Short Communication

ANTIDEPRESSANT EFFECT OF *SOLANUM SURATTENSE* BURM. F.

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ABSTRACT

Solanum surattense Burm. f. is used in traditional medicine for various health problems, including depression. This research was conducted to explore the antidepressant effect of *Solanum surattense* in order to validate its therapeutic use in depression. Forced swim test (FST), tail suspension test (TST) and open field test models of mice were used for the investigation of antidepressant effect of *Solanum surattense* crude extract (Ss.Cr) by the determination of behavioural responses of mice like swimming, climbing, immobility time, ambulations and rearings in these test models. Ss.Cr tested positive for alkaloids, flavonoids, saponins, steriods and tannins. It exhibited antidepressant effect by dose dependently (100-200 mg/Kg) decreasing immobility time ($P < 0.001$ vs normal saline respectively) in both FST and TST, while increased swimming duration ($P < 0.01$, $P < 0.001$ vs normal saline respectively), as exhibited by fluoxetine (20 mg/Kg). Ss.Cr did not significantly alter ambulation and rearing frequencies in open field test. SS.Cr did not produce any mortality up to 5 g/Kg dose in acute toxicity test. These results indicate that *Solanum surattense* possess antidepressant activity. The presence of phytochemicals, such as flavonoids and saponins argue the cogency of the proclaimed folk medicinal effect in depression.

Keywords: *Solanum surattense* Burm. f, Antidepressant, Forced swim test, Tail suspension test, Open field test, Mice

INTRODUCTION

Solanum surattense Burm. f. belongs to family Solanaceae, its english name is "yellow berried nightshade" (Rasheeduz and Parisa, 2015), locally called "Mokri", "Kandiari" (Marwat *et al*., 2014) and in domestic language Pashto called "Khraan Maraghoonra" in Lakki Marwat (Shafiullah *et al*., 2014). It is a natural growing perennial herb found in Pakistan and India (Ahmed *et al*., 2016). The plant is traditionally used for cough, leprosy, dropsy, fever, dysmenorrheal, hypertension, cardiac disorders, asthma, epilepsy and depression (Singh *et al*., 1979; Vaidyaratnam, 1994; Khan *et al*., 2019). The chemical constituents of *Solanum surattense* include solasodine, alkaloids, Sterols, saponins, flavonoids and glycosides (Ramar and Nandagopalam, 2011). It has been pharmacologically evaluated for analgesic (Amirtharaj *et al*., 2015), antidiabetic, antibacterial, antinociceptive, antioxidant, antifungal and larvicidal (Ramar and Nandagopalam, 2011) activities. In this study, we reveal antidepressant effect of *Solanum surattense* Burm. f, which elucidate its traditional use in depression.

MATERIALS AND METHODS

Animals: Both male and female albino mice, having weight 25-30 g, were utilized for this research. Mice were kept in animal house under standard laboratory conditions; 25°C, light-dark with equal 12 h period and were free for eating and drinking diet and water. This research study (Reference No: REC/RIPS/2015/006.) was performed according to the guidelines set by Commission on Life Sciences University, Institute of Laboratory Animal Resources, National Research Council and recommended by of Riphah Institute of Pharmaceutical Sciences' Ethical Committee.

Plant Material: *Solanum surattense* Burm. f. whole plant (2 Kg) was collected from district Lakki Marwat, Khyber Pakhtunkhwa. A plant taxonomist, Dr. Mushtaq Ahmad, Quaid-e-Azam University, Islamabad, verified the plant and a reference number ISL-12410 was submitted for future reference at the said department.

Extraction: After shade drying and grinding, 1.5 Kg of coarse powder was obtained and macerated in 70% methanol-water for 15 days, periodically mixed with stirrer. The extract was refined by filtration and then concentrated through rotavaps to get a black moist paste of *Solanum surattense* burm. f. crude extract (Ss.Cr). The % yield of Ss.Cr was found to be 16.66% w/w.

Chemicals: Fluoxetine was purchased from Hygeia Pharmaceuticals, Industrial Triangle Kahuta Road, Islamabad, Pakistan

Preliminary Phytochemical screening: Phytochemical tests were performed for screening of alkaloids, flavonoids, saponins, steriods and tannins complying to standard techniques (Harborne, 1984; Evans, 1996) with little bit modifications. Dragendorff's and Mayer's reagent test was performed for detection of alkaloids. The

extract was marked positive for flavonoids if yellow color was obtained with sodium hydroxide. The presence of saponins was identified when foam was produced on vigorously shaking of diluted sample of extract. Steroids were considered positive, if plant material treated with chloroform and sulfuric acid subsequently produced red coloration. On treatment with lead acetate, appearance of cream yellow color revealed presence of tannins.

Forced swim test (FST): FST formerly used for evaluating antidepressant activity (Harquin *et al.*, 2014) was applied. The test model consist of a cylindrical glass (30 cm in height and 20 cm in width) filled up to 2/3rd portion of it with water and maintained at 25 ± 2°C. Mice were separated into 5 groups (each group with 5 animals), administered normal saline (NS) 10 mL/Kg, Ss.Cr 30-200 mg/Kg and fluoxetine 20 mg/Kg body weight once/day for seven days intraperitoneally. On 7th day, 30 min. later to administration of NS, Ss.Cr, and fluoxetine, each mouse was allowed to swim in tank for five min. and duration of immobility, swimming and climbing were recorded via digital video camera. Animal that remained floating over water without scuffling or showing only little movements to save itself from dipping into water, will be considered immobile. Swimming is large horizontal movements of mice with forepaws, displacing mice body around cylinder while climbing is vibrant upright movements of mice with front paws against tank's wall, resulting in displacement of mice body around cylinder. The decrease in immobility time while increase in swimming and/or climbing behaviors show antidepressant activity.

Tail suspension test (TST): Tail suspension test which was previously described by (Chatterjee *et al.*, 2012; Aslam, 2016) was followed for measuring immobility time with little modification. In this test, mice were hanged 50cm over the ground on table's edge by sticky strip placed about one cm from tail's tip. Mice were separated into 5 groups (each group with 5 animals), administered NS 10 mL/Kg, Ss.Cr 30-200 mg/Kg and fluoxetine 20 mg/Kg body weight once/day for seven days intraperitoneally. On 7th day, 30 min. later to administration of NS, Ss.Cr, and Fluoxetine, each mouse was suspended and immobility duration was recorded for 5 min. via digital video camera. Animal will be considered immobile when it becomes completely motionless and hanged passively.

Open field test: This test was performed to distinguish between general stimulation of motor activity and antidepressant effect of Ss.Cr. It is a wooden apparatus with glass walls dimensions (50×25×50 cm) and its base is divided into 12 equal squares. Mice were separated into 5 groups (each group with 5 animals), administered NS 10 mL/Kg, Ss.Cr 30-200 mg/Kg and fluoxetine 20 mg/Kg body weight once/day for seven days

intraperitoneally. On 7th day, 30 min. later to administration of NS, Ss.Cr, and Fluoxetine, mice were placed in the side square to search the test model and number of ambulations and rearings were recorded via digital video camera (Khan *et al.*, 2016). The total numbers of squares crossed by a mouse are ambulations, the number of times a mouse stood on its rear legs is rearing and the number of times a mouse get into middle boxes with its all legs is central squares crossings. When a mouse enters in a square with its all four legs, is counted as one square crossed.

Acute toxicity test: Mice were placed in three groups, each having five animals. The test was conducted using high strength of Ss.Cr (3 and 5 g/Kg) administered in 10 mL/Kg volume. NS 10 mL/Kg was administered orally to one group. After 24 hours of study, mice were observed for mortality (Khan *et al.*, 2016).

Statistical analysis: The one-way analysis of variance, followed by Tukey post-hoc test, was used for statistical analysis. $P < 0.05$ was deemed to be significantly different. Data exhibited are mean ± standard error of mean (S.E.M). Bar graphs were analyzed by using Graph-Pad Prism (San Diego, CA, United States).

RESULTS

Phytochemical analysis: Ss.Cr tested positive for presence of saponins, flavonoids, alkaloids, tannins and steroids.

Effect on immobility, swimming and climbing times in FST: Ss.Cr (30-200 mg/Kg) decreased dose dependently immobility time, while increased swimming and non-significantly the climbing times in FST, as shown in (Figure 1). In NS group, the respective values of immobility, swimming and climbing times were 169.2 ± 5.88, 91.8 ± 6.78 and 39 ± 3.96 sec. In Ss.Cr (30 mg/Kg) group, immobility time was 155.6 ± 3.61 sec., while swimming and climbing times were 102.2 ± 4.21 and 42.2 ± 2.04 sec. respectively ($P > 0.05$ vs. NS). In Ss.Cr (100 mg/Kg) group, immobility time was reduced to 122.60 ± 6.24 sec. ($P < 0.001$ vs. NS), while swimming and climbing times were increased to 128.4 ± 6.91 sec. ($P < 0.01$ vs. NS) and 49 ± 4.09 sec. ($P > 0.05$ vs. NS) respectively. In Ss.Cr (200 mg/Kg) group, immobility time was reduced to 84.60 ± 5.66 sec. ($P < 0.001$ vs. NS), while swimming and climbing times were increased to 165 ± 7.48 sec. ($P < 0.001$ vs. NS) and 50.40 ± 4.67 sec. ($P > 0.05$ vs. NS) respectively. In fluoxetine (20 mg/Kg) group, immobility, swimming and climbing times were 64.40 ± 4.52, 183.60 ± 4.80 and 52 ± 3.33 sec. ($P < 0.001$, $P > 0.05$ vs. NS) respectively.

Effect on immobility time in TST: Ss.Cr (30-200 mg/Kg) decreased dose dependently immobility time in

TST as showed in (Figure 2). In NS group, immobility time was 178.4 ± 6.43 sec. In Ss.Cr (30 mg/Kg) group, immobility time was 166.8 ± 4.75 sec. ($P > 0.05$ vs. NS). In Ss.Cr (100 mg/Kg) group, immobility time was reduced to 130.40 ± 6.96 sec. ($P < 0.001$ vs. NS). In Ss.Cr (200 mg/Kg) group, immobility time was reduced to 80.20 ± 4.66 sec. ($P < 0.001$ vs. NS). In fluoxetine (20 mg/Kg) group, immobility time was decreased to 71.40 ± 5.42 sec. ($P < 0.001$ vs NS).

Effect on number of ambulations and rearings in open field test: Ss.Cr at (30-200 mg/Kg) did not significantly changed animals locomotors activity i.e. number of ambulations and rearings as shown in (Figure 3). In NS group, numbers of ambulation and rearing were 79 ± 4.72

and 41 ± 3.61 respectively. In Ss.Cr (30 mg/Kg) group, the respective values of numbers of ambulation and rearing were 80.40 ± 4.06 and 39.60 ± 3.70 ($P > 0.05$ vs. NS). In Ss.Cr (100 mg/Kg) group, numbers of ambulation and rearing were 74.80 ± 3.84 and 38 ± 3.12 ($P > 0.05$ vs. NS) respectively. In Ss.Cr (200 mg/Kg) group, numbers of ambulation and rearing were 71 ± 4.85 and 36 ± 4.54 ($P > 0.05$ vs. NS) respectively. In fluoxetine (20 mg/Kg) group, numbes of ambulation and rearing were 72.80 ± 5.28 and 35.60 ± 3.39 ($P > 0.05$ vs. NS).

Acute Toxicity: At orally administered higher doses (3 and 5 g/Kg), Ss.Cr did not cause any mortality of mice after 24 hours of observation.
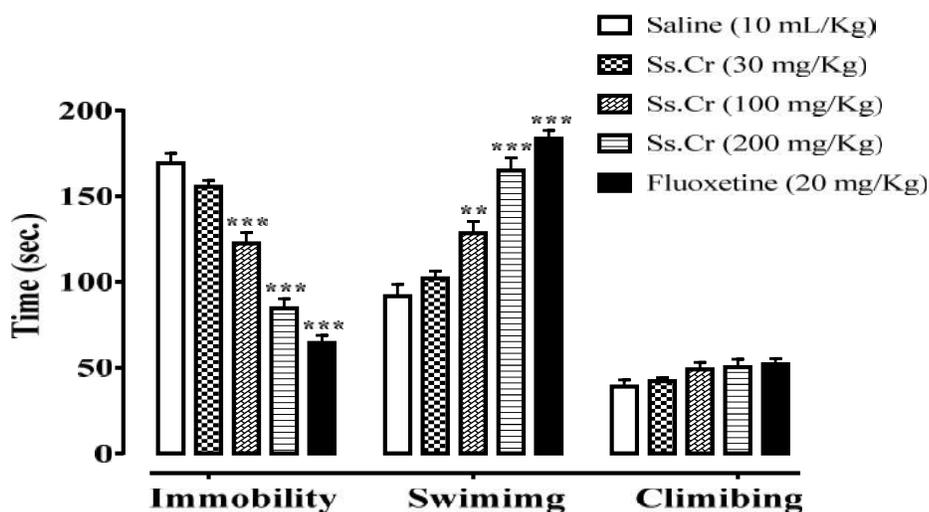

Figure 1. Bar-graph showing effect of *Solanum surattense* crude extract (Ss.Cr) and fluoxetine on immobility, swimming and climbing times in forced swim test in mice. Data expressed as mean ± SEM, n=5. **$P <$ 0.01, ***$P < 0.001$ vs. NS, one-way ANOVA with post-hoc Tukey test.
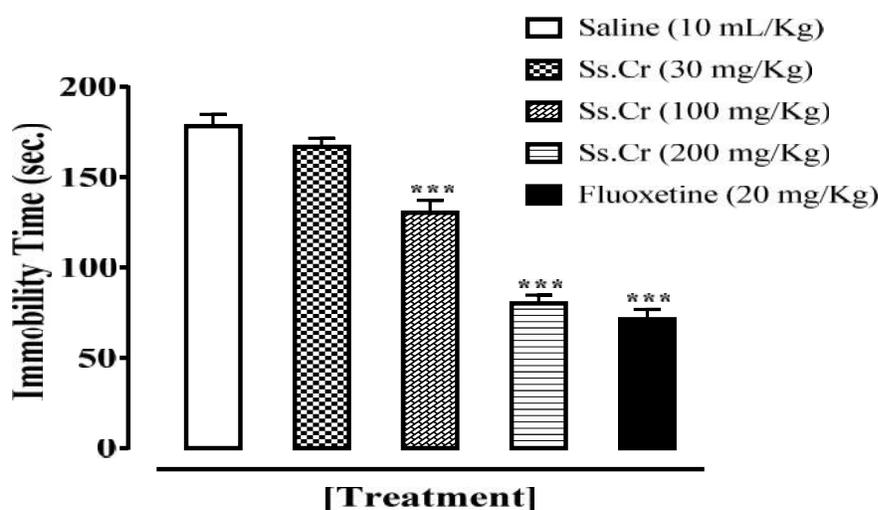

Figure 2. Bar-graph showing effect of *Solanum surattense* crude extract (Ss.Cr) and fluoxetine on immobility time in tail suspension test in mice. Data expressed as mean ± SEM, n=5. ***$P < 0.001$ vs. NS group, one-way ANOVA with post-hoc Tukey test.
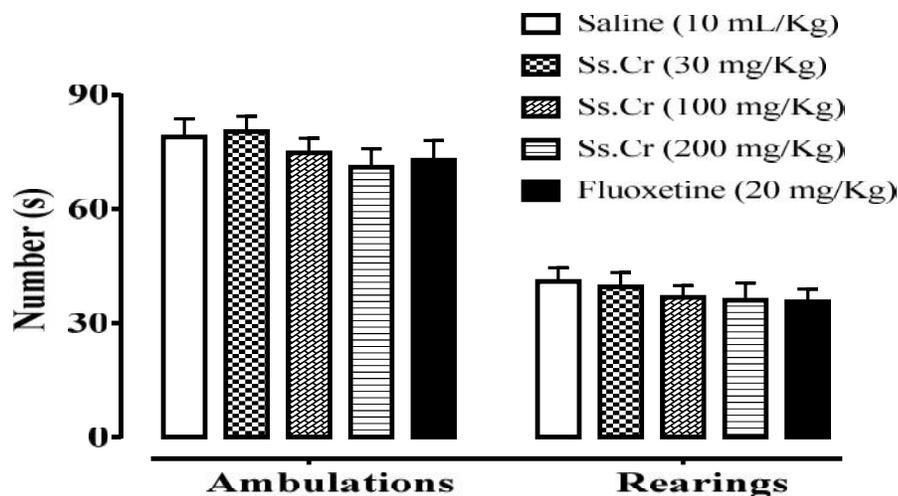
Figure 3. Bar-graph showing effect of *Solanum surattense* crude extract (Ss.Cr) and fluoxetine on number of mice ambulations and rearings in open field test. Data expressed as mean ± SEM, n=5, one-way ANOVA with post-hoc Tukey test.

DISCUSSION

Drugs which decrease the immobility duration in FST and TST, while increased the behavioral activities like swimming and/or climbing of mice in FST, often have antidepressant effects (El Tanbouly *et al.*, 2017; Benneh *et al.*, 2018). Ss.Cr reduced immobility time in both FST and TST, while increased swimming time in FST, exhibiting antidepressant effect. Just before FST, mice were tested in open field model in order to eliminate false-positive results that can be obtained with certain psychomotor stimulants, which by stimulating locomotors activity, decrease immobility time (Bourin *et al.*, 2001). The results revealed that Ss.Cr at doses, at which it exhibited antidepressant effect, did not notably change locomotors activities like ambulations and rearings frequencies. Hence, Ss.Cr shows to exhibit particular antidepressant effect. Climbing behavior is sensitive to noradrenergic while swimming behavior is sensitive to serotonergic neurotransmissions (Detke *et al.*, 1995). In FST, like flouxetine, Ss.Cr decreased immobility time while increased swimming time without significantly disturbing climbing behavior. This may suggest that serotonergic neurotransmissions may be responsible for antidepressant effect of Ss.Cr. The leaves and seeds of Ss.Cr have been known for flavonoids (kaempferol, quercetin) and ascorbic acid (Mali and Harsh, 2015) and these constituents are known for their antidepressant effects (Binfaré *et al.*, 2009; Park *et al.*, 2010). Depression can result from reduction of monoamine neurotransmitters (norepinephrine, dopamine and serotonin) in brain (Delgado, 2000). Ss.Cr constituents (Kaempferol and quercetin) are known for increasing level of these neurotransmitters and reduce serotonin metabolism in mice brain of FST and TST (Yan *et al.*, 2015). It is known that ascorbic acid shows its antidepressant effect via activation of phosphatidylinositol 3-kinase and mammalian target of rapamycin, inhibition of glycogen synthase kinase-3β and also via induction of hemeoxygenase-1 (Moretti *et al.*, 2014). Sc.Cr was found to be safe in acute toxicity test up to the highest tested dose (5 g/Kg), which shows the wide therapeutic range of *Solanum surattense*.

Conclusions: The present study reveals antidepressant effect of *Solanum surattense*, which affirms its medicinal application in neuronal diseases such as depression. Further advanced investigations are vindicated to identify the active principals and explicate the mechanism basis of the observed neuropharmacological effect.

Conflict of Interest: The authors have no conflict of interest.

Contribution of authors: The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

REFERENCES

Ahmed, M. M., S. Andleeb, F. Saqib, M. Hussain, M.N. Khatun, B.A. Chaudhry., and H. Rahman (2016). Diuretic and serum electrolyte regulation potential of aqueous methanolic extract of *Solanum surattense* fruit validates its folkloric use in dysuria. BMC Complement Altern Med. 16: 166.

Amirtharaj, L.V., N. Srinivasan, S. Abburi, K. Karthikeyan, and S. Mahalaxmi (2015). Evaluating the Analgesic Efficacy of *Solanum surattense* (Herbal Seed Extract) in Relieving Pulpal Pain-An In-vivo Study. Dentistry. 5: 1.

Aslam, M. (2016). Tail suspension test to evaluate the antidepressant activity of experimental drugs. Bangladesh J. Pharmacol. 11: 292-294.

Benneh, C.K., R.P. Biney, D.W. Adongo, P.K. Mante, F.A. Ampadu, A. Tandoh, J. Jato, and E. Woode (2018). Anxiolytic and Antidepressant Effects of *Maerua angolensis* D C. Stem Bark Extract in Mice. Depress Res Treat. https://doi.org/10.1155/2018/1537371

Binfaré, R.W., A. O. Rosa, K.R. Lobato, A. R. Santos and A.L. Rodrigues (2009). Ascorbic acid administration produces an antidepressant-like effect: evidence for the involvement of monoaminergic neurotransmission. Prog Neuropsychopharmacol Biol Psychiatry. 33: 530-540.

Bourin, M., A.J. Fiocco, and F. Clenet (2001). How valuable are animal models in defining antidepressant activity? Hum Psychopharmacol Clin Exp. 16: 9-21.

Chatterjee, M., M. Jaiswal, and G. Palit (2012). Comparative evaluation of forced swim test and tail suspension test as models of negative symptom of schizophrenia in rodents. ISRN Psychiatry, 2012.

Delgado, P.L. (2000). Depression: the case for a monoamine deficiency. J Clin Psychiatry. 61: 7-11

Detke, M.J., M. Rickels, and I. Lucki (1995). Active behaviors in the rat forced swimming test differentially produced by serotonergic and noradrenergic antidepressants. Psychopharmacology. 121: 66-72.

El Tanbouly, N., A.M. El Sayed, Z.Y. Ali, S.A. Wahab, S.H. El Gayed, S.M. Ezzat. and E.A Sattar (2017). Antidepressant-like effect of selected Egyptian cultivars of flaxseed oil on a rodent model of postpartum depression. Evid Based Complement Alternat Med. 2017.

Evans, W.C. (1996). Trease and Evan's Pharmacognosy: 14th edn. London: WB Sounders. 161-408.

Harborne, J.B. (1984). Phytochemical Methods: 2nd edn. New York: Chapman and Hall. 73-89.

Harquin, S.F., E.T. David, and N.A. Hervé (2014). Enhancing spatial memory: anxiolytic and antidepressant effects of *Tapinanthus dodoneifolius* (DC) Danser in mice. Neurol Res Int. 2014.

Khan, A.W., A.U. Khan, and A. Touqeer (2016). Anticonvulsant, anxiolytic, and sedative activities of *Verbena officinalis*. Front Pharmacol. 7: 499.

Khan, A.W., A.U. Khan, S.M.M. Shah, A. Ullah, M. Faheem, and M. Saleem (2019). An updated list of neuromedicinal plants of Pakistan, their uses, and phytochemistry. Evid Based Complement Alternat Med. https://doi.org/10.1155/2019/6191505

Mali, M.C., and N. Harsh (2015). Nutritional value estimation of the leaves and seeds of *Solanum surattense*. J. Med. Plants. Stud. 3: 27-29.

Marwat, S.K., E.A. Khan, A.A. Khakwani, I. Ullah, K.U. Khan, and I.U. Khan (2014). Useful ethnophytomedicinal recipes of angiosperms used against diabetes in South East Asian Countries (India, Pakistan & Sri Lanka). Pak J Pharm Sci. 27: 1333-1358.

Moretti, M., J. Budni, A.H. Freitas, P.B. Rosa, and A.L. Rodrigues (2014). Antidepressant-like effect of ascorbic acid is associated with the modulation of mammalian target of rapamycin pathway. J Psychiatr Res. 48: 16-24.

Moretti, M., J. Budni, A.H. Freitas, P.B. Rosa, and A.L. Rodrigues (2014). Antidepressant-like effect of ascorbic acid is associated with the modulation of mammalian target of rapamycin pathway. J Psychiatr Res. 48: 16-24.

Park, S.H., Y.B. Sim, P.L. Han, J.K. Lee, and H.W. Suh (2010). Antidepressant-like Effect of Kaempferol and Quercitirin, Isolated from *Opuntia ficus*-indica var. saboten. Exp Neurobiol. 19:30-38.

Ramar, K., and V. Nandagopalam, (2011). Rapid in vitro propagation of medicinally important plant *Solanum surattense*. Int. J. Pharm. Life Sci. 2: 499-501.

Rasheeduz, Z., and H. Parisa (2015). Quantification of Solasodine in Callus and Suspension Cultures of *Solanum xanthocarpum* Schrad. & Wendl by RP-HPLC. Int. J. Pharmacogn. Phytochem. Res. 7: 206-214.

Shafiullah, M.R. Khan, N.A. Shah, S.A. Shah, M. Majid, and M.A. Farooq (2014). Ethnomedicinal plant use value in the Lakki Marwat district of Pakistan. J. Ethnopharmacol. 158: 412-422.

Singh, M.P., S.B. Malla, S.B. Rajbhandari, and A. Manandhar. (1979). Medicinal plants of Nepal-retrospects and prospects. Econ. Bot. 33: 185-198.

Vaidyaratnam, P.V. (1994). Indian medicinal plants: a compendium of 500 species. Madras: Orient Longman Ltd. 59-64.

Yan, S.X., J.L. Lang, Y.Y. Song, Y.Z. Wu, M.H. Lv, X. Zhao, Y.H. Liu, and C.Y. Xu (2015). Studies on anti-depressant activity of four flavonoids isolated from *Apocynum venetum* Linn (Apocynaceae) leaf in mice. Trop J Pharm Res. 14: 2269-2277.