

Short communication

**URINARY BLADDER RELAXANT EFFECT OF *ARTEMISIA VULGARIS* AND
*ASPALATHUS LINEARIS***

Arif-ullah Khan^{1*} and A. H. Gilani²

¹Department of Pharmacology, Riphah Institute of Pharmaceutical Sciences, Riphah International University, Islamabad, Pakistan

²Natural Products Research Unit, Department of Biological and Biomedical Sciences, The Aga Khan University Medical College, Karachi-74800, Pakistan

*Corresponding authors e-mail: arif.ullah@riphah.edu.pk, anwarhgilani@yahoo.com

ABSTRACT

In isolated rabbit urinary bladder preparations, *Artemisia vulgaris* (Av.Cr) crude extract inhibited the contractions produced by carbachol (CCh, 1 μ M) and high K⁺ (80 mM) in a concentration-dependent (0.03-10 mg/mL) manners. The crude extract of *Aspalathus linearis* (Al. Cr) relaxed the contractions produced by low K⁺ (25 mM) at concentration range of 0.3-1.0 mg/mL, having moderate inhibitory effect on contractions produced by K⁺ (80 mM). Contractions induced by low K⁺ were partially antagonized by glibenclamide (3 μ M). These results indicate that urinary bladder relaxation produced by *Artemisia vulgaris* extract is mediated via dual, anticholinergic and Ca⁺⁺ antagonist mechanisms, while that of *Aspalathus linearis* via dominant K_{ATP} channel opening and weak Ca⁺⁺ channel blockade pathways. Thus the present study reveals the *Artemisia vulgaris* and *Aspslathus linaeris* medicinal usefulness in hyperactive bladder disorders

Key words: *Artemisia vulgaris*, *Aspalathus linearis*, urinary bladder relaxation.

INTRODUCTION

Hyperactivity of urinary bladder is mostly associated with urinary frequency and nocturia, resulting due to their involuntary contraction which leads to incontinence with and without urge. All of these symptoms are usually experienced by patients during filling phase of micturition cycle due to involuntary contractions of the bladder. Symptoms associated with dysfunction of the bladder are highly prevalent which deeply impair the quality of life of peoples, resulting in socio-economic burden on society. Urinary bladder contractility is predominantly controlled by muscurinic acetylcholine receptor system (Borchert *et al.*, 2004). We previously observed that *Artemisia vulgaris* Linn. commonly known as Mugwort (Compositae) exhibits antispasmodic, bronchodilatory and antidiarrheal properties, which is mediated through dual pathways i.e. Ca⁺⁺ antagonist and anticholinergic (Khan and Gilani, 2009). Similarly, *Aspalathus linearis* Burm. (Rooibos tea, Fabaceae) is reported to possess spasmolytic, airways relaxation, hypotensive and vasodilatory effects, occurred via predominant K⁺ channel activation and weak Ca⁺⁺ channel blockade mechanisms (Gilani *et al.*, 2006; Khan and Gilani, 2006, 2010). In present research, *Artemisia vulgaris* and *Aspalathus linearis* were investigated for the possible urinary bladder-relaxant action.

MATERIALS AND METHODS

Extraction of plant material: *Artemisia vulgaris* aerial parts were collected and shade dried followed by crushing. Then the crushed plant material was soaked in hydro-methanol (70%), filtered through filter paper and evaporated to obtain crude extract of *Artemisia vulgaris* (Av.Cr). *Aspalathus linearis* aqueous concentrate was evaporated at 45°C in rotary evaporator to obtain brown colored crude extract of *Aspalathus linearis* (Al. Cr).

Rabbit urinary bladder tissues: From rabbit whose neck was cervically dislocated, urinary bladder was isolated and sectioned into four vertical strips (Gilani *et al.*, 2008). Each tissue was hanged in tissue bath filled with 20 mL of Kreb's-Henseleit solution (pH 7.4), supplied continuously with carbogen gas. The inhibitory effects of the test material against CCh and/or K⁺ induced contractions were evaluated by adding test stock solution in cumulative fashion. The results observed after applying test materials were evidenced through Grass Model 7 Polygraph (Grass instrument company, USA).

RESULTS

When tested in urinary bladder strips, Av.Cr relaxed the contractions produced by K⁺ (80 mM) and CCh (1 μ M) (Figure 1), resulting with EC₅₀ values of 0.26 (0.14-0.5, 95% CI, n=4) and 3.4 mg/mL (2.5-4.9, n=4) respectively. On the other hand Al. Cr weakly effected (40%, n=3) the contractions produced by K⁺ (80

mM), while full relaxation was observed when applied on contractions produced by K^+ (25 mM). The EC_{50} value of 0.34 mg/mL (0.13-0.44, $n=4$) was calculated. In the presence of glibenclamide (3 μ M), the inhibitory effect of Al.Cr was partially blocked against K^+ (25 mM)-induced contraction and right shift in the curve was observed with an EC_{50} value of 2.4 mg/ml (1.6-3.7, $n=4$) as shown in Figure 2.

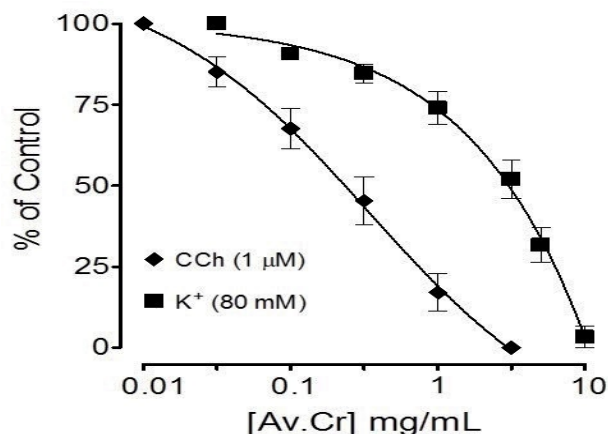


Figure 1. Concentration-response curves showing inhibitory effect of *Artemisia vulgaris* (Av.Cr) against carbachol (CCh) and K^+ -induced contractions in isolated rabbit urinary bladder preparations. Values shown are mean \pm SEM, $n=4$.

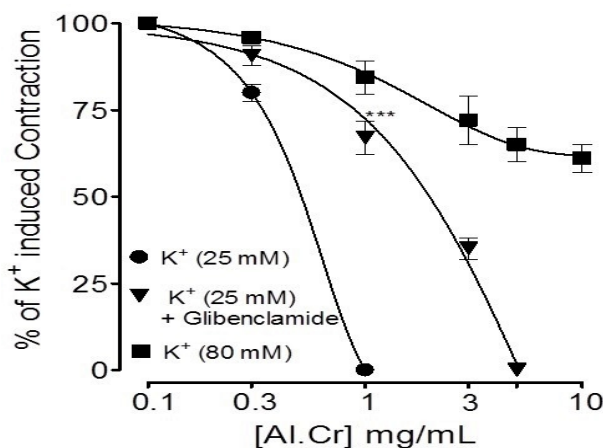


Figure 2. Concentration response curves showing effect of *Aspalathus linearis* (Al.Cr) for inhibitory effect against low K^+ (25 mM), in absence and presence of glibenclamide (3 μ M) and high K^+ (80 mM)-induced contractions in isolated rabbit urinary bladder preparations. Values shown are mean \pm SEM, $n = 3-4$. $***P < 0.001$ compared to respective concentrations values in absence of glibenclamide curve, two-way ANOVA followed by Bonferroni test.

DISCUSSION

In traditional system of medicine, *Artemisia vulgaris* and *Aspalathus linearis* are considered useful therapeutic agents in relieving smooth muscle spasms (Duke *et al.*, 2002). We therefore examined their effects on urinary bladder contractility. As expected, *Artemisia vulgaris* and *Aspalathus linearis* caused relaxation of urinary bladders tissues via various pharmacological mechanisms. The *Artemisia vulgaris* extract inhibited contractions induced by CCh more effectively than contractions induced by high K^+ , indicating that it mediate urinary bladder relaxation through dual muscarinic receptors and Ca^{++} entry blockade. *Aspalathus linearis* produced glibenclamide, a K_{ATP} channel blocker (Gopalakrishnan *et al.*, 2004) resistant inhibition of contractions produced by low K^+ , and with moderate effect against high K^+ . All of this reveals that a dual pathway of dominant ATP-dependent K^+ channel opening and weak Ca^{++} antagonism account for its urinary bladder relaxant effect. It is known that anticholinergics, Ca^{++} channel blockers and K^+ channel activating agents are the potential drugs for treatment of bladder hyperactivity (Empfield *et al.*, 1995; Andersson *et al.*, 2001). In conclusion, *Artemisia vulgaris* and *Aspalathus linearis* showed urinary bladder relaxant activity. Further detail clinical studies are warranted to confirm their pharmaceutical efficacy in remedy of overactive status of the urinary bladder.

REFERENCES

- Andersson, K. E., C. Chapple, and A. Wein (2001). The basis for the drug treatment of the overactive bladder. *World J. Urol.* 19:294-298.
- Borchert, V. E., P. Czyborra, C. Fetscher, M. Geopel, and M. C. Michel (2004). Extracts from *Rhois aromatica* and *Solidaginis virgaurea* inhibit rat and human bladder contraction. *Naunyn-Schmiedeberg's Arch. Pharmacol.* 369:281-286.
- Duke, J. A., M. J. Bogenschutz-Godwin, J. Duccellar, and P. A., Duke (2002). *Handbook of Medicinal Herbs*. CRC Press, Boca Raton. pp. 513-514.
- Empfield, J. R., K. Russell, and D. A. Trainor (1995). Potassium channel openers: Therapeutic possibilities. *Pharm. News* 6:23-27.
- Gilani, A. H., A. U. Khan, M. N. Ghayur, S. F. Ali, and J. W. Herzig (2006). Antispasmodic effect of Rooibos Tea (*Aspalathus linearis*) is mediated predominantly through K^+ channel activation. *Basic Clin. Pharmacol. Toxicol.* 99:365-373.
- Gilani, A. H., A. U. Khan, M. Raof, M. N. Ghayur, B. A. Siddiqui, W. Vohra, and S. Begum (2008). Gastrointestinal, selective airways and urinary bladder relaxant effects of *Hyoscyamus niger* are

- mediated through dual blockade of muscarinic receptors and Ca⁺⁺ channels. *Fund Clin. Pharmacol.* 22:87-99.
- Gopalakrishnan, M., S. A. Buckner, C. C. Shieh, T. Fey, A. Fabiyi, K. L. Whiteaker, R. D. Taber, I. Milicic, A. V. Daza, V. E. S. Scott, N. A. Castle, D. Printzenhoff, B. London, S. C. Turner, W. A. Carroll, J. P. Sullivan, M. J. Coghlan, and M. E. Brune (2004). *In-vitro* and *in-vivo* characterization of a novel naphthylamide ATP-sensitive K⁺ channel opener, A-151892. *Br. J. Pharmacol.* 143:81-90.
- Khan, A. U., and A. H. Gilani (2006). Selective bronchodilatory effect of Rooibos Tea (*Aspalathus linearis*) and its flavonoid: chrysoeriol. *Eur. J. Nutr.* 45:463-469.
- Khan, A. U., and A. H. Gilani (2009). Antispasmodic and bronchodilator activities of *Artemisia vulgaris* are mediated through dual blockade of muscarinic receptors and calcium influx. *J. Ethnopharmacol.* 126:480-486.
- Khan, A. U., and A. H. Gilani (2010). *In vivo* studies on bronchodilatory and analgesic activities of *Hysocyamus niger* and *Aspalathus linearis*. *Lat. Am. J. Pharm.* 29:777-782.