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Original Article

The Antioxidative, and antimicrobial activity of 2-amino substituted halochalcone N-glycoside derivative compounds

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Abstract

Introduction: The aim of this study was to specify the antioxidant and antimicrobial activity synthesized 2-amino substituted halochalcone N-glycoside derivative compounds.

Methods: The antioxidant capacity of synthesized compounds (1-4) was determined by cupric ion reducing antioxidant capacity (CUPRAC), and ferric reducing antioxidant power (FRAP). Antimicrobial activity was determined on 9 microorganism by agar well diffusion method.

Results: According to the study results, compound 3 showed the highest antioxidant activity. The compound 3 showed antimicrobial activity against *Yersinia pseudotuberculosis, Pseudomonas aeruginosa, Candida albicans* while compound 4 showed antimicrobial activity against *Escherichia coli, Yersinia pseudotuberculosis, Pseudomonas aeruginosa, Enterococcus faecalis, Bacillus cereus, Staphylococcus aureus.*

Conclusion: 2-amino substituted halochalcone *N*-glycoside derivative compounds could be evaluated in the pharmaceutical and cosmetic fields due to their antioxidant and antimicrobial potential.

Keywords: Antimicrobial activity, antioxidant activity, halochalcone, *N*- glycoside

1. Introduction

Chalcones, known as sub-members of flavonoids, are the common word given to substances containing the 1,3-diaryl prop-2-en-1-one carbon skeleton (1). Some chalcone species can be obtained from natural sources as well as synthesized (1, 2). Chalcones, which are commonly found in plants but in small amounts, have important pharmacological activities, which has led researchers to study the synthesis and biological activities of these compounds (3). The interest in chalcone compounds, which have attracted the attention of the scientific world with their industrial, biological and pharmacological properties, is increasing day by day (4). The substituted aromatic rings and functional α,β-

unsaturated carbonyl groups of chalcone compounds are important in terms of their biological activities (2). The functional groups carried by chalcone and its derivatives isolated or synthesized from plants enable them to exhibit biological activities such as anticancer (5), anti-inflammatory (6), antihyperglycemic (7), anti-HIV (8), antifungal (4), antibacterial (6), antioxidant (9), antimitotic (10) and antituberculosis (11). Chalcones have biological activities such as anticancer, anti-inflammatory, antibacterial, antituberculosis, antidiabetic, antioxidant, antimicrobial, antiviral, antimalarial and neuroprotective effects (12).

Nevertheless, there is insufficient information examining the antioxidant, and antimicrobial activities of 2-amino substituted halochalcone N-glycoside derivative compounds in the literature. That is why antioxidant, and antimicrobial activitiy of the compounds were examined in present study.

2. Methods

2.1. Chemicals and instrumentation

2,2-Diphenyl-1-picrylhydrazyl (DPPH) were purchased from Sigma-Aldrich (St. Louis, MO, USA). Methanol, ethanol, acetic acid, and acetonitrile were obtained from Merck (Darmstadt, Germany). Trolox (6-hydroxy-2,5,7,8-tetra- methylchroman-2- carboxylic acid), TPTZ (2,4,6-tripyridyl-s-triazine) and Folin-Ciocalteu's phenol reagent were purchased from Fluka Chemie GmbH (Buchs, Switzerland). Ampicillin and Fluconazole were purchased from Mustafa Nevzat and Phizer, respectively.

2.2. Supply of compounds

The names of the compounds used in the study are given in Table 1. The compounds (1-4) used in the study were synthesized in our previous studies (13) and used in experiments by taking sufficient amounts.

2.3. Antioxidant activity

In order to determine the ferric reduction antioxidant power, FRAP method was performed as stated in the literature (14). Trolox was prepared as standard in a range of concentrations (62.5, 125, 250, 500, 1000 µM). The methanolic extract and FRAP reagent was added in test tubes. All samples were incubated in dark conditions at 37 °C during 20 minutes. The absorbance was read 595 nm against a blank. CUPRAC method was applied to investigate the cupric ion reducing capacity of the compounds (15). The absorbance of the samples was measured at 450 nm. Whole processes was repeated in triplicate. The CUPRAC values were expressed as µM Trolox equivalent per gram of sample (15).

2.4. Antimicrobial activity

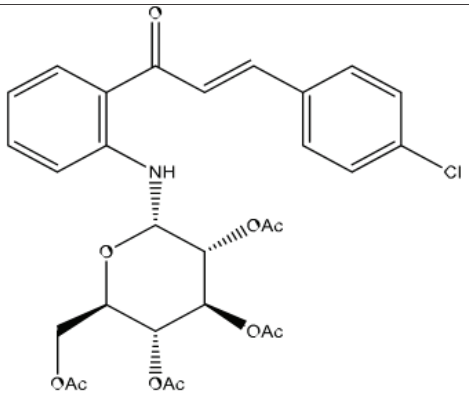
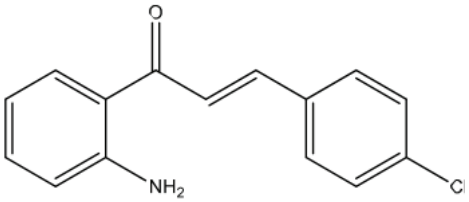
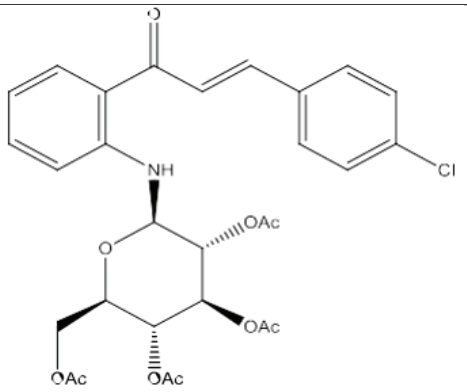
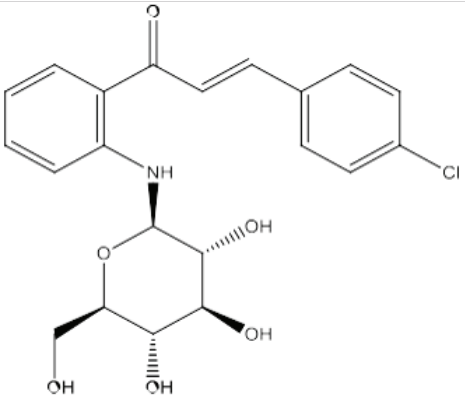
2.4.1. Test microorganisms

All microorganisms used in the study were provided from Refik Saydam Hıfzıssıhha Institute (Ankara, Turkey). *Escherichia coli* ATCC 25922, *Yersinia pseudotuberculosis* ATCC 911, *Pseudomonas aeruginosa* ATCC 43288 from Gram negative bacteria, *Staphylococcus aureus* ATCC 25923, *Enterococcus faecalis* ATCC 29212, *Bacillus cereus* 702 ROMA from Gram positive bacteria, and *Mycobacterium smegmatis* ATCC607 from no Gram were chosen as test bacteria. Moreover, *Candida albicans* ATCC 60193 and *Saccharomyces cerevisiae* RSKK 251 were chosen as yeast.

2.4.2. Antimicrobial assay

In order to detect the antimicrobial activity, some modifications were made in agar well diffusion method (16). Each bacterium was suspended in Mueller-Hinton (MH) broth (Difco, Detroit, MI). Yeast-like fungi were suspended in Yeast extracts broth. Micro-organisms were subsequently diluted to approximately 10^6 colony forming units (cfus) per ml. Potato Dextrose (PD) Agar (Difco, Detriot, MI) was used for yeast-like fungi and Brain Heart Infusion (BHI) Agar for *M. smegmatis* (17). These were first "flood-inoculated" onto the surface of MH and PD agars and subsequently dried. Wells with a diameter of 5 millimeters were opened from the agar using a sterile cork borer and 50 µL of extract was added to the wells. The plates were then incubated at 35°C for 18 hours. Antimicrobial activity was studied by comparing the zone of inhibition with the test organism. In this study, ampicillin, fluconazole and streptomycin as the standard drug were preferred (16,17).

Table 1. Compounds used in the study

Code of the compound	Full name of the compound	Explicit formulas of compounds
1	(2*E*)-1-[2-(2,3,4,6-tetra-*O*- acetyl-*N*-*α*-*D*-glucopyranosyl)phenyl]-3-(4- bromophenyl)prop-2-en-1-on	
2	[(2*E*)-1-(2- aminophenyl)-3-(4-chlorophenyl)prop-2-en-1-on]	
3	(2*E*)-1-[2-(2,3,4,6-tetra-*O*- acetyl -*N*-*β*-*D*-glucopyranosyl)phenyl]-3-(4- bromophenyl)prop-2-en-1-on	
4	(2*E*)-1-[2-(*N*- *β* -*D*- glucopyranosyl) phenyl]- 3-(4-chlorophenyl) prop-2-en-1-on	

2.5. Statistical Analysis

Statistical analysis of all data was evaluated with the Statistics Program for Social and Science (SPSS). Calibration graphs were created according to the absorbance against the concentration of the standard. Experimental results were given as means ± standard deviation.

3. Results

3.1. Antioxidant activities of compounds

The results of antioxidant activities of the compounds are presented in Table 2. Antioxidant activity of compounds was identified by using two different methods i.e. cupric ion reducing antioxidant capacity (CUPRAC), and reducing antioxidant power (FRAP). The compound 3 showed the highest antioxidant activity. Then compounds 2, 4 and 1 followed in that order. CUPRAC and FRAP results of the compound 3 were found as 172.778 ± 3.068 µM Trolox/g sample and 287.067 ± 8.994 µM Trolox/g sample, respectively.

Table 2. The antioxidant activities of compounds

Test Compounds	CUPRAC[1]	FRAP[2]
1	25.139 ± 1.641	80.733 ± 5.715
2	93.7501 ± 1.021	55.733 ± 3.399
3	172.778 ± 3.068	287.067 ± 8.994
4	33.333 ± 1.483	78.733 ± 5.907

[1]CUPRAC value represents the copper reducing antioxidant power (µM trolox equivalent/gram).

[2]FRAP value indicates iron reducing antioxidant power (µM trolox equivalent/gram).

3.2. Antimicrobial activities of compounds

While compound 2 showed antimicrobial activity against *E. coli*, *Y. pseudotuberculosis*,

P. aeruginosa, *E. faecalis*, *M. smegmatis* and *C. albicans*, compound 1 showed activity only against *M. smegmatis.* The compound 3 showed antimicrobial activity against *Y. pseudotuberculosis*, *P. aeruginosa*, *C. albicans.* While compound number 4 showed antimicrobial activity against *E. coli*, *Y. pseudotuberculosis*, *P. aeruginosa* among gram negative bacteria, showed activity against *E. faecalis*, *B. cereus*, *S. aureus* among gram positive bacteria (Table 3).

Table 3. Inhibition zone values of compounds

Tested Compounds	Microorganisms and Inhibition Zone (mm)								
	Gram negative			Gram positive			No gram	Yeast Like Fungi	
	Ec	Pa	Yp	Ef	Bc	Sa	Ms	Ca	Sc
1	-	-	-	-	-	-	6	-	-
2	7	6	6	-	6	-	15	6	-
3	-	7	6	-	-	-	-	6	-
4	8	6	8	6	10	7	-	-	-
Ampicillin	10	10	18	10	35	15	-	-	-
Fluconazole	-	-	-	-	-	-	-	25	25
Streptomycin	-	-	-	-	-	-	35	-	-

Q. Ec: E. coli ATCC 25922, Pa: P. aeruginosa ATCC 43288, Yp: Y. pseudotuberculosis ATCC 911, Ef: E. faecalis ATCC 29212, Bc: B. cereus 702 Roma, Sa: S. aureus ATCC 25923, Ms: M. smegmatis ATCC607, Ca: C. albicans ATCC 60193, Sc: S. cerevisiae RSKK 251, (-): no activity

4. Discussion

Chalcones are an important member of the flavonoid family (18). Many heterocyclic compounds of biological importance such as flavones, pyrazolines and indoles etc. can be synthesized using chalcones. Chalcones consist of a 15-carbon propane chain structure to which two phenyl rings are attached at the 1,3 positions (19). Chalcones containing oxygen atoms in their aromatic ring structure are of great biological importance (20). Chalcones are reported to have a wide range of pharmacological properties such as anticancer, antioxidant, antimalarial, antitubercular, antiviral, anti-inflammatory, antidiabetic, antihistamine, antiulcer and antibacterial (21-24).

It is known that free radicals are the basis of various diseases such as cardiovascular diseases, cancer, chronic inflammation and the like. It has been determined that flavonoid components prevent the formation of these radicals, can prevent lipids from undergoing oxidation by binding metal ions, and can inhibit the enzymatic systems that play a role in the formation of radicals (25). In our study, antioxidant activities of synthesized compounds were measured by using FRAP and CUPRAC determination methods. According to these methods, it was found that compound 3 showed the highest antioxidant activity. FRAP and CUPRAC methods are widely used methods to evaluate the in vitro reducing power of an antioxidant. Various chalcones have

been reported to have high antibacterial activity against gram- positive bacteria. Chalcones have protective effects against many microorganisms. The compounds synthesized in our study were found to have moderate antibacterial and antifungal activity. Particularly, compound 4 was found to exhibit antimicrobial activity against most of the tested microorganisms. Sugamoto et al. investigated the antibacterial activity of the chalcones they synthesized against gram-negative bacteria (*Escherichia coli*, *Proteus mirabilis*, *Pseudomonas fluorescens*) and gram-positive bacteria (*Bacillus subtilis*, *Staphylococcus epidermidis*, *Micrococcus luteus*). They found that not all chalcones were effective against gram- negative bacteria. They found that 4-hydroxyderricin, isobavachalcone, xanthoangelol, xanthoangelol F, bavachalcone and broussochalcone B were active compounds against *Bacillus subtilis*, *Staphylococcus epidermidis*, *Micrococcus luteus* (26). Xanthoangelol and 4-hydroxyderricin isolated from Angelica keiskei root were found to exhibit antibacterial activity against *Bacillus subtilis, Bacillus cereus, Staphylococcus aureus, Staphylococcus epidermidis* (27). Kromann et al. showed that the lipophilic character of Licochalcone A is necessary for antibacterial activity (28). Many chalcones have been shown to inhibit the growth of various yeasts and fungi. The antifungal mechanism of action of chalcones is thought to be related to the inhibition of the fungal cell wall. ElSohly et al. evaluated all isolated compounds against the fungal pathogens *Candida albicans* and *Cryptococcus neoformans*. Compound 2, called isobavachalcone, was found to have inhibitory activity against the tested fungal pathogens (29). López et al. showed that chalcones with different substituents in the A and B rings were active against dermatophytes (30).

5. Conclusion

In conclusion, the 2-amino substituted halochalcone n-glycoside derivative compounds we synthesized were shown to have moderate antimicrobial and antioxidant properties. In our opinion, the study is important as it provides a reference for further studies to be conducted with these compounds.

Conflicts of interest: The authors have no conflicts of interest to declare.

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