SHORT COMMUNICATION

PLANTS AS A SOURCE OF DIURETIC ACTIVITY AND STUDY OF 3-(6-ARYLIMIDAZO[2,1-B]THIAZOL-3-YL)-2-METHYLCHROMONE SYSTEM AS DIURETIC AGENT

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Abstract: Diuretic agents increase urine volume and are effective in heart failure , renal failure and maintain Na^+ ion balance. They are also effective in hypertension and nephrosis. Though plants possess diuretic activity , but their delayed action needs to use quickly acting agents . In this paper study on 3-(6-Arylimidazo[2,1-b]thiazol-3-yl)-2-methylchromones as diuretic agents is being discussed . Lead for diuretic activity has been found in this system .

Keywords: Diuretic activity, Chromones, Lead, Structure activity relationship (SAR)

INTRODUCTION

Diuretics are the drugs that increase urine volume as well as flow and clinically useful diuretics increase the rate of excretion of Na^+ ions (natriuresis) and accompanying ions like Cl^- ions (Jackson, 2001) . They adjust urine volume and composition of body fluids in situations like hypertension, heart failure, renal failure , nephrosis etc. (Jackson, 2001) . Most of the diuretics have adverse effects like fatigue, weakness and impotence. Plant based diuretics include caffeine present in tea, coffee and cola which inhibit sodium ion re-absorption . Most of the diuretics are effective in promoting sodium ion excretion; but all cause potassium ion loss (Vanamala *et al.* , 2012) . Moreover, resistance develops to diuretics (Brater, 1983). More than 650 herbal preparations in the form of tablets, decoctions, tinctures etc. have shown diuretic activity (Chopra *et al.*, 1986). *Achyranthes aspera* Linn .also possess diuretic activity (Srivastava *et al*., 2011). Aqueous extract of mango bark (*Mangifera indica*) is also diuretic (Shree Devi , 2011). Kane et al. (2009) reported potentiation of diuretic activity through ethanolic extract of *Euphorbia thymifolia*. Thus, various plant parts are good diuretic agents (Dutta et al. , 2014) ; but their action is delayed . Therefore, there is need to develop other diuretics which are non-resistant and non-toxic. Probably diuretic activity in plants is due to the presence of flavonoids and alkaloids in them (Vanamala et al., 2012) . Few chromone derivatives have shown diuretic activity in past (Sharma, 2015). Hence, it was thought to study diuretic activity in 3-(6-Arylimidazo[2,1-b]thiazol-3-yl)-2-methylchromones .

MATERIAL AND METHOD

3-(6-Arylimidazo[2,1-b]thiazol-3-yl)-2-methylchromones were synthesized by author in the Department of chemistry , Kurukshetra University , Kurukshetra (Garg et al. , 1985 ; Sharma , 2005) . The diuretic activity was tested at CDRI , Lucknow . Activity of compounds was compared with Chlorothiazide standard (value for which is taken as 100) [Table-1] .

RESULT AND DISCUSSION

6-Chloro-3-(6-phenylimidazo[2,1-b]thiazol-3-yl)-2-methylchromone (VPS-10) showed diuretic activity equal to 100 which is same as for chlorothiazide standard . However, compound is a bit toxic with ALD_{50} = 681 . VPS-11 with two halogens (chlorine atoms) , one at C_6 of chromone ring and other at *p*-position of phenyl ring present at C_6- position of imidazothiazolyl moiety , shows decrease in activity which becomes equal to 93 . This compound becomes safer [ALD_{50} > 1000] . Here one additional chlorine atom at conjugated position of phenyl ring decreases activity and toxicity as well. VPS-12 has one additional methyl group compared to VPS-10 at C_7- position of chromone ring; it exhibited less activity than VPS-10. It is inferred that additional methyl groups result in reduction of diuretic activity (*c. f.* Gupta , 2014) . One additional methyl group also reduced toxicity as ALD_{50} changes from 681 to 1000.

VPS-13 has two halogen atoms , Cl at C_6- position of chromone moiety and Br at *p*- position of phenyl ring present at C_6 – of imidazothiazolyl moiety . This compound also possesses a methyl group at C_7 – of chromone ring. Here reduction in diuretic activity is due to substituent Br and methyl group . Therefore , activity is much reduced and becomes equal to 68 because of the additive effect of Br and CH_3 . Toxicity of this compound is low because both Br and CH_3 decrease toxicity. 3-(6-(*p*)-chlorophenylimidazo[2,1-b]thiazol-3-yl)-2,6-dimethylchromome (VPS-14) has intermediate activity of 87 as methyl group decreases the activity and Cl substituent increases the activity in comparison to methyl group. As both these

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substituent decrease the toxicity the compound is safer for use with ALD_{50} value of 1000.

A look at these activities shows that additional halogen atom either Cl or Br decreases activity to same extent [activity of VPS-10 > VPS-11 by 7-units and activity of VPS-12 is > VPS-13 by 8-units] which may be ascribed to their same electronic effects (Silverman , 2004). Replacement of Cl by CH_3 group decreases the activity by 6-units [*c.f.* activity of VPS-11 and VPS-14].

Table 1. Effect of substitution on the diuretic activities of 3-(6-arylimidazo[2,1-b]thiazol-3-yl)-2-methylchromones :

S.No.	Code	Name of the compound	Activity	ALD_{50}
1.	VPS-10	6-chloro-3-(6-phenylimidazo[2,1-b]thiazol-3-yl)-2-methylchromone	100	681
2.	VPS-11	6-chloro-3-(6-(*p*)-chlorophenylimidazo[2,1-b]thiazol-3-yl)-2-methylchromone	93	>1000
3.	VPS-12	6-chloro-3-(6-phenylimidazo[2,1-b]thiazol-3-yl)-2,7-dimethylchromone	76	1000
4.	VPS-13	6-chloro-3-(6-(*p*)-bromophenylimidazo[2,1-b]thiazol-3-yl)-2,7-dimethylchromone	68	1000
5.	VPS-14	3-(6-(*p*)-chlorophenylimidazo[2,1-b]thiazol-3-yl)-2,6-dimethylchromone	87	1000
6.	Standard	Chlorothiazide	100	Drug

CONCLUSION

Methyl group at C_6 and C_7 – positions of chromone ring decreases the activity and introduction of halogen atom at *p*- position of aryl group present at 6-position of imidazothiazolyl moiety of 3-(6-arylimidazo[2,1-b]thiazol-3-yl)-2-methylchromones though decreases the activity but increases the diuretic activity in comparison to methyl group which may be attributed to their electronic effects . As all the tested 3-(6-arylimidazo[2,1-b]thiazol-3-yl)-2-methylchromones exhibited good diuretic activity so this system is a lead for this activity .

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