Volume 1 Issue 1 2012

ISSN: 2320- 480X

The Journal of Phytopharmacology

(Pharmacognosy and Phytomedicine Research)

Ethnopharmacology of selected Herbal plants used in Hypolipidemic complications

Aseem Sharma^{*1}, Gajraj Singh¹, Krishna Tripathi¹

1. Pinnacle Biomedical Research Institute (PBRI), Bhopal-462003 [Email: sharma.aseem04@gmail.com]

Abstract: The plant kingdom is a wide field to search for natural effective oral hypolipidemic agents that have slight or no side effects. The search for natural substances with hypolipidemic effects is therefore desirable, particularly in countries with a persistent incidence of hyperlipidemia and cardiovascular diseases. The consumption of synthetic drugs leads to hyperurecemia, diarrhoea, nausea, myositis, gastric irritation, flushing, dry skin and abnormal liver function. More recent ethnopharmacological studies shows these plants used in many parts of the world for the treatment of a number of diseases, e.g. as an hepatoprotective, hypotensive, hyperglycaemic, dibetes, antioxidant, antiinflammatory, anti-allergic, anti-tumor etc.

Keywords: Terminalia bellerica, Momordica cymbalaria, Camellia sinensis, Helicteres isora, Capparis spinosa, Perilla Frutescens & Ajuga iva

Introduction: Medicinal plants are gaining importance in the fields of research. Medicinal plants originate from almost every part of the globe. Such plants serve the primary healthcare needs of up to 80 % of people in developing countries where

there is increasing awareness of and demand for medicinal plants for healthcare and dietary supplements that often help to save lives. A significant number of modern pharmaceutical drugs are based on or derived from medicinal plants. In India;

4

drugs of herbal origin have been used in traditional systems of medicines such as Unani, Siddha and Ayurveda since ancient times.

Ethnopharmacology of selected Herbal plants used in Hypolipidemic complications are describe bellow.

Terminalia bellerica:

Botanical description-

Terminalia bellerica Roxb. (Combretaceae) is a large deciduous tree which occurs widely in the moist valleys of India and its fruits are most commonly used in Indian traditional systems ofmedicine.¹

Ethnobotany-

The fruit of T. bellerica has been used in traditional medicine for the treatment of anaemia, asthma, cancer, colic, constipation, diarrhoea, dysuria, headache, hypertension, inflammation and rheumatism.² The fruit is reported to have hepatoprotective^{3, 4} hypotensive⁵, anti-mutagenic⁶, antimicrobial and anti-HIV- 1 activity.⁷ The plant is known to lower the levels of lipid in hypercholesterolemic animals and prevent the development of atherosclerosis and myocardial infarction.⁸⁻¹⁰ Triphala and T.

bellerica crude extracts were found to reduce serum glucose level and have marked antioxidant properties in alloxan-induced diabetic rats.¹¹ In a recent study, the aqueous extract of T. Bellerica was found to stimulate insulin secretion in the clonal pancreatic β -cell line.¹² Phytochemically, the fruits of T. bellerica have been reported to contain β -sitosterol, gallic acid, ellagic acid, ethyl gallate, chebulagic acid, galloyl glucose, mannitol, glucose, galactose, fructose, rhamnose¹³, arjungenin, belleric acid, bellericoside¹⁴ and three lignans and one flavan.¹⁵

It has already reported the antidiabeticand protective effects of T. bellerica fruit extracts on certain biochemical parameters in streptozotocin induced diabetic rats.¹⁶

Hypolipidemic activity-

GA (galoic acid) isolated from T. bellerica and synthetic GA was administered to streptozotocin (STZ)-induced diabetic male Wistar rats at different doses for 28 days. Plasma glucose level was significantly (p <0.05) reduced in a dose-dependent manner when compared to the control.Histopathological examination of the pancreatic sections showed regeneration of -

5

cells of islets of GA-treated rats when compared to untreated diabetic rats. In addition, oral administration of GA (20 mg/kg bw) significantly decreased serum total cholesterol, triglyceride, LDLcholesterol, urea, uric acid, creatinine and at the same time markedly increased plasma insulin, C-peptide and glucose tolerance level.

Gallic acid present in fruit rind of T. bellerica is the active principle responsible for the regeneration of β -cells and normalizing all the biochemical parameters related to the patho-biochemistry of diabetes mellitus and hence it could be used as a potent antidiabetic agent.¹⁷

Momordica cymbalaria:

Botanical description-

M. cymbalaria Hook. (MC) belongs to the family Cucurbitaceae. MC is a species found in Deccan, Mysore and Konkan regions of India. The other members from the same genus, M. charantia Linn., and M. foetida.¹⁸

Ethnobotany-

MC is routinely used as a vegetable and also for the treatment of diabetes mellitus by the local people. The hypoglycaemic activity of MC was reported earlier.¹⁹ Its tuber is used as an abortificient.¹⁸

Hypolipidemic activity-

A significant decrease in blood glucose levels was observed in diabetic treated group from an initial level of 295 ± 25 to the level of 225 ± 31 mg/dl after treatment (P<0.001), while no significant decrease in blood glucose levels was observed in normal treated group (initial value 93.5 ± 2.5 and after treatment 104 ± 9.0 mg/dl.²⁰

Camellia sinensis:

Botanical description-

Green tea is a popular beverage, derived from the tea plant Camellia sinensis. Its peculiar green color results from the inactivation of polyphenol oxidase by treating fresh tea leaves with hot steam and air.²¹

Ethnobotany-

Evidence from animal studies indicates that green tea and its catechins retard the development or progression of

6

atherosclerosis in apoE-deficient mice^{22, 23} and hypercholesterolemic hamsters .^{24, 25}

Hypolipidemic activity-

Using ovariectomized rats with mesenteric lymph-duct cannula showed that fresh green tea extract, intraduodenally infused at the doses equivalent to one to two cups of tea, significantly lowered the lymphatic absorption of cholesterol in a dose-dependent manner in rats with mesenteric lymph-duct cannula.²⁶

Helicteres isora:

Botanical description-

Helicteres isora Linn., (Sterculiaceae) occurs, often gregariously, throughout India, from

Jamuna eastwards to Bihar and Bengal and southwards in central, western and southern India and Andaman islands. The roots and bark have been used as expectorant, demulcent, astringent, antigalactagogue, a cure for scabies and to lessen griping. Juice of the root is used in emphysema, stomach afflictions and diabetes.

Ethnobotany-

Fruits are demulcent, mildly astringent and useful in griping and flatulence.²⁷

Hypolipidemic activity-

Ethanolic extract of H. isora root caused significant reduction in plasma glucose, triglyceride and insulin levels at 300 mg/kg dose after 9 days of administration to insulin resistant and diabetic C57BL/KsJdb/db mice. In normoglycemic and mildly hypertriglyceridemic Swiss albino mice, the extract also showed significant reduction in plasma triglyceride and insulin levels, without affecting plasma glucose level.²⁸

Capparis spinosa:

Botanical description-

Capparis spinosa L. (CS) (Capparidaceae), locally known as "Kebbar" is a native shrub widely distributed throughout the southeastern region of Morocco (Tafilalet). This plant is traditionally used in diabetes control and treatment according to our previous ethnopharmacological surveys in two great areas of Morocco, Tafilalet and Fez-Boulemane regions.^{29, 30}

7

Ethnobotany-

CS is used in phytomedicine around the world as anti-oxidative³¹ antifungal³², antihepatotoxic, anti-inflammatory³³ and anti-diabetic³⁴. In the south-eastern region of Morocco (Tafilalet), CS fruits are recognized as potent hypoglycaemic agents by several traditional healers. ³⁵

Hypolipidemic activity-

The aqueous extract of Capparis spinosa L. (CS) induced a significant decrease on plasma triglycerides concentrations 1 week (p < 0.05) and 2 weeks (p < 0.01) after once daily repeated oral administration. A significant decrease of plasma cholesterol levels was also observed 4 days (p < 0.05) and 1 week (p < 0.05) after repeated oral administration. In diabetic rats, CS treatment caused a significant decrease of plasma triglycerides levels after repeated oral administration. Four days after repeated oral administration of aqueous CS extract, the plasma cholesterol levels were significantly decreased (p < 0.05) and still dropped after 2 weeks (p < 0.01). On the other hand, the repeated oral administration of CS aqueous extract caused a significant decrease of body weight 4 days after repeated oral treatment in diabetic rats (p < 0.05).

We conclude that the aqueous extract of CS (20 mg/kg) exhibits a potent lipid lowering activity in both normal and severe hyperglycaemic rats after repeated oral administration of CS aqueous extract.³⁶

Perilla Frutescens:

Botanical description-

Perilla frutescens, which belongs to the family Labiatae, having opposite leaves, square stems, and axillary clusters of purplish to white flowers, has been used extensively as a traditional medicinal herb in East Asian countries for centuries, especially in Japan and China.³⁷

Ethnobotany-

It shows potent antioxidant, antiinflammatory, anti-allergic and antitumor promoting substances contained in perilla plants.³⁸⁻⁴²

Hypolipidemic activity-

The levels of TC and TG in the High-fat control group (HFC) group were

significantly higher than those in the NC group (both Pb0.05 for TG and TC), which indicated that the model was successful in inducing hyperlipidemia in rats. Over a period of 4 weeks, compared with the HFC group, the levels of serum TC and TG were suppressed significantly (Pb0.05) by TFP treatments at a dose of 50–300mg/kg. The degree of suppression of TC and TG levels induced by TFP at a high dose of 200 mg/ kg was similar to that of lovastatin at a dose of 2.5 mg/kg, suggesting that TFP had a potent lipid lowering effect in the hyperlipidemia rats.

<u>Ajuga iva:</u>

Botanical description-

Ajuga also known as bugleweed, ground pine, carpet bugle, or just bugle, is a genus of about 40–50 species of annual and perennial herbaceous flowering plants in the mint family Lamiaceae, with most species native to Europe, Asia, and Africa, but also two species in southeastern Australia. They grow to 5–50 cm tall, with opposite leaves. Ajuga iva is one of them.

Ethnobotany-

According to several ethnopharmacological surveys, Ajuga iva (L.) Shreiber (Labiatae), is used in folk medicine for a variety of ailments, including diabetes.⁴³⁻⁴⁵ It also shows hypoglycemic activity in normal and streptozotocin (STZ)-induced diabetic rats⁴⁶, and the relative non-toxic nature of the plant extract both after acute and chronic oral and intraperitoneal administration in rats and mice.⁴⁷ It show hypoglycaemic action, after acute and sub-chronic oral administration, in normal and STZ-diabetic rats, using the latter animals as a model for human type 1 diabetes.⁴⁸

A preliminary phytochemical analysis of the AI-extract, carried out by the method of revealed that it contains several flavonoids, tannins, terpenes and steroids (unpublished data).⁴⁹

Hypolipidemic activity-

The effect of single oral doses of water (T) and the test materials, AI-extract, TR(Taurine) and GLB(Glibenclamide), on blood CHL levels at 6 h post dose in control (Fig. 1, Panel a) and STZ-diabetic rats (Fig.

9

1, Panel b) as compared to the baseline values (0 h). In normal (control) rats, a single oral dose of the AI-extract (AI10; 10 mg/kg BW) produced significant reduction (14%; P < 0.05) in plasma CHL, while TR (10 mg/kg BW) reduced it by 31% (P < 0.01). Administration of GLB (2.5 mg/kg BW) caused a small non-significant decrease (9%), while water (T) had no effect on CHL levels.

In the STZ-diabetic rats, a single oral dose of the AI-extract (AI10; 10 mg/kg BW) induced a highly significant reduction (44%) in plasma CHL level at 6 h (Fig. 1, Panel b) as compared to the pretreatment value $[1.64\pm0.2 \text{ mmol/L} (6 \text{ h}) \text{ versus } 2.95\pm0.03 \text{ mmol/L} (0 \text{ h}); P < 0.01]$. Administration of single oral doses of TR (10 mg/kg BW) and GLB (2.5 mg/kg BW) produced plasma CHL lowering (at 6 h) of 34% (P < 0.01) and 25% (P < 0.05), respectively.

The effect of administration of single oral doses of the test materials, at the doses indicated above, on plasma TG levels in normal and diabetic rats is shown in Fig. 2 (Panels a and b). Only TR produced a significant lowering of plasma TG (P < 0.05) in both the normal (28%) and STZ-diabetic (30%) rats. Both the AI-extract

and GLB caused insignificant decreases in plasma TG in normal and diabetic rats (13 and 16%, respectively; P = NS).

The AI-extract (10 mg/kg; oral) reduced plasma glucose levels after acute (single) and sub-chronic (3 weeks) dosing both in normal and diabetic rats. In normal rats, single and repeated oral administration of the AI-extract, at a dose of 10 mg/kg produced a small but significant decrease in plasma CHL levels (P < 0.05). A single dose of the AI-extract did not produce a significant change in plasma TG, but subchronic dosing (for up to 21 days) caused a significant decrease in plasma TG (P < 0.05). In STZ-diabetic rats, a single dose as well as repeated (3 weeks) treatment with the AI-extract produced a significant decrease in plasma CHL (P < 0.01), and triglyceride (P < 0.01) levels. The AI-extract also prevented weight loss in the diabetic animals. In summary, an aqueous extract of the Ajuga iva whole plant showed hypolipidemic activity, in addition to its hypoglycaemic effect in normoglycemic and diabetic rats.⁵⁰

Conclusion:

From the above literature it concluded that these plants have numerous medicinal uses.

Reference:

- R.N. Chopra, S.L. Nayar, I.C. Chopra, Glossary of Indian Medicinal Plants, C.S.I.R. Publication, New Delhi, 1996.
- J.A. Duke, M.J. Bogenschutz-Godwin, J. Ducelliar, P.A.K. Duke, Handbook of Medicinal Herbs, 2nd ed., Boca Raton, FL, CRC Press, 2002, pp. 70–71.
- K.K. Anand, B. Singh, A.K. Saxena, B.K. Chandan, V.N. Gupta, V. Bhardwaj, 3,4,5- Trihydroxy benzoic acid (gallic acid), the hepatoprotective principle in the fruits of Terminalia bellericabioassay guided activity, Pharmacol. Res. 36 (1997) 315–321.
- J. Anjana, B. Monika, S. Sangeeta, Protective effect of Terminalia bellerica Roxb. and gallic acid against carbon tetrachloride induced damage in albino rats, J. Ethnopharmacol. 109 (2007) 214– 218.

- R.D. Srivastava, S. Dwivedi, K.K. Sreenivasan, C.N. Chandrashekhar, Cardiovascular effects of Terminalia species of plants, Indian Drugs 29 (1992) 144–149.
- S. Kaur, S. Arora, K. Kaur, S. Kumar, The in vitro antimutagenic activity of Triphala, an Indian herbal drug, Food Chem. Toxicol. 40 (2002) 527–534.
- 7. R Valsaraj, P. Pushpangadan, U.W. Smitt. S.B. A. Adsersen, Christensen, A. Sittie, U. Nyman, C. Nielsen, C.E. Olsen, New anti-HIVantimalarial, and 1, antifungal Terminalia compounds from bellerica, J. Nat. Prod. 60 (1997) 739-742.
- M. Tariq, S.J. Hussain, M. Asif, M. Jahan, Protective effect of fruit extracts of Emblica officinalis (Gaertn) & Terminalia bellerica (Roxb.) in experimental myocardial necrosis in rats, Indian J. Exp. Biol. 15 (1977) 485–486.
- C.P. Thakur, B. Thakur, S. Singh,
 P.K. Sinha, S.K. Sinha, The ayurvedic medicines Haritaki, Amala and Bahira reduce cholesterol

induced atherosclerosis in rabbits, Int. J. Cardiol. 21 (1988) 167–175.

- 10. H.P. Shaila, A.L. Udupa, S.L. Udupa, Preventive actions of Terminalia bellerica in experimentally induced atherosclerosis, Int. J. Cardiol. 49 (1995) 101–106.
- M. Sabu, C.R. Kuttan, Anti-diabetic activity of medicinal plants and its relationship with their antioxidant property, J. Ethnopharmacol. 81 (2002) 155–160.
- 12. V. Kasabri, P.R. Flatt, Y.H.A. Abdel-Wahab, Terminalia bellerica stimulates the secretion and action of insulin and inhibits starch digestion and protein glycation in vitro, Br. J. Nutr. 103 (2010) 212–217.
- L.R. Row, P.S. Murty, Chemical examination of Terminalia bellerica Roxb., Indian J. Chem. 8 (1970) 1047–1048.
- 14. A.K. Nandy, G. Podder, N.P. Sahu,
 S.B. Mahato, Triterpenoids and their glucosides from Terminalia bellerica,
 Phytochemistry 28 (1989) 2769–2772.
- 15. T.H. Huang, G. Peng, B.P. Kota, G.Q. Li, J. Yamahara, B.D.

Roufogalis, Y. Li, Antidiabetic action of Punica granatum flower extract: activation of PPAR and identification of an active component, Toxicol. Appl. Pharmacol. 207 (2005) 160–169.

- 16. R.C.R. Latha, P. Daisy, Influence of Terminalia bellerica Roxb. fruit extracts on biochemical parameters in streptozotocin diabetic rats, Int. J. Pharmacol. 6 (2010) 89–96.
- 17. R. Cecily Rosemary Latha, P. Daisy. Insulin-secretagogue,

antihyperlipidemic and other protective effects of gallic acid isolated from Terminalia bellerica Roxb. in streptozotocin-induced diabetic rats.Chemico-Biological Interactions.2011; 189 (1-2):112-118.

- Nadkarni AK, Indian Materia Medica, Popular Prakashan Private Ltd: Bombay, India Vol I, edited by K Nadkarni, (1994) 67-71.
- Nagaraju N. Biochemical studies on some medicinal plants of Rayalaseema region. PhD thesis.
 S.V. University; Tirupathi: 1992.
- 20. B. Kameswara Rao, M.M. Kesavulu,R. Giri, Ch. Appa Rao. Antidiabetic

and hypolipidemic effects of Momordica cymbalaria Hook. fruit powder in alloxan-diabetic rats. Journal of Ethnopharmacology 67 (1999) 103–109.

- Harbowy ME, Balentine D. Tea chemistry. Critical Rev Plant Sci 1997;16:415–80.
- 22. Hayek T, Fuhrman B, Vaya J, Rosenblat M, Belinky P, Coleman R, et al. Reduced progression of atherosclerosis in apolipoprotein Edeficient mice following consumption of red wine, or its polyphenols quercetin or catechin, is associated with reduced susceptibility of LDL to oxidation aggregation. and Arterioscler Thromb Vasc Biol 1997; 17:2744-52.
- 23. Chyu KY, Babbidge SM, Zhao X, Dandillaya R, Rietveld AG, Yano J, et al. Differential effects of green tea-derived catechin on developing versus established atherosclerosis in apolipoprotein E-null mice. Circulation 2004;109:2448–53.
- 24. Yang TTC, Koo MWL. Hypocholesterolemic effects of

Chinese tea. Pharmacol Res 1997;35: 505–12.

- 25. Vinson JA, Teufel K, Wu N. Green and black teas inhibit atherosclerosis by lipid, antioxidant, and fibrinolytic mechanisms. J Agric Food Chem 2004;52:3661–5.
- 26. Sung I. Kooa, Sang K. Noh. Green tea as inhibitor of the intestinal absorption of lipids: potential mechanism for its lipid-lowering effect Journal of Nutritional Biochemistry 18 (2007) 179–183.
- Kirthikar K.R., Basu B.D., 1981. An ICS. Indian Medicinal Plants, VI, II, Lalit Mohan Basu, Allahabad, India, pp. 370_372.
- 28. Ranjan Chakrabarti, Reeba K.
 Vikramadithyan, Ramesh Mullangi,
 V.M. Sharma, H. Jagadheshan et al.
 Antidiabetic and hypolipidemic activity of Helicteres isora in animal models. Journal of Ethnopharmacology 81 (2002) 343-349.
- 29. Jouad, H., Haloui, M., Rhiouani, H.,El Hilaly, J., Eddouks, M., 2001.Ethnopharmacological survey ofmedicinal plants used or thetreatment of diabetes, cardiac and

Volume 1 Issue 1 2012

renal diseases in the North centre region of Morocco (Fez-Boulemane). Journal of Ethnopharmacology 77, 175–182.

- 30. Eddouks, М.. Maghrani, М., Lemhadri, A., Ouahidi, M.-L., Jouad, Н., 2002. Ethnopharmacological survey of medicinal plants used for the treatment of diabetes mellitus, hypertension and cardiac diseases in the south-east region of Morocco (Tafilalet). Journal of Ethnopharmacology 82, 97–103.
- 31. Germano, M.P., De Pasquale, R., D'Angelo, V., Catania, S., Silvari, V., Costa, C., 2002. Evaluation of extracts and isolated fraction from *Capparis spinosa* L. buds as an antioxidant source. Journal of Agriculture and Food Chemistry 27, 1168–1171.
- 32. Ali-Shtayeh, M.S., Abu Ghdeib, S.L., 1999. Antifungal activity of plant extracts against dermatophytes. Mycoses 42, 665–672. Gadgoli, C., Mishra, S.H., 1999. Antihepatotoxic activity of *p*-methoxy benzoic acid from *Capparis spinosa*. Journal of Ethnopharmacology 66, 187–192.

- 33. Al-Said, M.S., Abdelsattar, E.A., Khalifa, S.I., El-feraly, F.S., 1988. Isolation and identification of an anti-inflammatory principle from *Capparis spinosa*. Pharmazie 43, 640–641.
- 34. Yaniv, Z., Dafni, A., Friedman, J., Palevitch, D., 1987. Plants used for the treatment of diabetes in Israel. Journal of Ethnopharmacology 19, 145–151.
- 35. Ziyyat, A., Legssyer, A., Mekhfi, H., Dassouli, A., Serhrouchni, M., Benjelloun, W., 1997. Phytotherapy of hypertension and diabetes in oriental Morocco. Journal of Ethnopharmacology 58, 45–54.
- 36. M. Eddouksa, A. Lemhadria, J.-B. Michel. Hypolipidemic activity of aqueous extract of Capparis spinosa L. in normal and diabetic rats. Journal of Ethnopharmacology. 2005; 98(3):345-350.
- 37. Li-Jun Fenga, Chen-Huan Yub, Ke-Jing Yinga, Jian Huac, Xiao-Yan Dai. Hypolipidemic and antioxidant effects of total flavonoids of Perilla Frutescens leaves in hyperlipidemia rats induced by high-fat diet. Food

Volume 1 Issue 1 2012

Research International. 2011; 44(1): 404-409.

- Ueda, H., Yamazaki, C., & Yamazaki, M. (2002). Luteolin as an anti-inflammatory and anti-allergic constituent of Perilla frutescens. Biological and Pharmaceutical Bulletin, 25, 1197–1202.
- 39. Ueda, H., Yamazaki, C., & Yamazaki, M. (2003). Inhibitory effect of perilla leaf extract and luteoin on mouse skin tumor promotion. Biological and Pharmaceutical Bulletin, 26, 560–563.
- 40. Makino, T., Furuta, Y., Wakushima, H., Fujii, H., Saito, K., & Kano, Y. (2003). Anti-allergic effect of Perilla frutescens and its active constituents. Phytotherapy Research, 17, 240–243.
- 41. Banno, N., Akihisa, T., Tokuda, H., Yasukawa, K., Higashihara, H., Ukiya, M., et al. (2004). Triterpene acids from the leaves of Perilla frutescens and their antiinflammatory and antitumorpromoting effects. Bioscience Biotechnology and Biochemistry, 68, 85-90.

- 42. Schirrmacher, G., Skurk, T., Hauner, H., & Grassmann, J. (2010). Effect of Spinacia oleraceae L. and Perilla frutescens L. on antioxidants and lipid peroxidation in an intervention study in healthy individuals. Plant foods for human nutrition, 65, 71–76.
- 43. Bellakhdar, J., Claisse, R., Fleurentin, J., Younos, C., 1991. Repertory of standard herbal drugs in the Moroccan pharmacopoea. Journal of Ethnopharmacology 35, 123–143.
- 44. Bnouham, M., Mekhfi, H., Legssyer,
 A., Ziyyat, A., 2002. Medicinal plants used in the treatment of diabetes in Morocco. International Journal of Diabetes and Metabolism 10, 33–50.
- 45. El-Hilaly, J., Hmammouchi, M., Lyoussi, B., 2003. Ethnobotanical studies and economic evaluation of medicinal plants in Taounate province (northern Morocco). Journal of Ethnopharmacology 86, 149–158.
- 46. El-Hilaly, J., Lyoussi, B., 2002.Hypoglycemic effect of the lyophilized aqueous extract of Ajuga

iva in normal and streptozotocin diabetic rats. Journal of Ethnopharmacology 80, 109–113.

- 47. El-Hilaly, J., Israili, Z.H., Lyoussi,
 B., 2004. Acute and chronic toxicological studies of Ajuga iva in experimental animals. Journal of Ethnopharmacology 91, 43–50.
- Houghton, P.J., Raman, A., 1998.
 Laboratory Handbook for the Fractionation of Natural Extracts, first ed. ITP®, London.
- 49. Tenner Jr., T.E., Zhang, X.J., Lombardini, J.B., 2003.
 Hypoglycemic effects of taurine in the alloxan-treated rabbit, a model for type 1 diabetes. Advances in Experimental and Medical Biology 526, 97–104.
- 50. El-Hilaly J,Tahraoui A, Israili ZH, Lyoussi B. Hypolipidemic effects of acute and sub-chronic administration of an aqueous extract of Ajuga iva L. whole plant in normal and diabetic rats. Journal of Ethnopharmacology 2006; 105: 441-448.