International Journal of Engineering Research & Management Technology
ISSN: 2348-4039
January-2016 Volume- 3, Issue-1
Email: editor@ijermt.org www.ijermt.org

REVIEW ON BACOPA MONNIERI: A MULTIPOTENTIAL MEDICINAL PLANT

VINEET KUMAR VISHNOI[1*], PEEUSH SINGHAL[2,] KAPIL KUMAR GOEL[3,] RITU VISHNOI SINGHAL[4]

[1*]Deptt. of Botany & Microbiology, Gurukul Kangri Vishwavidyalaya, Haridwar-249404, Uttarakhand
[2,3]Deptt. of Pharmaceutical Sciences, Gurukul Kangri Vishwavidyalaya, Haridwar-249404, Uttarakhand
[4]Department of Botany, Chinmaya Degree College, BHEL, Ranipur, Haridwar-249404, Uttarakhand

ABSTRACT:
In current periods, the consumption of herbal products has greater than before greatly in the western world as well as in developed countries. Recently, one of the excellently important medicinal plants, widely used therapeutically and becoming gradually popular in the west is Bacopa monnieri, well-known cognitive enhancers. It was widely used in traditional medicine to treat various diseases. The current analysis condenses our present information of pharmacological actions, preclinical and clinical studies, major bioactive, reported mechanisms of actions, clinical efficacy, safety and the possibility of interactions of the herb with the conventional drugs. Simultaneously, research updates as well as possibilities for additional research are also stated concerning the plant.

Key words: Bacopa monnieri, Neurotonics, Clinical studies, Herb-drug interactions, Biological activity, Brahmi

INTRODUCTION:

Recently, the interest in the use of herbal products has grown dramatically in the western world as well as in developed countries [1]. It is now becoming exceedingly apparent that available psychotherapeutics does not properly meet therapeutic demands of a vast majority of patients with mental health problems, and that herbal remedies remain to be the ultimate therapeutic hope for many such patients in the western world and elsewhere [2]. The vast majorities of currently available psychoactive drugs as herbal remedies today seem to be a reflection of such a situation. In the folklore of Indian medicine, several herbs have been used traditionally as brain or nerve tonics. One of the most popular of these herbs is Bacopa monniera (BM), a well-known memory booster. This comprehensive review summarizes our current knowledge of the major bioactivities and clinical efficacy of BM, one of the currently popular central nervous system (CNS)-activating herbal plants.

EXPLANATION OF THE PLANT:

Bacopa monnieri (water hyssop, brahmi[2], thyme-leafed gratiola, water hyssop, herb of grace[2], Indian pennywort[2]) is a perennial, creeping herb native to the wetlands of southern and Eastern India, Australia, Europe, Africa, Asia, and North and South America[2].Bacopa is a medicinal herb used in Ayurveda, where it is also known as "Brahmi", after Brahmā , the creator God of the Hindu pantheon. It is a non-aromatic herb. The leaves of this plant are succulent, oblong and 4–6 mm (0.16–0.24 in) thick. Leaves are oblanceolate and are arranged oppositely (opposite decussate) on the stem. The flowers are small, actinomorphic and white, with four to five petals. Its ability to grow in water makes it a popular aquarium plant. It can even grow in slightly brackish conditions. Propagation is often achieved through cuttings [3]. It commonly grows in marshy areas throughout India, Nepal, Sri Lanka, China, Pakistan, Taiwan, and Vietnam. It is also found in Florida, Hawaii and other southern states of the United States where it can be grown in damp conditions by a pond or bog garden [4]. This plant can be grown hydroponically. Brahmi is also the name given to Centellaasiatica, particularly in North India, and Kerala where it is also identified in

Malayalam as muttil (മുത്തിള്) or kodakan. This identification for long in northern India, as Hē mā dri's Commentary on Aṣ ṭ ā ṅ gahṛ dayaṃ (Ā yuṛ vē darasā yanaṃ) treats maṇ ḍ ū kapaṛ ṇ ī (C. asiatica) as a synonym of brahmi[6;7], although that may be a case of mistaken identification that was introduced during the 16th century[8].Bacopamonnieri was initially described around the 6th century A.D. in texts such as the Charaka Samhita, Atharva-Veda, and Susrut Samhita as a medhyarasayana–class herb taken to sharpen intellect and attenuate mental deficits. The herb was allegedly used by ancient Vedic scholars to memorize lengthy sacred hymns and scriptures.

Figure 1: Bacopamonniera herb

Scientific classification:

Kingdom:	Plantae
(unranked):	Angiosperms
(unranked):	Eudicots
(unranked):	Asterids
Order:	Lamiales
Family:	Plantaginaceae (orScrophulariaceae)
Genus:	Bacopa
Species:	B. monnieri
Binomial name	Bacopamonnieri (L.) Pennell

CHEMICAL CONSTITUENTS:

The best characterized compounds in Bacopa monnieri are dammarane-type triterpenoidsaponins known as bacosides, with jujubogenin or pseudo-jujubogenin moieties as aglycone units [9].Bacosides comprise a family of 12 known analogs [10]. Other saponins called bacopasides I–XII have been identified more recently[11]. The alkaloids brahmine, nicotine, and herpestine have been catalogued, along with D-mannitol, apigenin, hersaponin, monnierasides I–III, cucurbitacin and plantainoside B[12;13;14].The constituent most studied has been bacoside A, which was found to be a blend of bacoside A3, bacopacide II, bacopasaponin C, and a jujubogenin isomer of bacosaponin C[15]. These assays have been conducted using whole plant extract, and bacoside concentrations may vary depending upon the part from which they are extracted. In one Bacopa monnieri sample, Rastogi et al. found this bacoside profile—bacopaside I (5.37%), bacoside A3 (5.59%), bacopaside II (6.9%), bacopasaponin C isomer (7.08%), and bacopasaponin C (4.18%)[16].

MECHANISM OF ACTION BASED ON PRECLINICAL STUDIES

The BM extracts and isolated bacosides have been comprehensively examined for their neuro-pharmacological effects. The triterpenoidsaponins and their bacosides are assumed to be responsible for BM's ability to enhance nerve impulse transmission. It was recommended that bacosides prompt membrane dephosphorylation, with a concomitant increase in protein and RNA turnover in specific brain areas [17].The other proposal that was put forward was that BM enhances protein kinase activity in the

hippocampus which may also contribute to its neurotropic action and thus it would aids in repair of damaged neurons by enhancing kinase activity, neuronal synthesis and restoration of synaptic activity and ultimately nerve impulse transmission[18].

RESEARCH:

Bacopa monnieri displays in vitro antioxidant and cell-protective effects [19]. In animals, it also inhibits acetylcholinesterase, activates choline acetyltransferase, and increases cerebral blood flow [20].Several studies have suggested that Bacopa monnieri extracts may have protective effects in animal models of neurodegeneration [21]. Small clinical trials in humans have found promising evidence for memory recall but research for other cognitive domains remains in its infancy [22; 23].

SEDATIVE AND TRANQUILLIZING PROPERTIES

Earlier studies reported a sedative effect of glycosides named hersaponins[24]. A subsequent study has found that the alcoholic extract, and to a lesser extent the aqueous extract of the whole plant exhibited tranquilizing effects on albino rats and dogs [25]. A previous study has reported that a single dose of the glycoside hersaponin is better than pentobarbitone in facilitating acquisition and retention of brightness discrimination reaction [26].

COGNITION

A team of other researcher reported that a standardized bacosides-rich extract of BM, reversed the cognitive deficits induced by intracerebroventricularly administered colchicines and injection of ibotenic acid into the nucleus Basalismagnocellularis [27].

ANTIDEPRESSANT AND ANTIANXIETY EFFECTS:

The antidepressant potential of BM has been evaluated in an earlier study, wherein it showed a significant antidepressant activity in the most commonly used behaviour paradigms in animal models of depression, namely, forced swim test and learned helplessness tests [28]. In the study, the BM extract in the dose range of 20-40 mg/kg was given once daily for 5 days and it was found comparable to standard anti-depressant drug imipramine in anti-depressant activity in rodent animals. The same study has postulated the role of serotonin and GABA (gamma amino butyric acid) in the mechanism of action attributed for its antidepressant action along with its anxiolytic potential, based on the compelling evidence that the symptoms of anxiety and depression overlap each other[29].

ANTI-EPILEPTIC EFFECTS

Although BM has been indicated as a remedy for epilepsy in Ayurvedic medicine[30], research in animals showed anticonvulsant activity only at high doses over extended periods of time. Early research in India demonstrated that hersaponin (an active constituent) exhibited protection against seizures in mice and mentioned the possibility of its use as an adjuvant in treatment of epilepsy[31].

GASTROINTESTINAL EFFECTS:

Some in vitro, animal and human studies have investigated the effects of BME on the gastrointestinal tract. In vitro studies have demonstrated direct spasmolytic activity on intestinal smooth muscle, via inhibition of calcium influx across cell membrane channels. This property suggests that BME may be of benefit in conditions characterized by intestinal spasm such as irritable bowel syndrome (IBS)[32;33]. A recent in vitro study also demonstrated its specific anti-microbial activity against Helicobacter pylori, a bacterium associated with chronic gastric ulcers. When the extract was incubated with human colonic muscosal cells and H. pylori, it resulted in the accumulation of prostaglandin E and prostacycline, prostaglandins known to be protective for gastric mucosa [34].

ANTIMICROBIAL EFFECTS:

Methanol extracts were found to be the most potent antimicrobial agent in comparison to other extracts. Aqueous extracts showed no activity against any of the microorganisms. Hexane and petroleum ether extracts showed similar antimicrobial activity but less significant in comparison to methanol extracts. The MIC of the methanol extracts was found to be the lowest against E.coli, Salmonellatyphimurium , Staphylococcus aureus and Saccharomyces cerevisae [35]. Methanolic extract (1mg/ml) of callus of Bacopa monnieri shows good activity against Staphylococcus aureus , Salmonella typhi and E. coli and maximum activity was observed against Staphylococcus aureus . No activity was observed against K. pneumoniae [36]. Ether extract of Bacopa monnieri showed antimicrobial activity against four bacteria and one fungus, Salmonella typhi, Pseudomonas aeruginosa, Staphylococcus aureus, Vibrio cholerae and Candida albicans [37].

MISCELLANEOUS STUDIES

In vitro research has shown a protective effect of BM against DNA damage in astrocytes [38] and human fibroblasts [39].In vitro research has suggested that an anticancer effect of BM extracts is possibly due to inhibition of DNA replication in cancer cell lines [40]. A study in mice demonstrated high doses (200 mg/kg) of BME increased the thyroid hormone, T4, by 41% when given orally. T3 was not stimulated, suggesting that the extract may directly stimulate synthesis and release of T4 at the glandular level, while not affecting conversion of T4 to T3. While this study indicated that BM extract did have a stimulatory effect on thyroid function, the doses were very high and it was assumed that the typical 200-400 mg daily dose in humans may not have the same effect[41]. BM was also reported to possess anti-inflammatory activity via inhibition of prostaglandin synthesis and lysosomal membrane stabilization[41,42]. In vitro research using rabbit aorta and pulmonary artery has demonstrated that BME exerts a vasodilatory effect on calcium chloride-induced contraction in both tissues. It is believed to exert this effect via interference with calcium channel flux in tissue cells [43]. Animal studies have demonstrated that BME have a relaxant effect on chemically-induced bronchoconstriction, probably via inhibition of calcium influx into cell membranes. An earlier in vitro study demonstrated the broncho-vasodilatory activity of BM on rabbit and guinea pig trachea, pulmonary artery and aorta[43].

CONTRAINDICATIONS AND INJURIOUSNESS

BM has a best ever of a number of hundred years of nontoxictherapeutic use in Herbal medicine. A double-blind, clinical trial of healthy male volunteers examined the safety of Therapeutic doses of isolated bacosides over a 4-week period. Concentrated bacosides given in single (20-30 mg) and multiple (100-200 mg) daily doses were well tolerated and without adverse effects[46].The LD 50 of aqueous and alcoholic extracts of BM in rats were 1000 mg and 15 g/kg by the intraperitoneal route respectively[47]. The aqueous extract given orally at a dose of 5 g/kg did not show any toxicity. The LD5of the alcoholic extract was 17 g/kg given orally. Both extracts did not produce any gross behavioural changes at these levels [44].

DOSAGE:

Regular doses of Bacopa are 5-10 g of non- standardized powder per day, infusion (8 - 16 mL), and 30 mL everyday of syrup. Prescribed amount of a 1:2 fluid extract are 5-12 mL per day for adults and 2.5 -6 mL per day for children ages 6-12. For Bacopa extracts standardized to 20 - percent bacosides A and B , the dosage is 200 -400 mg daily in divided doses for adults, and 100- 200 mg daily in divided doses for children [45].

HERB-DRUG INTERACTIONS

In vitro and animal studies have demonstrated that BME might potentiate the effect when taken with some synthetic drugs or it might have a protective effect against certain drugs and their negative side effects. BM has been noted in animal models to decrease the toxicity of morphine and phenytoin. Administration of BME with morphine significantly decreased LPO and increased levels of antioxidant enzymes and

glutathione in rat hepatic tissue, when compared to morphine alone. These results suggested a protective effect for BM on the hepatic antioxidant status in morphine-treated rats [46].

In mice, BM administration with phenytoin significantly reversed phenytoin-induced cognitive impairment, as noted by improved acquisition and retention of memory [47]. The mice received phenytoin (25 mg/kg orally for 14 days). BM (40 mg/kg for 7 days) given along with phenytoin in the second week of the 2-week regimen significantly reversed PHT-induced impairment of cognitive function as determined from the PA results. Both acquisition and retention of memory were improved without affecting the anti-convulsant activity of PHT. These effects were independent of motor stimulation. These results suggested a potential corrective effect of BME in phenytoin-induced cognitive deficit [48].

UPCOMING SCENARIOS: CONCLUSION

In light of many reports showing important activities of BME, the wide variety of neuropharmacological actions of BM opens up interesting avenues for further research and offers new perspectives in the treatment of these diseases. Larger clinical trials and further research are required to ascertain the findings mentioned in this review. While the activity of BM both as an anxiolytic and anti-depressant needs further evaluation, its potential as an anti-epileptic treatment and as a treatment to correct side effects of anti-epileptic drugs is another area to be studied in future. Also, the antioxidant capacity of BM may explain, at least in part, the reported antistress, immunomodulatory, cognition-facilitating, anti-inflammatory and antiageing effects produced by it in experimental animals as well as in clinical situations and may justify further investigation of its other beneficial properties. Moreover, these experimental evidences suggest that because of its antioxidant activity, it may be useful in the treatment of human pathologies in which free radical production plays a key role. Also, the antifertality potential of BM was recently disclosed in male mice, wherein it was shown to cause reversible suppression of spermatogenesis and fertility, without producing apparent toxic effects[49]. BM has also shown to have thrombolytic activity in one recent in vitro study [50]. In addition to all pharmacological studies mentioned above, herb-drug and herb-herb interactions of BM need to be studied. The diverse studies indicated that interactions between herbal medicines and synthetic drugs exist and can have serious consequences.[51;52] Therefore, it is necessaryto consider the possibility of BM-drug interactions.

. REFERENCES

1. "Bacopa monnieri information from NPGS/GRIN". Www.ars-grin.gov. Retrieved2008-03-13.
2. "USDA GRIN Taxonomy". Retrieved 20 March 2014.
3. Oudhia, Pankaj (2004). "Bramhi (Bacopa monnieri)".Society for PartheniumManagement (SOPAM).Retrieved July 30, 2017.
4. .IUCN. "Bacopamonnieri".Retrieved 19 July 2012.
5. Rajani, M.; et al. (2004). Ramawat, K. G., ed. Biotechnology of Medicinal Plants: Vitalizer and Therapeutic. Enfield, NH: Science Publishers.
6. Warrier, P. K.; Nambiar, V. P. K.; Ramankutty, C.; Ramankutty, R. Vasudevan Nair (1996). Indian Medicinal Plants: A Compendium of 500 Species. Orient Blackswan.p. 238. ISBN 978-81-250-0301-4.
7. Daniel, M. (2005). Medicinal Plants: Chemistry and Properties. Science Publishers.p. 225. ISBN 978-1-57808-395-4.
8. Khare, C. P. (2003). Indian Herbal Remedies: Rational Western Therapy, Ayurvedic, and Other Traditional Usage, Botany. Springer.p. 89. ISBN 978-3-540-01026-5.
9. Sivaramakrishna, C; Rao, CV; Trimurtulu, G; Vanisree, M; Subbaraju, GV (2005). "Triterpenoidglycosides from Bacopa monnieri". Phytochemistry. **66**:2719–2728.doi:10.1016/j.phytochem.2005.09.016.
10. Garai, S; Mahato, SB; Ohtani, K; Yamasaki, K (2009). "Dammaranetriterpenoidsaponins from Bacopamonnieri". Can J Chem. **87**: 1230–1234.
11. Chakravarty, A.K; Garai, S.; Masuda, K; Nakane, T; Kawahara, N. (2003). "Bacopasides III–V: Three new triterpenoid glycosides from Bacopamonniera". Chem Pharm Bull. **51**: 215–217. doi:10.1248/cpb.51.215. PMID 12576661.
12. Chatterji, N; Rastogi, RP; Dhar, ML (1965). "Chemical examination of BacopamonnieraWettst: Part II—Isolation of chemical constituents". Ind J Chem. **3**: 24–29.
13. Chakravarty, AK; Sarkar, T; Nakane, T; Kawahara, N; Masuda, K (2008). "New phenylethanoid glycosides from Bacopamonniera". Chem Pharm Bull. **50**: 1616–1618.
14. Bhandari P, Kumar N, Singh B, Kaul VK. Cucurbitacins from Bacopamonnieri.Phytochemistry 2007.

15. .Deepak, M; Sangli, GK; Arun, PC; Amit, A (2005). "Quantitative determination of the major saponin mixture bacosideA in Bacopamonnieri by HPLC". Phytochem Anal. **16**: 24–29. doi:10.1002/pca.805.
16. Rastogi, M; Ojha, R; Prabu, PC; Devi, DP; Agrawal, A; Dubey, GP (2012). "Amelioration of age associated neuroinflammation on long term bacosides treatment".Neurochem Res. **37**: 869–874. doi:10.1007/s11064-011-0681-1.
17. Singh HK, Rastogi RP, Srimal RC, Dhawan BN. Effect of bacosides A and B on avoidance responses in rats. Phytother Res 1988; 2:70-5.
18. Singh HK, Dhawan BN. Neuropsychopharmacological effects of the AyurvedicnootropicBacopamonniera Linn. (Brahmi).Ind J Pharmacol 1997; 29:S359-S65.
19. Russo A, Borrelli F (April 2005). "Bacopamonniera, a reputed nootropic plant: an overview". Phytomedicine (Review). **12** (4):30517.doi:10.1016/j.phymed.2003.12.008. PMID 15898709.
20. Aguiar S, Borowski T (August 2013). "Neuropharmacological review of the nootropic herbBacopamonnieri". Rejuvenation Res (Review). **16** (4):313–26.doi:10.1089/rej.2013.1431. PMC 3746283. PMID 23772955.
21. Dhanasekaran, M.; Tharakan, B.; Holcomb, L. A.; Hitt, A. R.; Young, K. A.; Manyam, B. V. (2007). "Neuroprotective mechanisms of ayurvedicantidementia botanical Bacopamonniera". Phytotherapy Research. **21** (10): 965–969. doi:10.1002/ptr.2195.PMID 17604373.
22. Pase MP, Kean J, Sarris J, Neale C, Scholey AB, Stough C (July 2012). "The cognitive-enhancing effects of Bacopamonnieri: a systematic review of randomized, controlled humanclinical trials". J.AlternComplement Med (Review). **18** (7):647-52.doi:10.1089/acm.2011.0367. PMID 22747190.
23. Russo and Borrelli (2005). "Bacopamonniera, a reputed nootropic plant: an overview". Phytomedicine. **12** (4):305-317. doi:10.1016/j.phymed.2003.12.008.PMID 15898709.
24. Malhotra CK, Das PK. Pharmacological studies of Herpestismonniera Linn (Brahmi). Ind J Med Res 1959; 47:294-305.
25. Aithal HN, Sirsi M. Pharmacological investigation on Herpestismonniera . Ind J Pharmacy 1961; 23:2-5.
26. Sinha MM. Some empiricalbehavioural data indicative of concomitant biochemical reactions. Proceeds Ind. Sci. Congress Part II, Bangalore: 1971. p. 1-26.
27. Bhattacharya SK, Kumar A, Ghosal S. Effect of Bacopamonniera on animal models of Alzheimer's disease and perturbed central cholinergic markers of cognition in rats. In: DV Siva Sankar, editors. Molecular Aspects of Asian Medicines. New York: PJD Publications; 1999. p. 27-58.
28. Sairam K, Dorababu M, Goel RK, Bhattacharya SK. Antidepressant activity of standardized extract of Bacopamonniera in experimental models of depression in rats. Phytomed 2002; 9:207-11.
29. Shader RI, Greenblatt DJ. Pharmacotherapy of acute anxiety. In: Bloom FE, Kupfer DJ. Editors. Psycopharmacology: Fourth generation of progress. New York: Raven Press; 1995. p. 1341-8.
30. Shanmugasundaram ER Akbar GK, Shanmugasundaram B, Rahmighritham KR. An Ayurvedic herbal formula for the control of epilepsy. J Ethnopharmacol 1991; 33:269-76.
31. .Martis G, Rao A, Karanth KS. Neuropharmacological activity of Herpestismonniera.Fitoterapia 1992; 63:399-404.
32. .Dar A, Channa S. Relaxant effect of ethanol extract of Bacopamonniera on trachea, pulmonary artery and aorta from rabbit and guinea-pig. Phytother Res 1997; 11:323-5.
33. Dar A, Channa S. Calcium antagonistic activity of Bacopamonniera on vascular and intestinal smooth muscles of rabbit and guinea-pig. J Ethnopharmacol 1999; 66:167-74.
34. Goel RK, Sairam K, Babu MD, Tavares IA, Raman A. In vitro evaluation of Bacopamonniera on anti- Helicobacter pylori activity and accumulation of prostaglandins. Phytomed 2003; 10:523-7.
35. Mathur A, Verma SK, Purohit R, Singh SK, Mathur D, Prasad G and Dua VK. Pharmacological investigation of Bacopamonnieri on the basis of antioxidant, antimicrobial and anti -inflammatory properties. J Chem Pharm. Res 2010, 2(6):191-198.
36. Sundriyal A, Rawat DS and Singh AK. Tissue culture, phytochemical and pharmacological study of Bacopamonnieri . Asian Journal of Biochemical and Pharmaceutical Research 2013;1(3): 243-260 .
37. Azad AK, Awang M, Rahman MM. Phytochemical and microbiological evaluation of a local medicinal plant Bacopamonnieri (l.) Penn. International Journal of Current Pharmaceutical Review and Research 2012;3(3), 66-78.
38. Russo A, Borrelli F, Campisi A, Acquaviva R, Raciti G, Vanella A. Nitric oxide-related toxicity in cultured astrocytes: Effect of Bacopamonniera . Life Sci 2003; 73:1517-26.
39. Russo A, Izzo AA, Borrelli F, Renis M, Vanella A. Free radical scavenging capacity and protective effect of Bacopamonniera L . on DNA damage. Phytother Res 2003; 17:870-5.
40. Elangovan V, Govindasamy S, Ramamoorthy N, Balasubramaanian K. In vitro studies on the anticancer activity of Bacopamonnieri . Fitoterapia 1995; 66:211-5.
41. Kar A, Panda S, Bharti S. Relative efficacy of three medicinal plant extracts in the alteration of thyroid hormone concentrations in male mice. J Ethnopharmacol 2002; 81:281-5.
42. Jain P, Khanna NK, Trehan T, Pendse VK, Godhwani JL. Anti-inflammatory effects of an Ayurvedic preparation, BrahmiRasayan, in rodents. Ind J ExpBiol 1994; 32:633-6.

43. Channa S, Dar A, Anjum S, Yaqoob M, Rahman A. Anti-inflammatory activity of Bacopamonniera in rodents. J Ethnopharmacol 2006; 104:286-9.
44. Monograph, Bacopamonniera . Alternative Medicine Review 2004; 9(1):79 -85.
45. Sumathy T, Subramanian S, Govindasamy S, Balakrishna K, Veluchamy G. Protective role of Bacopamonniera on morphine induced hepatotoxicity in rats. Phytother Res 2001; 15:643-5.
46. Smith DB. Cognitive effects of anti-epileptic drugs.AdvNeurol 1991; 55:197-212.
47. Vohora D, Pal SN, Pillai KK. Protection from phenytoin-induced cognitive deficit by Bacopamonniera , a reputed Indian nootropic plant. J Ethnopharmacol 2000;71:383-90.
48. Singh A, Singh SK. Evaluation of antifertality potential of brahmi in male mouse. Contraception 2009; 79:71-9.
49. Prasad S, Kashyap RS, Deopujari JY, Purohit HJ, Taori GM, Daginawala HF. Effect of Fagonia Arabica (Dhamasa) on in vitro thrombolysis. BMC Compl Alt Med 2007; 7:36.
50. Izzo AA, Ernst E. Interactions between herbal medicines and prescribed drugs: A systematic review. Drugs 2001; 61:2163-75.
51. Gohil KJ, Patel JA. Herb-drug interactions: A review and study based on assessment of clinical case reports in literature. Ind J Pharmacol 2007; 39:129 -39.