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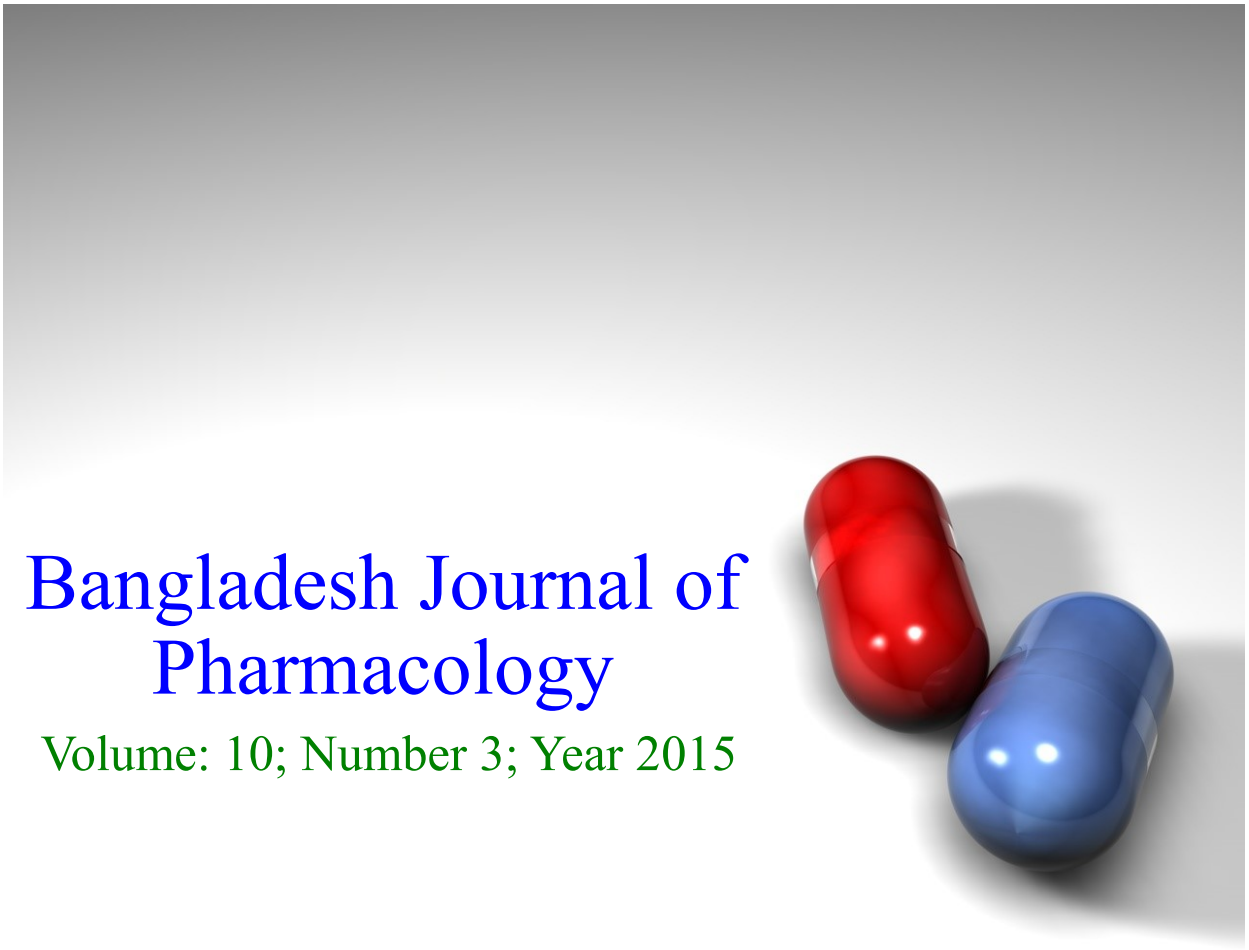

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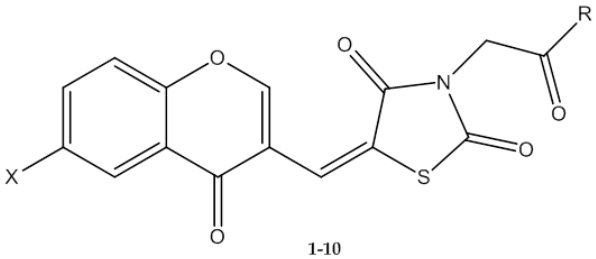
Letter to the Editor

Antimicrobial screening of new 5-(chromene-3-yl) methylene-2,4-thiazolidinediones

Sir,

Efforts are being made globally for the control of microbial resistance phenomenon, of its spread, effects, treatment costs and towards finding new effective protocols. One of the main objectives of medicinal chemistry is the design, synthesis and investigation of molecules having value as human therapeutic agents.

From the big family of heterocyclic compounds, 1,3-thiazolidine-2,4-diones show a wide spectrum of chemo -therapeutic properties and a considerable amount of work has been done on the synthesis of thiazolidine-dione derivatives as potent antibacterial and antifungal agents (Gouveia et al., 2009, Liu et al., 2011). Chromone and related compounds are wide-spread in nature and exhibit a wide range of pharmacological activity like antibacterial, antifungal (Hatzade et al., 2010, Ali and Ibrahim, 2010), antitumor, anti-oxidant, anti-HIV, antiulcerant, anti-inflammatory. As a continuation of our previous work (Nastasă et al., 2013), the present study shows the antimicrobial screening of a new series of 5-(chromene-3-yl)methy-lene-2,4-thiazolidinediones



1-10

Cp	X	R
1	CH_3	naphtyl
2	H	naphtyl
3	Cl	naphtyl
4	CH_3	4-methoxy-phenyl
5	H	4-methoxy-phenyl
6	CH_3	phenyl
7	H	phenyl
8	Cl	phenyl
9	CH_3	5-(2-hydroxy-benzamide)
10	Cl	5-(2-hydroxy-benzamide)

Figure 1: General structure of 5-(chromene-3-yl)methylene-2,4-thiazolidinediones

(Figure 1), for which the chemical synthesis and characterization haven't yet been revealed.

For this purpose, diffusion method was applied (Wayne, 1997), using gentamicin and fluconazole as reference drugs for the antibacterial and antifungal activity, respectively. There were three concentrations of compounds tested: 10, 5 and 1 mg/mL, prepared in dimethylsulfoxide (DMSO). Solvent was used as control and it didn't display antimicrobial inhibition. Six-millimeter diameter wells were cut from the agar using a sterile cork-borer. After drying for 10-15 min, the six millimeter diameter wells were inoculated with 50 µL from each solution. Plates inoculated with bacteria were incubated for 24 hours and those with fungus 48 hours, at 37°C. The effects of the new compounds were assessed by measuring the diameter of the growth inhibition zone. All the tests were performed in duplicate and the average was taken as final reading.

The antimicrobial effect was evaluated against two Gram-positive (*Listeria monocytogenes* ATCC 13932 and *Staphylococcus aureus* ATCC 49444) and two Gram-negative (*Escherichia coli* ATCC 25922, *Salmonella typhimurium* ATCC 14028) bacteriaand one fungal strain, *Candida albicans* ATCC 10231. The growth inhibitory effects displayed by the 5-(chromene-3-yl) methylene-2,4-thiazolidinedionesare presented in Table I.

All compounds displayed moderate to good antimicrobial activity on the selected strains. The most powerful effect was showed against *Salmonella typhimurium* ATCC 14028, where all molecules, excepting **8**, had a very good growth inhibitory activity, even superior to gentamicin, the reference antibacterial drug. The most promising compounds against this Gram negative strain were **2**, **3**, **7** and **9**, for which all concentrations used showed to be very active. The strongest inhibitory effect was displayed by compound **3**, at a concentration of 10 mg/mL and compound **4**, at a concentration of 5 mg/mL. The second Gram-negative bacterium used in the antimicrobial screening, *Escherichia coli* ATCC 25922, was less sensitive to the activity of the new synthesized chromenyl-thiazolidine-dione derivatives. Thus, best effect was noted for compounds **9** and **10**, at the concentration of 10 mg/mL, but inferior to that of the antibacterial reference drug. Same substances proved to be the most powerful inhibitors of the growth of *Listeria monocytogenes* ATCC 13932, their activity being superior to gentamicin. The

Table I

Diameters of the growth inhibition zones (mm) for the new 5-chromenyl-thiazolidinediones

Cp	Gram-positive bacteria (mm)		Gram-negative bacteria (mm)		Fungus (mm)
(10/5/1 mg/mL)	*L. monocytogenes*	*S. aureus*	*E. coli*	*S. typhi*	*C. albicans*
1	18/10/12	20/12/12	16/18/18	20/20/18	24/16/16
2	14/14/14	18/12/12	18/18/18	20/20/22	16/16/16
3	16/8/8	20/12/10	14/14/14	24/20/20	22/18/16
4	18/16/16	16/12/12	14/14/14	18/24/20	20/16/16
5	14/16/14	12/14/12	16/16/16	22/18/18	20/18/12
6	16/16/16	28/14/10	18/16/16	18/20/18	22/18/16
7	18/8/10	22/10/10	16/18/18	20/20/20	20/18/18
8	16/16/18	10/12/12	18/18/16	18/18/18	14/14/14
9	20/18/20	20/14/14	20/16/16	22/20/20	20/18/18
10	26/14/14	26/14/12	20/18/16	22/18/18	22/16/14
Gentamicin	18	19	22	18	NT
Fluconazole	NT	NT	NT	NT	28

diameters measured on *Staphylococcus aureus* ATCC 49444 revealed that compounds were more efficient at 10 mg/mL concentration and that compound **6** was the most active.

The compounds showed a moderate activity on *Candida albicans* ATCC 10231. The most powerful was compound **1**, at 10 mg/mL concentration. The less active was compound **8**, which displayed a modest antibacterial effect, also.

For substances displaying the same R, substitution of chromone with methyl group in position 6 was favorable for the activity against *Staphylococcus aureus*. Comparing with molecules which have alkyl substitutes at the level of thiazolidinedione nitrogen (Nastasă et al., 2013), the introduction of aryl fragment increased the effect against *S. aureus* bacterial strain. Better growth inhibitory activities expressed by compounds **9** and **10** could be explained by the capacity of amides to form complexes with metals required for microorganism survival.

As shown in our previous study, there was not a direct relationship established between the concentration and the effect of the 5-(chromene-3-yl)methylene-2,4-thiazolidinediones. The results obtained may suggest that, for these molecules, the antimicrobial activity is not dose dependent.

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