Antimicrobial activity of undecan-3-one, undecan-3-ol and undec-3-yl acetate

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Abstract

The antimicrobial activity of undecan-3-one, undecan-3-ol and its acetate was studied with respect to bacteria Escherichia coli and Bacillus subtilis, yeast Candida mycoderma and mould Aspergillus niger. The viability of the populations of the microbial strains tested in the presence of the studied compounds was assessed with the impedimetric method. It was found that the ketone did not cause a total inhibition of the growth of the studied bacteria populations, but it effectively affected the fungi. Alcohol obtained as a result of undecan-3-one reduction revealed better bacteriostatic activity while it was not active with respect to C. mycoderma. Undecan-3-ol ester was characterized by the poorest antimicrobial activity.

Key words: *undecan-3-one, undecan-3-ol, acetate, antimicrobial activity.*

(Centr Eur J Immunol 2009; 34 (3): 154-157)

Introduction

Since time immemorial people have used plants a source of food, spices, scents or cures for a number of diseases. The world of plants is the greatest "factory" of organic compounds. With the development of analytical methods and techniques of refining substances, more and more organic compounds were found in plant extracts and essential oils, and their structures were identified. At the same time, some chemical compounds were found to reveal biological activity. What is particularly interesting is the biological activity of those ingredients of plants that may be produced in a relatively simple and efficient manner by chemical synthesis. Those compounds are deemed identical with the natural ones and may be used as substitutes for the natural components. The chemical synthesis of organic compounds identical to the natural ones, their isomers and derivatives is usually economically beneficial. In recent years, a number of scientific studies have focused on the bactericidal, fungicidal, and virucidal activity of plant based compounds. Particular focus is on research into the biological activity of compounds that are used as cosmetic scents or cooking essences. Examples of such compounds are undecanones. Undecan-2-one, undecan-2-ol and undec-2-yl acetate are quite widespread in the plant world. They are components of essential oils and extracts obtained from some plants, including very exotic ones. Sizeable amounts of undecan-2-one are found in oils obtained from plants of the *Rutaceae* family.

Depending on the variety of rue, cultivation conditions and part of the plant from which they are obtained, oils contain from several to several dozen percent of this ketone [1-4]. Undecan-2-ol in amounts of several percent is present in e.g. oil from the herb *Ruta graveolens* [5], *Ruta chalepensis* [3, 6], oil from the roots of *Philodendron acutatum Scott*. [7], oil from *Glycosmis pentaphylla* bark [8], curcuma, cocoa butter, sweet corn, and many fruits, e.g. fresh apples, bananas, and strawberries [9]. *Ruta graveolens* is also a natural source of undec-2-yl acetate [1]. Synthetic undecan-2-one, undecan-2-ol, and its acetate have a fruity-floral scent with an orange-herbaceous or fatty note [5].

Undecan-3-one occurs in 0.6% in brown seaweed *Dictyopteris membranacea* coming from the Mediterranean French coast [10] and is produced in putrefying trees under the influence of the fungi *Fomitopsis piniola* [11]. It is also the orientation feromone of the African ants *Decophylla longinoda*, which works at short distances [12]. It is only undecan-3-one that has the status of a compound identical to a natural one, while undecan-3-ol and its acetate obtained through organic synthesis [12, 13] have not been identified

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in nature. These compounds are characterized by pleasant floral odors [5, 14].

Our research into the antimicrobial activity of undecan-2-one and undecan-2-ol and their acetates obtained through organic synthesis showed that the ketone and alcohol inhibit yeast *Candida mycoderma*, mould *Aspergillus niger* and bacteria *Bacillus subtilis*. Even though undec-2-yl acetate did not reveal any significant antimicrobial activity, for most ester-microorganism systems statistically significant differences were found in its activity depending on the concentration [15, 16]. Due to the specific pleasurable smell and antimicrobial activity of undecan-2-one and undecan-2-ol, it is possible to use them as preservatives in foods and cosmetics. Furthermore, experiments with mice indicate that these compounds stimulate the immunological system.

It was expected that isomeric undecan-3-one, undecan-3-ol and its acetate, which differ in the place in the carbon chain, might also have preserving properties. It was found interesting and relevant to examine the antimicrobial activity of these compounds. Previous immunological studies show that these compounds also stimulate the immunological system in mice [18].

Materials and Methods

Synthesis of the ketone

Undecan-3-one was prepared by the ketonization of a mixture of propanoic and nonanoic acids in the presence of 20 wt% MnO_2/Al_2O_3 catalyst under flowing conditions. The yield of the ketone was 69.2%, and its purity was 98.9% (GC), n^{20}_D = 1.4271 (exp). A comprehensive description of its synthesis as well as physical and spectral properties has been given elsewhere [12, 13]. The undecan-3-one obtained as above had a fruity odor with an apple-like note [14].

Synthesis of the alcohol

Undecan-3-ol was prepared by the reduction of undecan-3-one using sodium borohydride in a water/propan-2-ol solution [19]. The yield of undecan-3-ol was 98%, its purity 99.2% (GC), n^{20}_D = 1.4382 (exp). It had a fine woody and floral odor [14].

Synthesis of the acetate

The acetate was prepared by the esterification of undecan-3-ol with acetic anhydride in the presence of anhydrous sodium acetate. The yield of undec-3-yl acetate was 81% and its purity was 99.1%, n^{20}_D = 1.4259 [19]. It had a faint, soap-fatty odor [14].

Microorganisms

Bacteria *B. subtilis* ATCC 6633 and *E. coli* ATCC 8793; yeast *C. mycoderma* ŁOCK 0008 and mould *A. niger* ŁOCK 0436 were used in the experiments. The microorganisms originated from the ATCC Collection and the Pure Culture Collection of the Institute of Fermentation Technology and Microbiology, Łódź Technical University ŁOCK 105. Double passaging activated the microorganisms: bacteria on TSB medium (Trypticase Soy Broth) Oxoid (*B. subtilis* temperature 30°C, 48 h; *E. coli* temperature 37°C, 48 h), yeast and mould on Sabouraud Agar, bioMerieux (temperature 28°C, 72 h).

Determination of antimicrobial activity

The antimicrobial activity of undecan-3-one, undecan-3-ol and undec-3-yl acetate was determined by the impedimetric method using a Bactometer M64 System (bioMerieux). A suspension of the tested microbial cells in physiological salt solution (0.85% NaCl) was standardized to the density of about 10^7 CFU/ml. Each well of the impedimeter module was filled with 0.1 ml of the cell suspension, 1, 5, 10, 20 or 30 µl of undecan-3-one, undecan-3-ol, or undecan-3-one acetate and completed with a medium to 1 ml volume. The positive control sample was a suspension of microorganisms in a medium without undecan-3-one and its derivatives. The negative control was a culture of bacteria and fungi with the addition of novobiocin (0.5 µg/ml) and cycloheximide (0.2 µg/ml), respectively. The samples were incubated for 72 h at temperatures optimal for the growth of particular microorganisms, as described in the strain activation procedure. After incubation in the bactometer, the viability of the microorganism was controlled by a surface culture on the PCA medium (Plate Count Agar, bioMerieux). The plates were incubated for 3 days in the case of bacteria and yeasts and for 5 days in the case of the mould at temperatures optimal for the growth of particular microorganisms.

Minimal Inhibitory Concentration (MIC) was assigned as the lowest concentration inhibiting the growth of microorganisms in the bactometer at parallel growth on the PCA plates. Minimal Bactericidal Concentration (MBC) or Minimal Fungicidal Concentration (MFC) was the lowest concentration of undecan-3-one or its derivatives at which no microbial growth was observed either in the bactometer wells or on the PCA plates.

Statistical analysis of the results

Results were analyzed using a 3-way ANOVA at a confidence level of $p < 0.05$. The results of population viability were presented as an arithmetic mean of three assays with standard deviation not exceeding 0.2 logarithmic units.

Results

Undecan-3-one revealed low bacteriostatic activity against Gram-positive bacteria *B. subtilis*, but did not work on Gram-negative bacteria *E. coli*. The ketone was active against the tested fungal strains, and affected the mould *A. niger* 3-4 times more strongly. No statistically significant differences were found ($p < 0.05$) in the bacteriostatic activity of undecan-3-one in concentrations from 1 to 10 µl/ml with respect to the

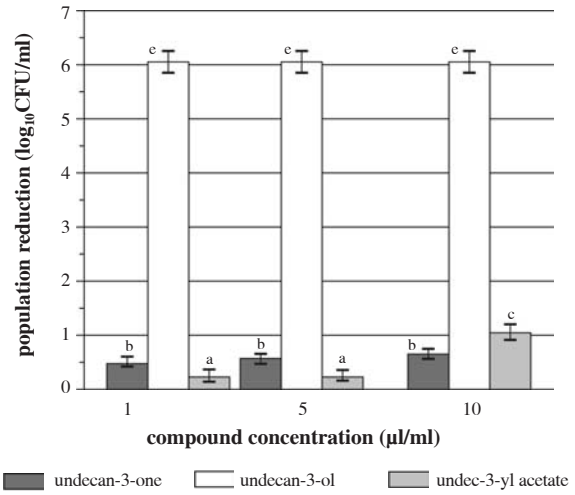

Fig. 1. Reduction in the size of the population of *B. subtilis* in the presence of undecan-3-one, undecan-3-ol and its acetate. Values with different superscripts (a, b, c, e) are significantly ($p < 0.05$) different.

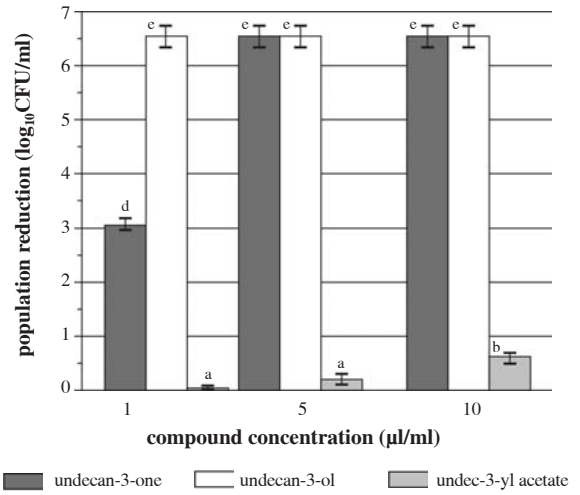

Fig. 2. Reduction in the size of the population of *A. niger* in the presence of undecan-3-one, undecan-3-ol and its acetate. Values with different superscripts (a, b, d, e) are significantly ($p < 0.05$) different.

bacteria *B. subtilis* (Fig. 1). Undecan-3-one started to affect *A. niger* mould at a concentration of 1 µl/ml limiting its growth by 3 logarithmic units (Fig. 2).

The alcohol and acetate, in the tested concentration ranges, did not affect *E. coli* and *C. mycoderma* (Tab. 1). The alcohol showed strong static activity on *B. subtilis* and *A. niger* (MIC 1 µl/ml). Even though undec-3-yl acetate did not reveal significant antimicrobial activity (MIC > 10 µl/ml), in both systems: ester-*B. subtilis* and ester-*A. niger*, statistically significant differences were found ($p < 0.05$) in the activity of the compounds with increased concentration to 10 µl/ml (Figs. 1 and 2).

Due to its fungistatic properties, undecan-3-one may be a substance supporting the microbiological stability of food and cosmetic products. Even though the sanitizing role of undecan-3-ol in these systems is lesser, it may also be used as a supportive element in systems preserving scent matrices.

Discussion

Due to the fact that there are no data in the literature concerning the biological activity of undecanones, it is only possible to compare their activity to plant extracts containing undecan-2-one. It was found that undecan-3-one did not cause a total inhibition of the growth of the studied bacteria populations, but it effectively acted against the fungi. Similarly as in the case of undecan-3-one, extracts from *Ruta graveolens* leafs, containing a substantial amount of undecan-2-one [1-4], did not show activity with respect to *E. coli* [20, 21]. *B. subtilis* did not reveal sensitivity either to undecan-3-one or *Ruta graveolens* extracts [20-22]. Furthermore, what is interesting, undecan-3-one shows high fungistatic activity in contrast to that of the plant extracts [20]. Studies on the antimicrobial activity of various essential oils indicate that yeasts and moulds are more sensitive to them as compared to bacteria [23-25], which is consistent with our results for undecan-3-one.

Even though in antimicrobial activity rankings alcohols usually come only after ketones [26], undecan-3-ol obtained by reduction of undecan-3-one revealed better bacteriostatic activity, but it did not affect *C. mycoderma*. The greater activity of preparations with respect to *A. niger* as compared to yeast of the genus *Candida* are confirmed by studies on a variety of essential oils [24, 25].

Table 1. The antimicrobial activity of undecan-3-one and its derivatives expressed as MIC and MBC/MFC in µl/ml

Compound	*B. subtilis*		*E. coli*		*C. mycoderma*		*A. niger*	
	MIC	MBC	MIC	MBC	MIC	MFC	MIC	MFC
undecan-3-one	> 30	> 30	> 30	> 30	20	30	5	10
undecan-3-ol	1	20	> 30	> 30	> 30	> 30	1	20
undec-3-yl acetate	> 10	> 10	> 10	> 10	> 10	> 10	> 10	> 10

Undecan-3-ol ester was characterized by the weakest bacteriostatic and fungistatic activity, which is consistent with the standard classification of antimicrobial activity [26-27].

Our previous studies show that the profile of antimicrobial activity changes with the place of the function group in undecan-2-one [15, 16], undecan-3-one, and their derivatives. It is particularly visible in systems where these compounds do not cause a total inhibition of population growth. Even for the esters that only poorly affect microbes, at concentrations of 5 and 10 µl/ml, statistically significant ($p < 0.05$) differences in the size of microbial populations were observed. However, the relationship between structural changes and the antimicrobial activity of the preparations requires further research. Earlier attempts to describe such relationships for various components of essential oils were not successful [28-30].

However undecan-3-one did not cause a total inhibition of the growth of *E. coli* and *B. subtilis*, it effectively affected *C. mycoderma* and *A. niger*. Undecan-3-ol revealed better bacteriostatic activity while it was not active with respect to *C. mycoderma*. The poorest antimicrobial activity was observed for undecan-3-ol ester. Our previous studies [18] of undecan-3-one and undecan-3-ol showed their stimulatory effect on cellular and humoral immunity. They produced strong stimulation of antibody production, enhanced metabolic and phagocytic activity of blood leukocytes and the proliferative response to mitogens of blood and splenic T (Con A) and B (LPS) lymphocytes in mice. Research results indicate that the compounds under study may fulfill both the function of preservatives and food aroma, at the same time having a positive effect on the immunological system.

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