Application of the Principles of “Green Chemistry” for the Synthesis of 10-Undecylenic Aliphatic Esters with Antimicrobial Activity

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Received: 29 November 2019; Accepted: 09 March 2020

Abstract: Undecylic acid (10:1) is known as an antifungal agent and an active ingredient of many topical medicines [1–6]. The present research investigates the preparation of aliphatic esters of 10-undecylic acid with butanol and i-amyl alcohol by the conventional and ultrasound-assisted syntheses as well as the structural elucidation of the resulting compounds, by FTIR and NMR spectroscopy. The antimicrobial properties of the obtained 10-undecylenic esters were tested against Gram-positive bacteria (Staphylococcus aureus; Enterococcus faecalis; Listeria monocytogenes), Gram-negative bacteria (Escherichia coli; Salmonella sp.) and filamentous fungi (Penicillium sp.; Aspergillus niger; Fusarium moniliforme) using the conventional agar-well diffusion assay. The results demonstrated that all esters had insignificant antibacterial activity. i-Amyl-10-undecylenate and t-butyl-10-undecylenate showed activity against both Gram-positive and Gram-negative bacteria, while i-butyl-10-undecylenate and n-butyl-10-undecylenate were effective only against Gram-positive bacteria tested. In contrast, all 10-undecylenic esters demonstrated high antifungal activity, which was most pronounced in i-Amyl-10-undecylenate. Therefore, the obtained products can be successfully used as promising antifungal agents for various pharmaceutical formulations as well as biocontrol means against plant pathogens.

Keywords: 10-undecylenate alkyl esters; FTIR and NMR spectroscopy; antimicrobial activity

1 Introduction

Undecylenic acid (10-) is known as an antifungal agent and is the active ingredient in many topical active medicines [1,2]. It is approximately six times more effective as an antifungal substance than caprylic acid. Wyss demonstrated as early as 1945 that the greater the number of carbon atoms in the fatty acid chain, the greater the fungicidal activity to the point of exceeding eleven carbon atoms, where the solubility became a limiting factor [1–3].

During 1949, Perlman proposed the use of undecylenic acid as a therapeutic agent for psoriasis, neurodermatitis, and related arthropathies. Moreover, undecylenic acid and its salts are also used as topical agents for the treatment of various fungal skin infections [4].

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The commercial product Leucidal® Liquid PT is used as a broad-spectrum antimicrobial preparation whose action is due to the presence of water-soluble undecylenates obtained from Lactobacillus during the fermentation process. Undecylenic acid is an oil-soluble, unsaturated fatty acid, which is usually obtained by the thermal conversion of castor oil derived from castor oil. Castor oil is 100% biodegradable, natural and renewable resource [5].

Undecylenic acid based products have been used by Yong and co-authors in the preparation of formula that improves the intratumoral distribution of the anticancer agents, with significant stability under physiological conditions [6].

Bigot uses undecylenic monoglycerides as a synthon when performing polymerization processes [7].

Grafting of undecylenic acid on the ethyleneoctene copolymer in the molten state has been investigated by He et al. [8].

Lee et al. have investigated the use of undecylenic acid as a non-peptide inhibitor of 1-calpain with a good cell permeability and a potent neuroprotective effect in Alzheimer’s disease [9].

In addition, unsaturated undecylenic ester of sucrose showed also very well antimicrobial activity against Candida albicans, exhibited an inhibition activity against the Gram-positive bacteria: Bacillus subtilis and Bacillus cereus, and Gram-negative E. coli, as also inhibited the growth of Pseudomonas aeruginosa, against which undecylenic acid was inactive. On the base of this investigation sucrose undecylenic and sucrose laurate ester could be used as potential antimicrobial agent for protecting plants and foods against some microorganisms [10].

The antimicrobial activity of ultrasound-assisted synthesized octa-O-acetylsucrose was also studied against seventeen microorganisms (Gram-positive and Gram-negative bacteria, yeasts and fungi). Octa-O-acetylsucrose inhibited the growth of fungi Penicillium sp., Rhizopus sp. and Fusarium moniliforme at 5 mg/ml and yeasts Candida albicans at 1 mg/ml. No inhibition against the Gram-positive and Gram-negative bacteria was observed [11]. Sucroesters are used in cosmetics as detergents and for medical purposes [12]. Their bactericidal activity depends on their nature—the length of the alkyl chain, as well as the strain of microorganisms. The commercial sucroesters are also used as antimicrobial agents in canned foods and beverages mainly in Japan to stabilize emulsions during the sterilization process and to inhibit bacterial spores [13,14].

Inulin esters was potential antimicrobial and antifungal agents. The results from antibacterial assay showed that 1% inulin laurinate inhibited the growth of some food borne pathogenic bacteria—Escherichia coli, Salmonella and B. cereus. Inulin 10-undecylenate and laurinate were active against Candida albicans and Penicillium [15–18].

Ultrasonic chemistry (sonochemistry) is one of the modern trends in “green” chemistry that deals with the application of ultrasonic waves to chemical effects. The main advantages of sonochemistry are the use of less hazardous chemicals and solvents, the reduction of the energy consumption and the increase in the selectivity of the reaction. In this regard, the ultrasonic waves in many cases facilitates the management of chemical reactions, stimulating greater efficiency and effectiveness.

Current approaches to the synthesis and modification of organic compounds target “green technologies” through the use of ultrasound. It is well known that the supportive effect of ultrasound is due to the formation of cavitation bubbles in the liquid medium. The rapid implosion of these bubbles induces a high pressure gradient and a sharp increase in temperature.

Aliphatic esters were obtained by esterification of fatty acids with ethanol and methanol in the presence of sulfuric acid under ultrasound irradiation (20 kHz) for 15–30 min at room temperature [19]. However, until now the information about ultrasound-assisted esterification of 10-undecylenic acid is undufficient.
Therefore, the esterification of 10-undecylenic acid with n-butyl, i-butyl, t-butyl and i-Amyl alcohols under ultrasonic irradiation remained challenge.

The synthesis of aliphatic esters of 10-undecylenic acid is examined in this article, comparing classical and ultrasonic synthesis, and elucidation of the structure of the compounds obtained. The aliphatic 10-undecylenic esters were subjected to an experimental study for an evaluation of their antifungal and antimicrobial activities against *Staphylococcus aureus*, *Enterococcus faecalis*, *Listeria monocytogenes*; *Escherichia coli*; *Salmonella* sp.; *Penicillium* sp.; *Aspergillus niger* and *Fusarium moniliforme*.

2 Experimental

2.1 Materials and Methods

The following reagents were used to synthesize the studied esters: n-butanol, i-butanol, t-butanol, i-amyl alcohol, methanol, n-hexane, dimethyl sulfoxide (DMSO) (Panreac); 10-undecylenic acid (Reachim); anhydrous Na₂SO₄ (Riedel-de Haen); K₂CO₃, NaCl, acetone, HCl, ethyl acetate (Chimtex); tetrahydrofuran (Panreac).

2.1.1 Conventional Synthesis of 10-Undecylenic Esters

In a 300 ml Erlenmeyer flask was place 0.5 mol of the corresponding alcohol, 2 mmol conc. H₂SO₄ was added as catalyst, followed by the addition of 4 mmol 10-undecylenic acid. The flask was connected to the reflux with water cooling and the samples were heated under reflux at the boiling point of the alcohol used. After 120 min, the reaction was quenched, the reaction mixture was cooled to room temperature and the sample was poured into 100 ml of distilled water. The sample was extracted with 50 ml of hexane in triplicate. The combined hexane extracts were washed with 10% Na₂CO₃ and dried with anhydrous Na₂SO₄, after which the hexane was distilled. The ester obtained was separated and the yield determined by weight.

2.1.2 Ultrasound Synthesis of 10-Undecylenic Esters

In a 300 ml Erlenmeyer flask was place 0.5 mol of selected alcohol, 2 mmol conc. H₂SO₄ (as catalyst), and 4 mmol 10-undecylenic acid. The flask was connected to a water-cooled reflux condenser and placed in a Dimoff A-2/2 ultrasonic bath (100 W, 44 kHz). It was sonicated for 15 min at room temperature. After completion of the reaction, the reaction mixture was cooled vigorously with 100 cm³ of ice-cold water and neutralized with 10% Na₂CO₃. Triple extraction with 20 cm³ of diethyl ether was carried out. The extracts were combined and dried with anhydrous Na₂SO₄. The ester was obtained after the distillation and the yield determined by weight.

FTIR Spectroscopy

FTIR spectra of the synthesized esters were recorded on a Nicolet Avatar spectrometer (Thermo Scientific, USA, ZnSe crystal, resolution 4 cm⁻¹), on KBr pellets, in the frequency range of 4000–500 cm⁻¹.

¹H and ¹³C NMR Spectroscopy

The ¹H and ¹³C NMR spectra were recorded on a Bruker spectrometer at a frequency of 500 MHz in CDCl₃ with a tetramethylsilane (TMS) as standard.

Gas Chromatography (GC)

Identification of synthesized aliphatic esters was performed by gas chromatography with a flame ionization detector (Shimadzu GC/FID), equipped with CP Wax 52 CB capillary column (30 m × 0.25 mm × 0.25 m) (Varian Chrompak, Netherland); a Flame-Ionization Detector (FID) and Shimadzu ER-5A integrator (Shimadzu GmbH, Duisburg, Germany). The carrier gas was nitrogen with flow 0.8 cm³ min⁻¹ and split 80:1. The gradient of temperature was in the range from 165 to 230°C, with 4°C min⁻¹, kept for
20 min at this temperature. The temperatures of the injector was 260°C and the operating temperature of detector 280°C, as previously described [20].

**Antimicrobial Activity**

**Test microorganisms.** Three Gram-positive bacteria (*Staphylococcus aureus* ATCC 25923; *Enterococcus faecalis* ATCC 12984; *Listeria monocytogenes* ATCC 8632), two Gram-negative bacteria (*Escherichia coli* ATCC 8739, *Salmonella* sp.—clinical isolate) and three fungi (*Fusarium moniliforme* ATCC 38932, *Aspergillus niger*, *Penicillium* sp.—plant isolates) from the collection of the Department of Microbiology at the University of Food Technologies, Plovdiv, Bulgaria, were selected for the antimicrobial assay.

**Culture media.** *Luria-Bertani glucose agar medium—LBG agar* (containing tryptone, yeast extract, NaCl, glucose and agar) was used for cultivation of Gram-positive and Gram-negative test bacteria, as well as for implementation of agar well diffusion assay. For these two purposes 50 g of LBG-agar were dissolved in 1 L of deionized water, the final pH was adjusted to 7.5, and then autoclaved at 121°C for 20 min before use.

*Malt extract agar medium* (containing malt extract, dextrose, peptone and agar) for the cultivation of the test fungi was used. For this purpose 33.6 g of malt agar were dissolved in 1 L of deionized water, the final pH was corrected to 5.5, and then autoclaved for 20 min at 121°C.

**Antimicrobial Assay**

The antimicrobial activity was determined by using the standard agar well diffusion method in LBG agar. The test bacteria were cultured on the LBG agar at 37°C for 24 h. The test fungi were grown on malt extract agar at 30°C for 7 days or until sporulation. The inocula of test bacteria were prepared by homogenization of a small amount of biomass in 5 ml of sterile 0.5% NaCl. The inocula of test fungi were prepared by addition of 5 ml of sterile 0.5% NaCl into the tubes and vigorous shaking, then filtered and replaced in another tubes before use. The concentrations of the viable bacterial cells and fungal spores in the inocula were determined using a Thoma’s counting chamber. Their final concentrations were adjusted to $1.0 \times 10^8$ cfu/ml for bacterial cells and $1.0 \times 10^5$ cfu/ml for fungal spores, then inoculated in preliminarily melted and tempered at 45–48°C LBG agar media. The inoculated LBG agar media were transferred in a quantity of 17 ml in sterile Petri dishes ($d = 90$ mm) and allowed to solidify. Then six wells ($d = 6$ mm) per dish were cut. The samples of the esters were pipetted in quantity of 50 μl into the agar wells.

Three antibiotics penicillin (1.2 mg/ml), Streptomycin (6 mg/ml) and nystatin (40 μg/ml) were used as controls. The inoculated Petri dishes were incubated at 37°C (for bacteria) and at 30°C (for fungi). The antimicrobial activity was determined by measuring and recording the diameter of the inhibition zones around the wells on the 24-th and 48-th hour of incubation. Microorganisms with inhibition zones of 18 mm or more were considered as sensitive (strong inhibitory effect); moderately sensitive were those in which the zones were from 12 to 18 mm (moderate inhibitory effect); resistant were those microorganisms, where the inhibition zones were up to 12 mm or completely missing (insignificant or no inhibitory effect) [21,22].

**3 Results and Discussion**

The synthesis of aliphatic esters of 10-undecylenic acid was performed by both conventional and ultrasound methods (Fig. 1).

The reaction time decreases from 2 h in the conventional synthesis to 15 min after the application of US irradiation.
The synthesis of aliphatic esters of 10-undecylenic acid was performed by both methods (conventional and US). The yield data shows an increase of 3 to 7 percentage after the application of the US method compared to the conventional one. The highest yield was observed with i-propanol and the least one with i-butanol (Tab. 1).

The aliphatic esters obtained were also identified by gas chromatography. The number of peaks and the retention time of the esters were determined (Tab. 2).

Table 1: Reaction time and yield data for the synthesis of aliphatic esters of 10-undecylenic acid

| Ester                  | Conventional method | Ultrasound method |
|------------------------|---------------------|-------------------|
|                        | Reaction time, min  | yield, %          | Reaction time, min | yield, % |
| i-Amyl-10-undecylenate | 120                 | 69                | 15                 | 76       |
| i-Propyl-10-undecylate | 120                 | 72                | 15                 | 75       |
| n-Butyl 10-undecylate  | 120                 | 70                | 15                 | 75       |
| i-Butyl 10-undecylate  | 120                 | 73                | 15                 | 80       |
| t-Butyl 10-undecylate  | 120                 | 75                | 15                 | 79       |

Table 2: Results from GC-FID analysis of the retention time for the synthesized aliphatic esters

| Aliphatic esters | The retention time, min |
|------------------|-------------------------|
| i-Amyl-10-undecylate | 15,0                   |
| i-Propyl-10-undecylate | 9,5                    |
| n-Butyl 10-undecylate  | 10,2                   |
| i-Butyl 10-undecylate  | 11,1                   |
| t-Butyl 10-undecylate  | 19,3                   |

The application of ultrasonic irradiation on organic molecules with a long carbon skeleton can lead to C–C rupture. According to Mason et al. [23], in cavitation bubbles the temperature can reach 1000 K and pressure of 100 atmospheres. Under these conditions, the carbon bond breaking and the isomerization cracking processes take place. In our case, only one major peak was observed in the gas chromatograms.
obtained. As a result of these observations, it can be concluded that under the reaction conditions—ultrasonic irradiation with a frequency of 44 kHz, power 100 W, a reaction time of 15 min and a catalyst concentrated H₂SO₄, the ultrasonic effect did not cause any breakage of C–C bonds.

The aliphatic esters of the 10-undecylenic acid obtained by ultrasonic esterification were characterized by FTIR spectroscopy.

In the FTIR spectra of the synthesized esters, several characteristic bands typical for esters were observed (Fig. 2).

![Figure 2: FTIR spectra of alkyl-10-undecylenate esters](image)

In the region between 600 and 1500 cm⁻¹ the absorption bands associated with the hydrocarbon chain appeared. The intense and narrow band in the spectrum at 1743 cm⁻¹ was due to the stretching vibrations (νC=O) of the carbonyl group in the ester. The stretching vibrations of the C–H bond appeared in a medium intensity band and they were observed at 2930 cm⁻¹. In esters, a band appeared at about 2850 cm⁻¹ corresponding to νC–Hₐₐ (CH₂). In addition, the bands characteristic of C–O–C of the ester group also appeared at 1270 and 1223 cm⁻¹.

The spectral data showed clearly the absorption bands characteristic of the vinyl group CH₂=CH– at the 10-undecylenic acid ester. No other absorption bands were observed to demonstrate a change in the position of the double C=C bond in the esters of 10-undecylenic acid.

The trend was also evident in the t-butyl ester. Theoretically, tertiary alcohols are the most difficult to esterify, and therefore, it can be expected that by the synthesis of their esters, isomeric and oxidation byproducts will be obtained. However, in the FTIR spectrum of the synthesized t-butyl 10-undecylenic ester did not observe characteristic OH groups of absorption bands (Fig. 2). The IR spectra of esters with different alcohols in the ultrasonic field did not show any isomerization and oxidation processes.

### 3.1 Nuclear Magnetic Resonance

In the ¹H NMR spectra of the i-propyl esters, resonance signals were observed in the range of 4.83–4.90 ppm characteristic of the methine protons CH of the i-propyl group. The methyl protons from the i-propyl group were observed at 1.35–1.39 ppm and the methyl protons from the aliphatic acid chain at 0.97–1.0 ppm.

The methylene protons were recorded in the spectrum at 1.29–2.31 ppm, with resonance signals for the CH₂ protons linked to the C=O group observed at 2.28–2.31 ppm. Characteristic resonance signals were appeared in the spectrum of i-propyl-10-undecnylenes in the range of 4.94–5.65 ppm due to olefin protons. The proton at the secondary carbon atom in the i-propyl group was observed at 4.94 ppm, and for the methyl groups at the range 1.41–1.42 ppm.
In the $^{13}$C NMR spectra, the signal for the carbonyl carbon atom was observed at 174.35 ppm and that of the secondary carbon atom of the $i$-propyl group at 70.04 ppm. Signals for the methylene groups are observed in the range 22.93–31.64 ppm, and those for the carbon of the methyl group of acid at 14.01 ppm, respectively for the carbon of the $i$-propyl group at 22.51 ppm. For $i$-propyl-10-undecylenate, characteristic double-bonded carbon atoms are observed at 115.34 and 138.99 ppm.

A number of characteristic resonance signals are observed in the $^1$H NMR spectra of the synthesized $t$-butyl ester. The displacement for the methyl protons from the aliphatic chain occurs at 0.99 ppm and those from the $t$-butyl moiety at 1.49 ppm. Metinic protons at the secondary carbon atom of the $i$-butyl group were observed at 2.21 ppm. The methylene protons stand out clearly as multiplets in the range of 1.30 to 4.06 ppm.

The methylene protons adjacent to the carbonyl carbon atom were observed at 2.29 ppm, respectively, for the C–O bound group in the spectrum of $n$-butyl esters at 4.06 ppm, for the $t$-butyl ester at 2.36 ppm and for $i$-butyl ester at 2.29 and 3.98 ppm.

It was of interest to investigate the effect of ultrasonic irradiation on the structure of 10-undecylenic acid as representative of non-saturated acids. The presence of a double bond permits the possibility of adverse reactions— isomerization, oxidation, polymerization.

In the $^1$H NMR spectrum of $t$-butyl-10-undecylene, the chemical displacements of protons for the vinyl group –CH=CH$_2$ at 4.99 and 5.65 ppm were clearly observed (Fig. 3). In the analyzed spectrum and in the data on spin-spin interactions characteristic of olefin protons, characteristic signals due to the spin-spin interaction were observed, both between olefin protons and protons from the double bond with adjacent carbon atoms. 

![Figure 3: $^1$H NMR spectrum of the $t$-butyl-10-undecylene for the vinyl group protons](image.png)
methylene protons. When a complex of protons was connected to two or more unequal adjacent protons, the so-called complex spin-spin interaction [24,25].

It was observed that the $H_c$ signal, which appeared at 4.97–5.01 ppm, was actually split in four (Fig. 4). $H_c$ interacts with $H_a$ and $H_b$, which can be read by two different $J$ constants. $H_a$ is transposed with $H_c$ relative to the double bond, and splits the $H_c$ signal in doublet with $J$ constant 17.1 Hz. An additional spin–spin interaction with $H_b$ is observed in each of these $H_c$ doublet signals (Figs. 5 and 6), resulting in two more doublets, each with a much smaller $J$ constant (3.5 Hz). This double spin-spin interaction is called a doublet of doublets or “double doublets” (abbreviation dd in the spectrum data).

![Figure 4: $H_c$ signal data in the $^1$H NMR spectrum of $t$-butyl-10-undecylenate](image)

![Figure 5: $H_b$ and $H_c$, signal data in the $^1$H NMR spectrum of $t$-butyl-10-undecylenate](image)
The signal for Hb at 4.93 ppm is cleaved by a doublet of the cis-arranged Hb, with each of them having a spin–spin interaction with Hc. As a result, a doublet of doublets is observed again, but this time with two sub-doublets that have the smaller $J$ constant.

In the proton spectrum of t-butyl-10-undecylenes, no changes in the resonance signals for vinyl protons were observed, as well as isomerization from cis-in trans-configuration, and compounds resulting from oxidation.

The $^1$H NMR spectra confirmed that under the ultrasonic irradiation with duration 15 min of the reaction mixture, no isomerization, oxidation and polymerization processes occur in the structure of the 10-undecylenic acid. Resonance signals for the carbonyl carbon atom at 172.83–174.36 ppm were observed in $^{13}$C NMR spectra. Signals for the C-atom of the t-butyl group were recorded at 81.62 ppm, and for the carbon atom the i-butyl group at 19.69 ppm. Signals for the carbon atoms of the three methyl groups in t-butanol were observed at 28.3 ppm and those from fatty acid and n-butanol at 14.02 ppm.

For n-, i- and t-butyl-10-undecylenates, two resonance signals were observed in the $^{13}$C NMR spectra—at 115.35 ppm (=CH–) and 139.0 ppm (CH$_2$=), and for carbon from methyl groups at the tertiary carbon atom were observed at 27.62 ppm, respectively.

3.2 Antimicrobial Activity of Synthesized Esters

The results from antimicrobial activity of testing esters were presented (Fig. 7 and Tab. 3).

The screening for antimicrobial activity showed that all the tested esters possessed mostly antifungal, rather than antibacterial activity. i-Amyl-10-undecylenate and t-butyl-10-undecylenate esters possessed insignificant antibacterial activity against Gram (+) and Gram (–) microorganisms. i-Butyl 10-undecylenate and n-butyl-10-undecylenate esters were inactive against Gram (–) microorganisms E. coli and Salmonella sp. i-Amyl-10-undecylenate demonstrated the highest antifungal activity against the molds Penicillium sp., A. niger and F. moniliforme. Promising antifungal potential was demonstrated also by i-butyl-10-undecylenate, t-butyl-10-undecylenate and n-butyl-10-undecylenate esters. Penicillin (1.2 mg/ml) was active only against L. monocytogenes, while Streptomycin (6 mg/ml) was effective against all tested bacteria. The antifungal antibiotic Nystatin showed negative results.
4 Conclusion

The intensifying effect of the ultrasonic effect on the synthesis of 10-undecylenic alcohol esters has been demonstrated. The reaction time is significantly reduced from 120 min to 15 min and the reaction temperature is lowered to room temperature, as the yield of esters increased up to 5% or remain constant. Under the conditions of ultrasound-assisted synthesis, the structure and composition of the esters obtained remained unchanged and was comparable with those ones obtained by the conventional method.

Antimicrobial properties of the obtained 10-undecylenic esters demonstrated that most of esters had insignificant antibacterial activity. However, \( i \)-Amyl-10-undecylenate and \( t \)-butyl-10-undecylenate showed activity against both Gram-positive and Gram-negative bacteria, while \( i \)-butyl-10-undecylenate and \( n \)-butyl-10-undecylenate were effective only against Gram-positive bacteria tested. In contrast, all 10-undecylenic esters demonstrated high antifungal activity, which was most pronounced in

**Figure 7:** Antifungal activity of aliphatic esters of 10-undecylenic acids, where K is Nystatin (40 µg/ml), 1. \( i \)-Amyl 10-undecylenate; 2. \( i \)-Butyl 10-undecylenate; 3. \( t \)-Butyl 10-undecylenate; 4. \( n \)-Butyl 10-undecylenate

**Table 3:** Antimicrobial activity of synthesized esters

| Sample                  | Gram (+) bacteria | Gram (-) bacteria | Fungi        |
|-------------------------|-------------------|-------------------|--------------|
|                         | \( S. \) aureus   | \( E. \) faecalis | \( E. \) coli | \( Salm. \) Penicillium | \( A. \) niger | \( F. \) moniliforme |
| \( i \)-Amyl 10-undecylenate | 11               | 11                | 12           | 13                | 11             | 30              | 30            | 22          |
| \( i \)-Butyl 10-undecylenate | 11               | 11                | 12           | –                 | –              | 25              | 25            | 13          |
| \( t \)-Butyl 10-undecylenate | 13               | 10                | 13           | 11                | 11             | 20              | 21            | 15          |
| \( n \)-Butyl 10-undecylenate | 10               | 10                | 13           | –                 | –              | 21              | 23            | 13          |
| Penicillin (1.2 mg/ml)  | –                 | –                 | 19           | –                 | –              | n/a             | n/a           | n/a         |
| Streptomycin (6 mg/ml)  | 15                | 15                | 30           | 23                | 12             | n/a             | n/a           | n/a         |
| Nystatin (40 µg/ml)     | n/a               | n/a               | n/a          | n/a               | n/a            | –               | –             | –           |
i-amyl-10-undecylenate. Therefore, the obtained products can be successfully used as promising antifungal agents for various pharmaceutical formulations as well as biocontrol means against plant pathogens.

**Funding Statement:** This research was financially supported by Fund Science Contract No 1805C, Technical University of Gabrovo, Bulgaria.

**Conflicts of Interest:** The authors declare that they have no conflicts of interest to report regarding the present study.

**References**

1. Shapiro, A. L., Rothman, S. (1945). Undecylenic acid in the treatment of dermatomycoses. *Archives of Dermatology and Syphilology*, 52, 166–171.

2. Neuhauser, I. (1954). Successful treatment of intestinal moniliasis with fatty acid-resin complex. *Archives of Internal Medicine*, 93(1), 53–60. DOI 10.1001/archinte.1954.00240250063005.

3. Wyss, O., Ludwig, B. J., Joiner, R. R. (1945). The fungistatic and fungicidal action of fatty acids and related compounds. *Archives of Biochemistry*, 7, 415.

4. Newell, G. W., Petretti, A. K., Reiner, L. (1949). Studies of the acute and chronic toxicity of undecylenic acid. *Journal of Investigative Dermatology*, 13(3), 145–149. DOI 10.1038/jid.1949.81.

5. **Antimicrobial Product List.** [www.activemicrotechnologies.com](http://www.activemicrotechnologies.com).

6. Yong, T., Hu, J., Zhang, X., Li, F., Yang, H. et al. (2016). Domino-like intercellular delivery of undecylenic acid-conjugated porous silicon nanoparticles for deep tumor penetration. *ACS Applied Materials & Interfaces*, 8(41), 27611–27621. DOI 10.1021/acsami.6b11127.

7. Bigot, S., Daghrir, M., Mnanna, A., Boni, G., Pourchet, S. et al. (2016). Undecylenic acid: a tunable bio-based synthon for materials applications. *European Polymer Journal*, 74, 26–37. DOI 10.1016/j.europoly.2015.11.008.

8. He, P., Huang, H., Zhang, Y., Liu, N. C. (2005). Undecylenic acid grafting on ethylene-octene copolymer in molten state. *Reactive and Functional Polymers*, 62(1), 25–29. DOI 10.1016/j.reactfunctpolym.2004.05.007.

9. Lee, E., Eom, J. E., Kim, H. L., Kang, D. H., Jun, K. Y. et al. (2012). Neuroprotective effect of undecylenic acid extracted from *Ricinus communis* L. through inhibition of μ-calpain. *European Journal of Pharmaceutical Sciences*, 46(1–2), 17–25. DOI 10.1016/j.ejps.2012.01.015.

10. Matev, G., Petkova, N., Vrancheva, R., Ivanov, I., Pavlov, A. et al. (2014). University of Plovdiv “Paisii Hilendarski”—Bulgaria. *Scientific Papers, 39*(5), 17–24.

11. Petkova, N., Vassilev, D., Grudeva, R., Tumbarski, Y., Vasileva, I. et al. (2017). Green synthesis of sucrose octaacetate and characterization of its physicochemical properties and antimicrobial activity. *Chemical and Biochemical Engineering Quarterly*, 31(4), 395–402.

12. Ferrer, M., Soliveri, J., Plou, F., Lopez-Cortes, N., Reyes-Duarte, D. et al. (2005). Ballesteros, synthesis of sugar esters in solvent mixtures by lipases from *Thermomyces lanuginosus* and *Candida antarctica* B and their antimicrobial properties. *Enzyme and Microbial Technology*, 36(4), 391–398. DOI 10.1016/j.enzmicrotec.2004.02.009.

13. Habulin, M., Šabeder, S., Knez, Ž. (2008). Enzymatic synthesis of sugar fatty acid esters in organic solvent and in supercritical carbon dioxide and their antimicrobial activity. *Journal of Supercritical Fluids*, 45(3), 338–345. DOI 10.1016/j.supflu.2008.01.002.

14. Stagner, W. C., Gaddam, S., Parmar, R., Ghanta, A. K. (2014). Sucrose octaacetate. *Profiles of Drug Substances, Excipients and Related Methodology*, 44, 267–291.

15. Shang, H. M., Zhou, H. Z., Yang, J. Y., Li, R., Song, H. et al. (2018). In vitro and in vivo antioxidant activities of inulin. *PLoS One, 13*(2), e0192273.

16. Matev, G., Petkova, N., Vrancheva, R., Ivanov, I., Pavlov, A. et al. (2014). Synthesis, characterization and application of sucroesters as antimicrobial agents, scientific papers of Plovdiv University “Paisii Hilendarski”. *Chemistry, 39*(5), 17–23.
17. Matin, M., Bhuiyan, M., Afrin, A., Debnath, D. (2013). Comparative antimicrobial activities of some monosaccharide and disaccharide acetates. *Journal of Scientific Research*, 5(3), 515–525. DOI 10.3329/jsr.v5i3.15695.

18. Birmani, M. W., Nawab, A., Ghani, M. W., Li, G., Xiao, M. et al. (2019). A review: role of inulin in animal nutrition. *Journal of Food Technology Research*, 6(1), 18–27. DOI 10.18488/journal.58.2019.61.18.27.

19. Hobuss, C. B., Venzke, D., Pacheco, B. S., Souza, A. O., Santos, M. A. Z. et al. (2012). Ultrasound-assisted synthesis of aliphatic acid esters at room temperature. *Ultrasonics Sonochemistry*, 19(3), 387–389. DOI 10.1016/j.ultsonch.2011.06.020.

20. Staykov, A., Vassilev, K., Dragoev, S., Balev, D., Vlahova-Vangelova, D. et al. (2015). Inhibition of lipid oxidation in different types packaged beef by a composition of natural antioxidants. *Oxidation Communications*, 38(2), 666–676.

21. Tumbarski, Y., Lincheva, V., Petkova, N., Nikolova, R., Vrancheva, R. et al. (2017). Antimicrobial activity of extract from aerial parts of potentilla (*Potentilla reptans* L.). *Industrial Technologies*, 4(1), 37–43.

22. Tumbarski, Y., Deseva, I., Mihaylova, D., Stoyanova, M., Krastev, L. et al. (2018). Isolation, characterization and amino acid composition of a bacteriocin produced by Bacillus methylotrophicus strain BM47. *Food Technology and Biotechnology*, 56(4), 546–552. DOI 10.17113/ftb.56.04.18.5905.

23. Mason, T. J., Peters, D. (2011). *Practical sonochemistry*. Cambridge: Horwood Publishing Limited.

24. Soderberg, T. (2013). *Organic chemistry with a biological emphasis*, vol. I. Morris: University of Minnesota.

25. Wei, W., Ye, W., Wang, J., Huang, C., Xiong, J. B. et al. (2019). Hydrangea-like α-Ni1/3Co2/3(OH)2 reinforced by ethyl carbamate Rivet for all-solid-state supercapacitors with outstanding comprehensive performance. *ACS Applied Materials & Interfaces*, 11(35), 32269–32281. DOI 10.1021/acsami.9b09555.