ref.) stimulated plant germination compared to the control (Fig. 5). Furthermore, it was observed that the maximum germination was obtained on day 3 for all the obtained salts and Biopower and on day 5 in the control experiment. However, the positive germination effect was not correlated with later root and shoot growth.

The analysis of the data presented in Fig. 6A and B resulted in a significant structural effect of the obtained ILs on the propagation of the mass or length increase of shoots and roots. The obtained data indicated the crucial influence of cation structure on plants, where three different plant behaviors were noted depending on the length of the alkyl substituent at the quaternary nitrogen atom. One behavior was the growth of all three parameters with the elongation of alkyl chains in the cation for salts **1–3a–c**. Similar results have already been observed previously and were explained by the increase in hydrophobicity of the products, which resulted in a reduced amount of chemical substances absorbed by plants and thus reduced phytotoxicity.[51] By contrast, salts **1–3d**, **e** and **g** exhibited an inverse relationship, where all measured parameters decreased with increasing alkyl substituent length.

This behavior is associated with the increasing water solubility for salts **1–3d**, **e** and **g**, which leads to improved migration of substances in soil to the roots.[52] The third category included ILs that, with the elongation of the alkyl chain, reduced length of roots and shoots but increased the mass of shoots relative to the control. This particular case occurred in ILs **1–3f**, where the plants had significantly thicker shoots and roots than the other tested salts, which increased the weight and may indicate an effect on the growth mechanism of plants and an impact similar to chlormequat chloride.[53]

Considering the effect of anions on the phytotoxicity of the examined salts, the emphasis should be on ILs **1a–g**, where the cation effect was limited owing to the use of glycine betaine, which has no negative effect on plant development. Moreover, glycine betaine is managed by plants and contributes to a positive effect during plant growth.[54] In addition, glycine betaine reduced the effect of cations and their molecular weight in prepared 0.1% water solutions.

Therefore, if we consider the data presented in Fig. 6, it can be observed that salts with cholate (**e**) and docusate (**f**) anions did not statistically inhibit root growth relative to salts with bis(2-ethylhexyl)phosphate (**g**) anions, which were the most phytotoxic. This result was astonishing because bis(2-ethylhexyl) phosphate has a very similar structure to docusate anions. However, minor differences in their structure affected their properties a large extent.[55,56] Moreover, bis(2-ethylhexyl)phosphate (1250 mg kg$^{-1}$ (rat)[57]) is more toxic to animals than docusate (3690 mg kg$^{-1}$ (rat)[58]), which may also lead to increased toxicity towards plants.

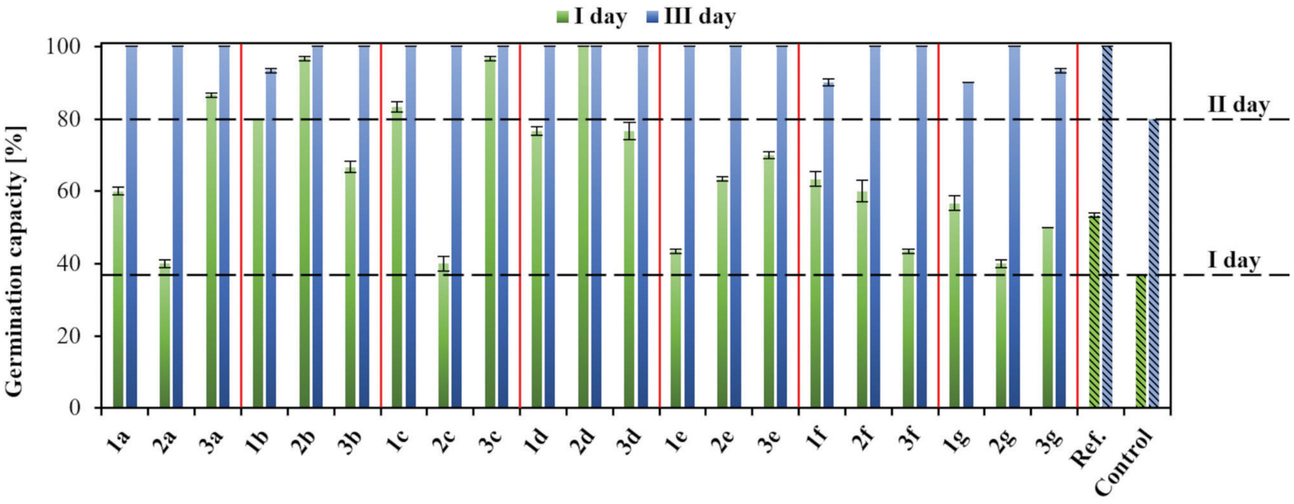


Fig. 5 Germination capacity of synthesized salts, Ref. – Biopower, and Control – water.

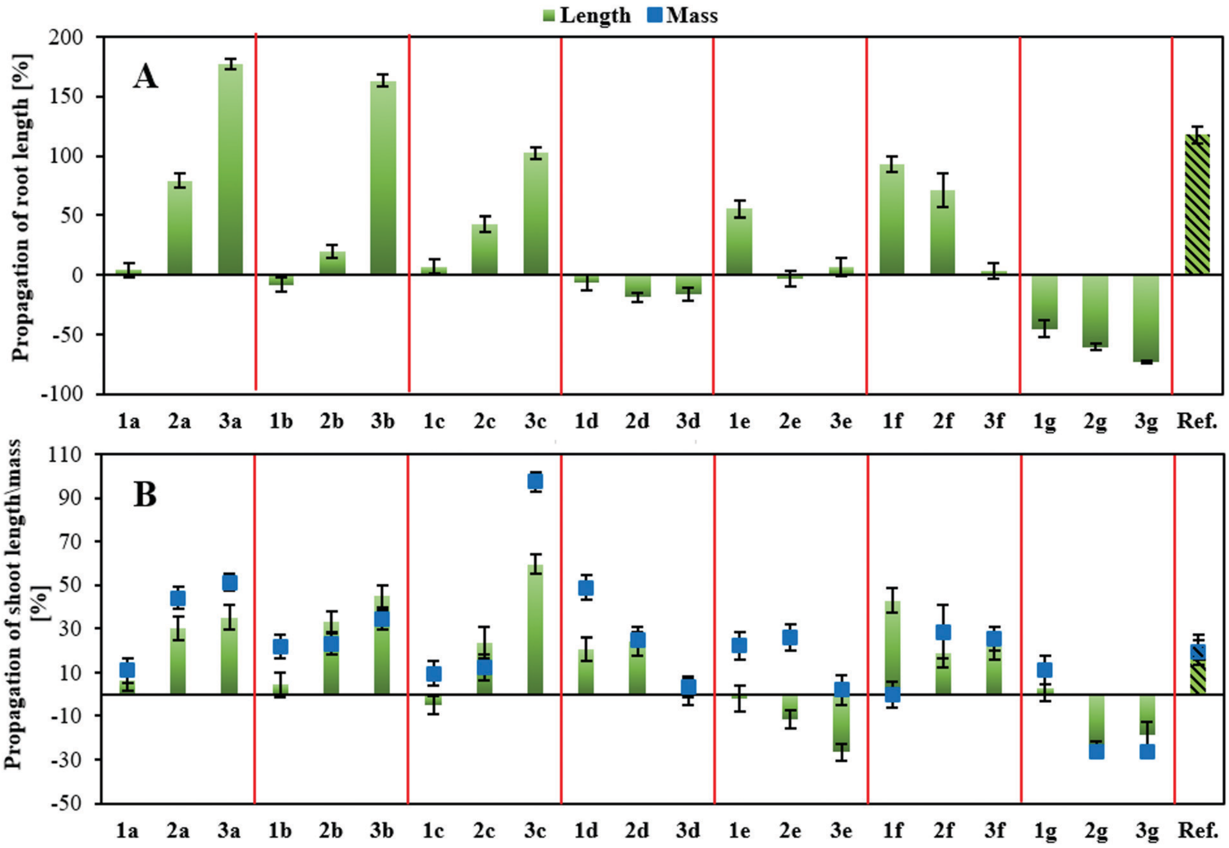


Fig. 6 Effects of synthesized salts **1–3a–g** on propagation of root length (A) as well as shoot length and mass (B) of cornflower seedlings, Ref. – Biopower.

In contrast, glycolate (**a**), D-gluconate (**b**), α-ketoglutarate (**c**), and L-pyroglutamate (**d**) anions did not contribute to abnormal growth of shoots and roots relative to the control. The nonphytotoxicity of these anions at the concentrations used was associated with the biocompatibility of anion sources and their use in the plant life cycle.[59–61]

It cannot be overlooked that appropriate modification of the cation by elongating the alkyl substituent and reducing the concentration of the relevant anions in the formulations enhances the propagation or inhibits the development of plants. Therefore, it can be unambiguously concluded that the proper design of new compounds is essential, which results

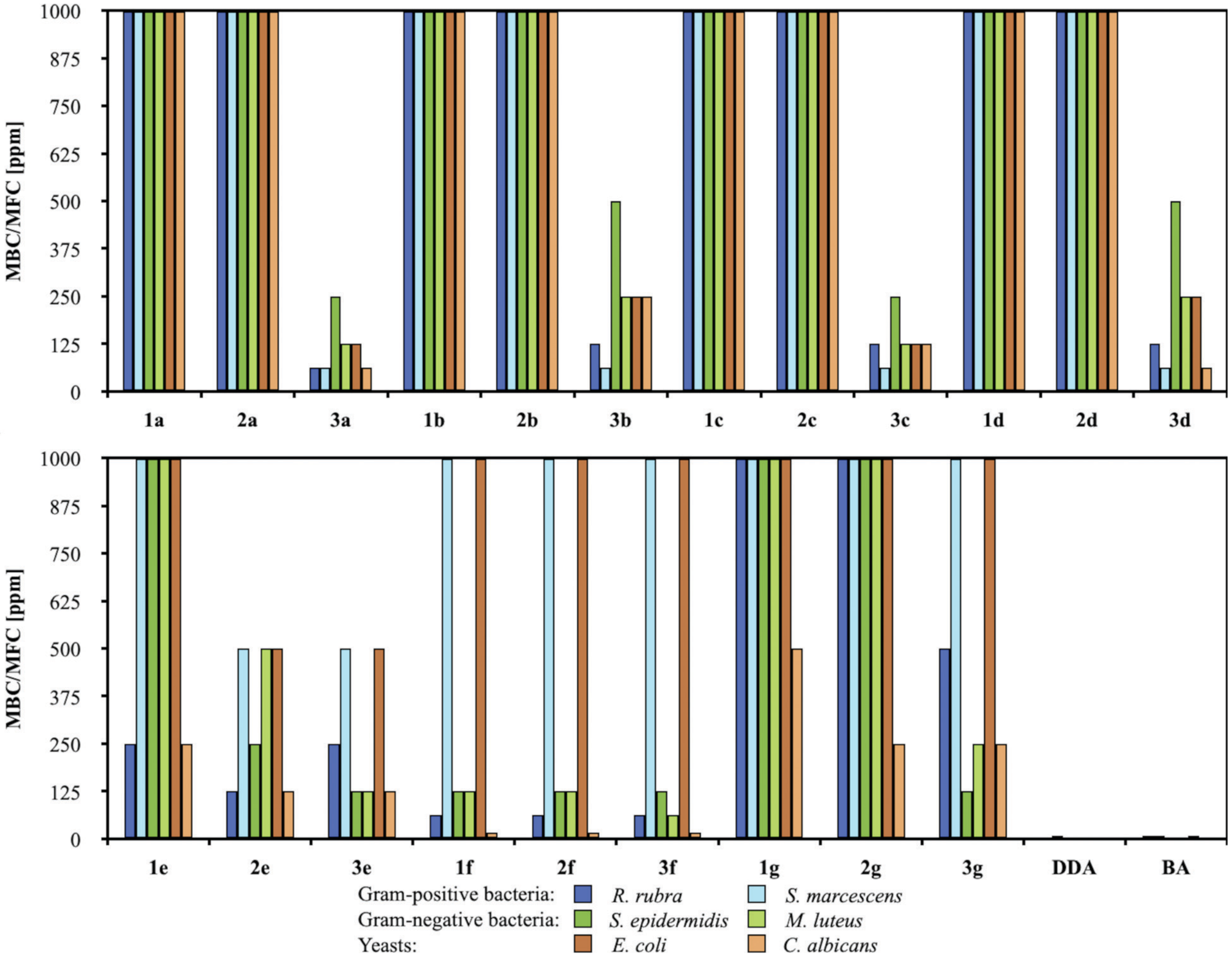


Fig. 7 MBCs and MFCs determined for the obtained ILs.

in obtaining appropriate phytotoxicity for plants, thus improving their condition.

**Toxicity to bacteria and fungi.** The results of toxicity tests of ILs against various groups of microorganisms are shown in Fig. 7 and Tables S5–S7 in the ESI† (the methodology is described in the ESI†). The obtained data proved that the susceptibility of microorganisms to the obtained salts increased with the elongation of alkyl substituents in the cation.[62] Moreover, Gram-positive bacteria were more susceptible to ILs than Gram-negative bacteria, which was associated with the difference in their cell wall structure. Gram-negative bacteria contain the outer membrane in the cell wall structure as the component responsible for resistance to antimicrobial substances. The difference leads to the slower transport of substances into the inside of the bacteria and simultaneously causes higher resistance to new compounds for Gram-negative bacteria.[63]

Moreover, **a–d**, and **g** anions were nontoxic to microorganisms, and only the elongation of the substituent in the cation to 12 carbon atoms reduced the resistance of the bacteria and yeasts. Such a phenomenon is well known and described in the scientific literature.[62]

It is worth noting that the docusate anion connected with alkylbetaine resulted in toxicity to Gram-positive bacteria and yeasts at concentrations $<125$ ppm. The results were unexpected, especially considering that ionic liquids described in the literature with dodecyl(2-hydroxyethyl)dimethylammonium cations exhibited their MBC/MFC at concentrations $>125$ ppm.[21] Further research is needed to assess the significance of the impact of changes in the cation structure to explain the mechanism of absorption and interaction of these salts with bacteria and yeasts.

Moreover, a comparison of the results obtained with those of didecyldimethylammonium chloride (DDA) and benzalkonium chloride (BA) showed that the obtained salts had potential impacts on microorganisms, although these effects were negligible compared to the aforementioned salts. Therefore, due to the limited toxicity to the microbes, the ILs obtained should also be poorly toxic or nontoxic to bacteria and fungi in the soil, which implies that soil microorganisms should biodegrade these substances.

## Conclusions

This study described and characterized a series of novel ionic liquids containing natural or synthetic anions and betaine-based cations. The synthesis methodology was performed under environmentally friendly conditions and allowed us to obtain all products with high efficiency (over 70%) and purity, which was confirmed by spectral analyses (FT-IR, $^1$H NMR and $^{13}$C NMR spectroscopy) and elemental analysis. The conducted experiments proved that the chemical structure of the cations strongly influenced the solubility in most of the organic solvents used. Moreover, anions and cations in synthesized ILs were associated with the surface activity of aqueous solutions. The obtained betaine ion derivatives with one or two amphiphilic ions were surface-active compounds and achieved a CMC at low concentrations. Moreover, the synergistic effect of both surface-active ions resulted in excellent surfactants. Additionally, synthesized salts were used as additives to herbicides. ILs with dodecylbetainium cations and α-ketoglutarate, cholate, docusate or bis(2-ethylhexyl)phosphate anions were the most effective in increasing the herbicide activity of iodosulfuron–methyl sodium. Further analysis of contact angles measured for spray solutions on the hydrophobic surface allowed us to identify a strong correlation between the wettability of herbicide solutions and the biological activity of these solutions towards weeds. This correlation confirms previous reports and represents a valuable tool that facilitates the design of new adjuvants.

Furthermore, the effects of the obtained salts on organisms, such as insects, plants and microorganisms, have been noted. Very good deterrent properties towards common pests in stored products have only been reported for ILs with glycolate or bis(2-ethylhexyl)phosphate anions. To our knowledge, this behavior is related to the deterrent activity of the previously mentioned ions, where the anions are the only ones described in the literature as a potential source of pest repellents. Moreover, the environmental toxicity data allowed us to clearly state that almost all synthesized salts were characterized by low phytotoxicity and microbiological toxicity, suggesting that they have a low environmental impact. Only salts with bis(2-ethylhexyl)phosphate anions exhibited phytotoxicity. The best intermediate results were recorded for bis(2-ethylhexyl)-phosphate, although its toxicity to plants excluded it. Similarly, excellent biological activity and low toxicity were observed for ILs with the docusate anion. The only drawback was that these formulations were weak insect deterrents. The obtained results prove that selecting the appropriate cation and anion can lead to ionic liquids, which are simultaneously good surfactants (adjuvants) and insect deterrents. Moreover, due to reports of low toxicity, these compounds are a potential source of new substances for agrochemical applications.

## Conflicts of interest

There are no conflicts to declare.

## Acknowledgements

This work was supported by the National Science Centre, Poland (PRELUDIUM 17:2019/33/N/ST4/02292).

## References

1 M. W. Aktar, D. Sengupta and A. Chowdhury, *Interdiscip. Toxicol.*, 2009, **2**, 1–12.

2 S. García-Salinas, H. Elizondo-Castillo, M. Arruebo, G. Mendoza and S. Irusta, *Molecules*, 2018, **23**, 1399.

3 C. Veeresham, *J. Adv. Pharm. Technol. Res.*, 2012, **3**, 200–201.

4 J. M. Cholewa, L. Guimaraes-Ferreira and N. E. Zanchi, *Amino Acids*, 2014, **46**, 1785–1793.

5 T. Ohnishi, S. Balan, M. Toyoshima, M. Maekawa, H. Ohba, A. Watanabe, Y. Iwayama, Y. Fujita, Y. Tan, Y. Hisano, C. Shimamoto-Mitsuyama, Y. Nozaki, K. Esaki, A. Nagaoka, J. Matsumoto, M. Hino, N. Mataga, A. Hayashi-Takagi, K. Hashimoto, Y. Kunii, A. Kakita, H. Yabe and T. Yoshikawa, *EBioMedicine*, 2019, **45**, 432–446.

6 M. Alirezaei, V. Jaldani, O. Dezfoulian and G. Shahsavari, *Herb. Med. J.*, 2017, **2**, 9–17.

7 Z. Nizioł-Łukaszewska, P. Osika, T. Wasilewski and T. Bujak, *Molecules*, 2017, **22**, 320.

8 R. Lan and I. Kim, *Arch. Anim. Nutr.*, 2018, **72**, 368–378.

9 M. M. Abdelsattar, M. N. Abd El-Ati, A. M. A. Hussein and A. M. Saleem, *SVU-International Journal of Agricultural Science*, 2019, **1**, 33–42.

10 W. Henke, K. Herdel, K. Jung, D. Schnorr and S. A. Loening, *Nucleic Acids Res.*, 1997, **25**, 3957–3958.

11 E. V. Capela, A. E. Santiago, A. F. C. S. Rufino, A. P. M. Tavares, M. M. Pereira, A. Mohamadou, M. R. Aires-Barros, J. A. P. Coutinho, A. M. Azevedo and M. G. Freire, *Green Chem.*, 2019, **21**, 5671–5682.

12 J. J. Parajó, I. P. E. Macário, Y. De Gaetano, L. Dupont, J. Salgado, J. L. Pereira, F. J. M. Gonçalves, A. Mohamadou and S. P. M. Ventura, *Ecotoxicol. Environ. Saf.*, 2019, **184**, 109580.

13 W. L. Hough, M. Smiglak, H. Rodríguez, R. P. Swatloski, S. K. Spear, D. T. Daly, J. Pernak, J. E. Grisel, R. D. Carliss, M. D. Soutullo, J. H. Davis, Jr. and R. D. Rogers, *New J. Chem.*, 2007, **31**, 1429–1436.

14 J. L. Shamshina, S. P. Kelley, G. Gurau and R. D. Rogers, *Nature*, 2015, **528**, 188–189.

15 R. M. Moshikur, M. R. Chowdhury, M. Moniruzzaman and M. Goto, *Green Chem.*, 2020, **12**, 8116–8139.

16 J. Pernak, D. K. Kaczmarek, T. Rzemieniecki, M. Niemczak, Ł. Chrzanowski and T. Praczyk, *J. Agric. Food Chem.*, 2020, **68**, 4588–4594.

17 M. Niemczak, Ł. Chrzanowski, T. Praczyk and J. Pernak, *New J. Chem.*, 2017, **41**, 8066–8077.

18 F. Goursaud, M. Berchel, J. Guilbot, N. Legros, L. Lemiègre, J. Marcilloux, D. Plusquellec and T. Benvegnu, *Green Chem.*, 2008, **10**, 310–320.

19 D. K. Kaczmarek, A. Parus, M. Łożyński and J. Pernak, *RSC Adv.*, 2020, **10**, 43058–43065.

20 J. Pernak, K. Czerniak, M. Niemczak, Ł. Ławniczak, D. K. Kaczmarek, A. Borkowski and T. Praczyk, *ACS Sustainable Chem. Eng.*, 2018, **6**, 2741–2750.

21 D. K. Kaczmarek, T. Rzemieniecki, D. Gwiazdowska, T. Kleiber, T. Praczyk and J. Pernak, *J. Mol. Liq.*, 2021, **327**, 114792.

22 D. K. Kaczmarek, T. Rzemieniecki, K. Marcinkowska and J. Pernak, *J. Ind. Eng. Chem.*, 2019, **78**, 440–447.

23 R. H. Broh-Kahn, A. Halpern, E. J. Sasmor and A. G. Mundipharma, GB1006728, 1962.

24 Centre d'Etudes et de Realisations Therapeutiques, FR 4529, 1966.

25 M. B. Hay and S. C. B. Myneni, *Geochim. Cosmochim. Acta*, 2007, **71**, 3518–3532.

26 M. Niemczak, A. Biedziak, K. Czerniak and K. Marcinkowska, *Tetrahedron*, 2017, **73**, 7315–7325.

27 Y. Fukaya, Y. Iizuka, K. Sekikawa and H. Ohno, *Green Chem.*, 2007, **9**, 1155–1157.

28 L. Wang, C. Z. Xing, L. Xu and G. J. Liu, *Russ. J. Phys. Chem. A*, 2018, **92**, 2204–2209.

29 A. Martin, P. L. Wu, Z. Liron and S. Cohen, *J. Pharm. Sci.*, 1985, **74**, 638–642.

30 M. Niemczak, D. K. Kaczmarek, T. Klejdysz, D. Gwiazdowska, K. Marchwińska and J. Pernak, *ACS Sustainable Chem. Eng.*, 2019, **7**, 1072–1084.

31 W. G. Gorman and G. D. Hall, *J. Pharm. Sci.*, 1964, **53**, 1017–1020.

32 G. Sharma, D. Singh, S. Rajamani and R. L. Gardas, *ChemistrySelect*, 2017, **2**, 10091–10096.

33 W. X. Li, A. Farajtabar, N. Wang, Z. T. Liu, Z. H. Fei and H. K. Zhao, *J. Chem. Thermodyn.*, 2019, **138**, 288–296.

34 W. Wang, J. Zhu, G. Tang, H. Huo, W. Zhang, Y. Liang, H. Dong, J. Yang and Y. Cao, *New J. Chem.*, 2019, **43**, 827–833.

35 H. Kumar and G. Kaur, *J. Dispersion Sci. Technol.*, 2020, DOI: 10.1080/01932691.2020.1724796.

36 B. Šarac, Ž. Medoš, A. Cognigni, K. Bica, L.-J. Chen and M. Bešter-Rogač, *Colloids Surf., A*, 2017, **532**, 609–617.

37 G. Kume, M. Gallotti and G. Nunes, *J. Surfactants Deterg.*, 2008, **11**, 1–11.

38 P. Brown, C. P. Butts, J. Eastoe, D. Fermin, I. Grillo, H.-C. Lee, D. Parker, D. Plana and R. M. Richardson, *Langmuir*, 2012, **28**, 2502–2509.

39 Z. Zhou, C. Cao, L. Cao, L. Zheng, J. Xu, F. Li and Q. Huang, *Colloids Surf., B*, 2018, **167**, 206–212.

40 A. Bejarano, U. Sauer and C. Preininger, *Appl. Microbiol. Biotechnol.*, 2017, **101**, 7335–7346.

41 L. Ling, L. Jiangang, S. Minchong, Z. Chunlei and D. Yuanhua, *Sci. Rep.*, 2015, **5**, 13033.

42 Q. Zhang, Y. Li, Y. Song, H. Fu, J. Li and Z. Wang, *J. Mol. Liq.*, 2017, **243**, 431–438.

43 M. Niemczak, Ł. Sobiech and M. Grzanka, *J. Agric. Food Chem.*, 2020, **68**, 13661–13671.

44 D. K. Kaczmarek, K. Czerniak and T. Klejdysz, *Chem. Pap.*, 2018, **72**, 2457–2466.

45 M. Tulp and L. Bohlin, *Bioorg. Med. Chem.*, 2005, **13**, 5274–5282.

46 M. A. Murcia Valderrama, R.-J. van Putten and G.-J. M. Gruter, *Eur. Polym. J.*, 2019, **119**, 445–468.

47 T. Yoshida and J. Yoshida, *J. Chromatogr. B: Anal. Technol. Biomed. Life Sci.*, 2012, **880**, 66–73.

48 K. Marcinkowska, T. Praczyk, B. Łęgosz, A. Biedziak and J. Pernak, *Weed Sci.*, 2018, **66**, 404–414.

49 R. C. Kirkwood, *Pest Sci.*, 1993, **38**, 93–102.

50 A. Parus and G. Framski, *Sci. Total Environ.*, 2018, **643**, 1278–1284.

51 M. Pan and L. M. Chu, *Ecotoxicol. Environ. Saf.*, 2016, **126**, 228–237.

52 R. E. Temple and H. W. Hilton, *Weeds*, 1963, **11**, 297–300.

53 J. Pernak, M. Niemczak, K. Materna, K. Marcinkowska and T. Praczyk, *Tetrahedron*, 2013, **69**, 4665–4669.

54 S. Ali, Z. Abbas, M. F. Seleiman, M. Rizwan, İ. Yavas, B. A. Alhammad, A. Shami, M. Hasanuzzaman and D. Kalderis, *Plants*, 2020, **9**, 896.

55 Y. Luan, G. Xu, S. Yuan, L. Xiao and Z. Zhang, *Langmuir*, 2002, **18**, 8700–8705.

56 S. Gao, X. H. Shen, Q. D. Chen and H. C. Gao, *Sci. China: Chem.*, 2012, **55**, 1712–1718.

57 U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, 1997, RTECS, Registry Of Toxic Effects of Chemical Substances.

58 M. M. Fiume, B. Heldreth, W. F. Bergfeld, D. V. Belsito, R. A. Hill, C. D. Klaassen, D. C. Liebler, J. G. Marks Jr., R. C. Shank, T. J. Slaga, P. W. Snyder and F. A. Andersen, *Int. J. Toxicol.*, 2016, **35**, 34S–46S.

59 I. Bargmann, M. C. Rillig, W. Buss, A. Kruse and M. Kuecke, *J. Agron. Crop Sci.*, 2013, **199**, 360–373.

60 H. Amano and H. Noda, *Fish. Sci.*, 1994, **60**, 449–454.

61 D. Jiménez-Arias, F. J. García-Machado, S. Morales-Sierra, J. C. Luis, E. Suarez, M. Hernández, F. Valdés and A. A. Borges, *Environ. Exp. Bot.*, 2019, **158**, 215–222.

62 A. Parus, W. Wilms, V. Verkhovetska, G. Framski, M. Woźniak-Karczewska, A. Syguda, B. Strzemiecka, A. Borkowski, Ł. Ławniczak and Ł. Chrzanowski, *New J. Chem.*, 2020, **44**, 8869–8877.

63 Z. Breijyeh, B. Jubeh and R. Karaman, *Molecules*, 2020, **25**, 1340.