

PHYTOCHEMISTRY AND PHARMACOLOGICAL ASPECTS OF *LEUCAS URTICIFOLIA* (VAHL) BENTH.

KALSOOM AKHTAR^a, SHER BAHADAR KHAN^{b,c*}, ABDUL MALIK^{d*},

For Author Affiliations, see end of the text

ABSTRACT:

Medicinal plants have attracted increased attention because of their beneficial effects on human health. Many medicinal plants are used as traditional medicine in various countries for long time. A large number of secondary metabolites with various biological activities have been discovered from various medicinal plants and some bioactive substances derived from plants have diverse functional roles as secondary metabolites and these properties can be applied to the developments of novel pharmaceuticals. *Leucas Urticifolia* (family-Lamiaceae) is an annual herbaceous plant and has various activities. Chemical studies have underlined the presence

of various classes of compounds, the main being triterpenes, diterpene, flavonoids and fatty acids. The extract of this plant as well as pure compounds isolated from this plant, have been demonstrated to possess multiple pharmacological activities. In this review, we have explored the phytochemistry and pharmacological activities of *Leucas Urticifolia* in order to collate existing information on this plant as well as highlight its multi-activity properties as a medicinal agent.

Keywords: *Leucas Urticifolia*, Lamiaceae, Phytochemistry, Pharmaceuticals, Pharmacological aspects

INTRODUCTION:

The genus *Leucas*, belonging to the family Lamiaceae, comprises about 100 species. In the Indo-Pakistani subcontinent, the genus is represented by 35 species which are mostly herbs or under shrubs found in temperate or hilly regions (1). *Leucas urticaefolia* is an annual herb distributed in the Punjab, Baluchistan, Sindh and Rajputana desert of Pakistan. At Gomawal in Baluchistan, the plant is used as a cure for fever. Its local name in Gujerati is Kubo (2) and in Tilla Gogian of the Potohar region, it is known as Goma or Guldora. The decoction of the leaves and apical shoots with gur is used locally as an abortifacient up to 3 months of pregnancy. Infusions of the flowers are used in skin diseases. It is also used to treat piles. *L. urticifolia* is astringent, stimulant, haemostatic, anthelmintic and diuretic. The plant is also used for the treatment of diarrhea, dysentery, uterine haemorrhages, dropsy, gravel, cystitis, calculus, bronchial catarrh, skin diseases, fever and various types of mental disorders (1).

DESCRIPTION:

The plant is taxonomically classified as follow:

Domain:	Eukaryota
Kingdom:	Plantae
Subkingdom:	Angiospermae

Phylum:	Eudicots
Subphylum:	core eudicots
Order:	Lamiales
Family:	Lamiaceae
Subfamilia:	Lamioideae
Genus:	<i>Leucas</i>
Species:	<i>Urticifolia</i>
Botanical name:	<i>Leucas urticifolia</i> (Vahl) Benth.
Synonyms:	<i>Phlomis urticifolia</i> Vahl (basionym)
Local name:	Gujerati is Kubo, Goma or Guldora.

DISTRIBUTIONAL RANGE:

Africa: Northern Africa: Egypt, Northeast Tropical Africa: Ethiopia; Sudan
Asia-temperate: Arabian Peninsula: Oman; Saudi Arabia; Yemen
Western Asia: Afghanistan; Iran
Asia-tropical: Indian Subcontinent: India; Pakistan

PHYTOCHEMISTRY:

The aerial parts of plant are well investigated for chemical information (3).

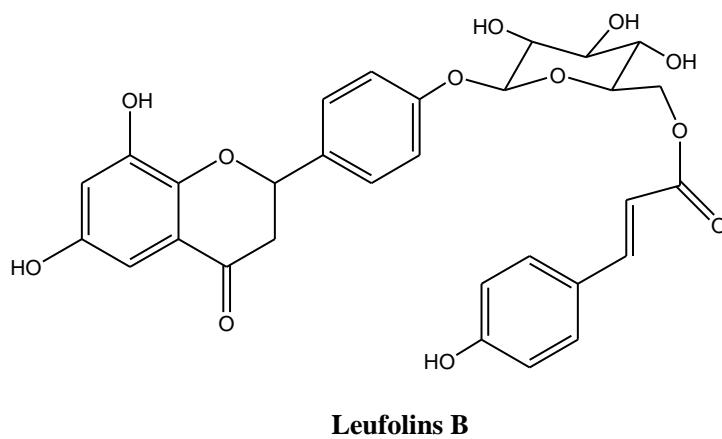
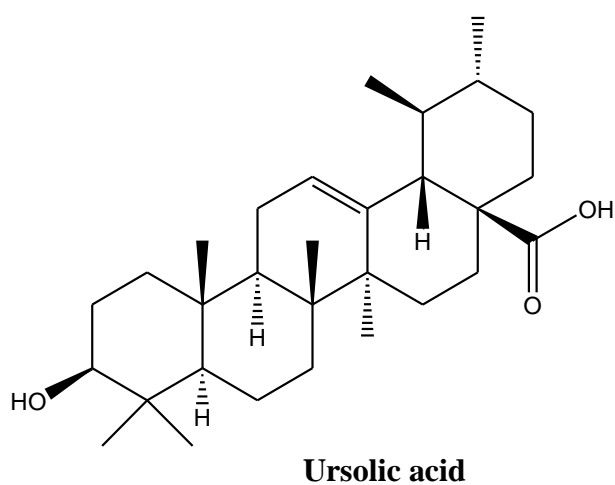
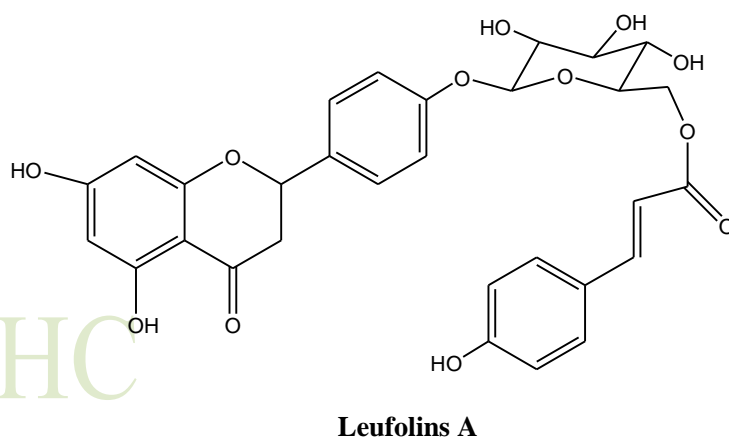
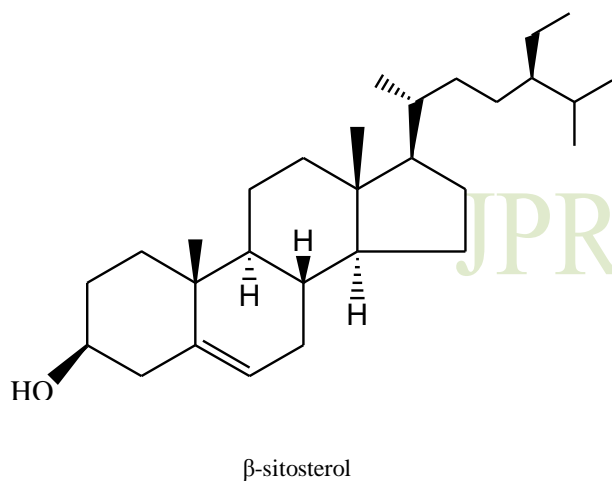
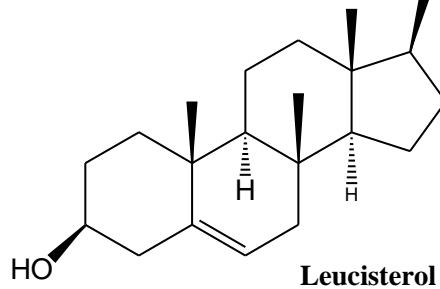
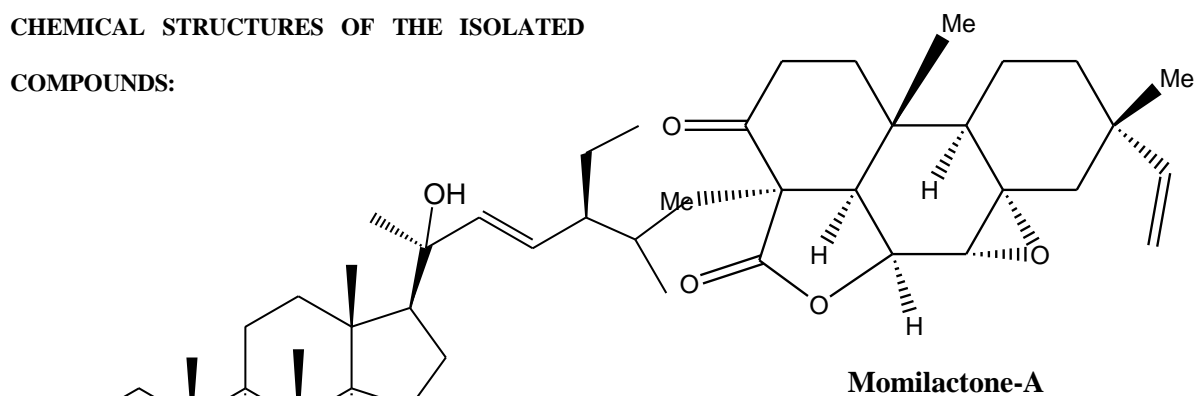
Triterpenes: Leucisterol, β -sitosterol, and ursolic acid (3),

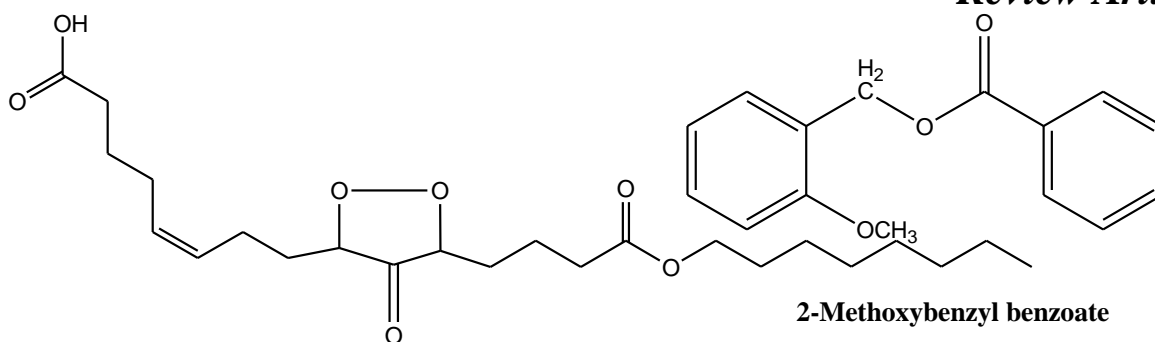
Diterpene: Momilactone-A (4)

Flavonoids: Leufolins A, Leufolins B (5).

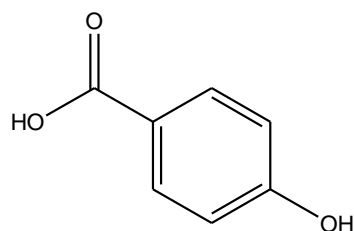
Acids and esters: Urticic acid, Methoxybenzyl benzoate, 4-hydroxy benzoic acid (3).

**CHEMICAL STRUCTURES OF THE ISOLATED
COMPOUNDS:**





Urtic acid



4-hydroxy benzoic acid

JPRHC

PHARMACOLOGICAL ASPECTS:

BUTYRYLCHOLINESTERASE ACTIVITY:

Leucisterol, Leufolins A and Leufolins B displayed inhibitory potential against butyrylcholinesterase. Butyrylcholinesterase (BChE, EC 3.1.1.8) inhibition may be an effective tool for the treatment of *Alzheimer's* disease (AD) and related dementias. These inhibitors may act as potential leads in the discovery of clinically useful inhibitors for nervous system disorders, particularly by reducing memory deficiency in *Alzheimer's* disease patients by potentiating and affecting the cholinergic transmission process (3,5).

Cholinesterases are enzymes that share extensive sequence homology and distinct substrate specificity and inhibition sensitivity. Cholinesterases are potent target for the symptomatic treatment of Alzheimer's disease and related dementia. It has been found that butyrylcholinesterase (BChE) inhibition is an effective tool for the treatment of AD and related dementias (6). It has been found that BChE is found in significantly higher quantities in Alzheimer plaques than in plaques of normal aged-related non-demented brains. It is general viewed as a back up for the homologous acetylcholinesterase and to act as a scavenger for anticholinesterase compounds (7). Butyrylcholinesterase is involved three different enzymatic activities in its structure like its sister enzyme, acetylcholinesterase: esterase, aryl acylamidase and pepti-

dase (or protease). Whereas the clear role of acetylcholinesterase in cholinergic neurotransmission is well defined, the real physiological function of butyrylcholinesterase is still unknown. Both enzymes have similar molecular forms with different tissue distribution. Esteratic activity of butyrylcholinesterase becomes more important in scavenging of organophosphate and carbamate inhibitors before they reach to acetylcholinesterase; in regulating cholinergic transmission in the absence of acetylcholinesterase and in inactivation of some drugs such as cocaine aspirin, amitriptyline or in activation of others such as bambuterol, heroin. It is suggested that aryl acylamidase activity plays a role in crosstalking between serotonergic and cholinergic neurotransmission systems. In addition, peptidase activity of butyrylcholinesterase has a function in the development and progression of Alzheimer disease due to cause the production of β -amyloid protein and to help its diffusion to β -amyloid plaques.

Animal cholinesterases are widespread enzymes present in cholinergic and noncholinergic tissues as well as in their plasma and other body fluids (8-11). They are divided into two classes according to differing in their substrate specificity, behaviour in excess substrate and susceptibility to inhibitors: acetylcholinesterase or “true cholinesterase” (AChE; acetylcholine acetylhydrolase, E.C. 3.1.1.7) and butyrylcholinesterase (BChE; acylcholine acylhydrolase, E.C. 3.1.1.8). BChE is also known as pseudocholinesterase, non-specific cholinesterase or simply cholinesterase. AChE hydrolyzes acetylcholine faster than other cholinesters and is much less active on

butyrylcholine. On the contrary, BChE preferentially acts on butyrylcholine, but also hydrolyzes acetylcholine (10,12). The inhibition of AChE by excess substrate is one of the key features that distinguishes it from BChE. BChE exhibits the substrate activation in excess substrate (13,14). Their tissue-specific distribution is also different from each other: AChE is known to be abundant in brain, muscle and erythrocyte membrane, whereas BChE has higher activity in liver, intestine, heart, kidney and lung (15,16). Many species such as human, horse, mice exhibit high BChE activity in their plasma, while rat has higher AChE activity than BChE in its plasma (10,16,17).

AChE and BChE share 65% amino acid sequence homology and have similar molecular forms and active center structure despite being products of different genes on human chromosomes 7 (specifically 7q22) and 3 (specifically 3q26), respectively (18). The main function of AChE is rapid hydrolysis of the neurotransmitter acetylcholine at cholinergic synapses, and it is one of the fastest enzyme known (19). But individuals whose BChE is absent does not correlate with any physiological abnormality. Its importance as a detoxification enzyme is growing interest in recent years. BChE is of pharmacological and toxicological importance, because it hydrolyzes ester-containing drugs and scavenges cholinesterase inhibitors including potent organophosphorus nerve agents before they reach their synaptic targets (20).

REFERENCES

1. S. M. H. Jafri, Flora of Karachi; The Book Corporation Karachi: Karachi, Pakistan, 1966; p. 391.
2. K. R. Kiritikhar, and B. D. Basu,. Indian Medicinal Plants, 2005, Vol. 3, 2nd ed., p. 2021. Dehradun: International Book Distributors.
3. I. Fatima, I. Ahmad, I. Anis, A. Malik, N. Afza, L. Iqbal, and M. Latif, New Butyrylcholinesterase Inhibitory Steroid and Peroxy Acid from *Leucas urticifolia*. Arch Pharm Res 2008, 31(8), 999-1003.
4. R. S. Habib, M. Jamshaid, M. N. Tahir, T. J. Khana, and I. U. Khan. (4R,5R,6S,7R,8S,9R,10S,13S)-7,8b-Epoxymomilactone-A. Acta Cryst 2008, E64, o892.
5. A. T. Noor, I. Fatima, I. Ahmad, A. Malik, N. Afza, L. Iqbal, M. Latif, and S. B. Khan. Leufofins A and B, Potent Butyrylcholinesterase-inhibiting Flavonoid Glucosides from *Leucas urticifolia*. Molecules 2007, 12, 1447-1454.
6. S. Q. Yu, H. W. Holloway, T. Utsuki, A. Brossi, N. H. Greig. Synthesis of novel phenserinebased-selective inhibitors of butyrylcholinesterase for Alzheimer's disease. J. Med. Chem 1999, 42, 1855-1861.
7. M. Schwarz, D. Glick, Y. Loewensten, H. Soreq. Engineering of human cholinesterase explains and predict diverse consequences of administration of various drugs and poisons. Pharmacol. Ther 1995, 67, 283-322.
8. A. N. Cokugras, Butyrylcholinesterase: Structure and Physiological Importance, Turkish Journal of Biochemistry - Turk J Biochem 2003, 28 (2), 54-61.
9. J. Massouliè, L. Pezzementi, S. Bon, E. Krejci, F.M. Valette. Molecular and cellular biology of cholinesterases. Neurobiology 1992, 41, 31-91.
10. A. Chatonnet, O Lockridge. Comparision of butyrylcholinesterase and acetylcholinesterase. Biochem. J 1989, 260, 625-634.
11. R.J.J. Ryhänen Pseudocholinesterase activity in some human body fluids. Gen. Pharmacol 1983,14, 459-460.
12. M. Ekholm. Predicting relative binding free energies as substrate and inhibitors of acetyl- and butyrylcholinesterase. Theo. chem 2001, 572, 25-34.
13. V. Tougu. Acetylcholinesterase: Mechanism of catalysis and inhibition. Curr. Med. Chem 2001, 1, 155-170.
14. P. Masson, W. Xie, M.T. Froment, O. Lockridge Effects of mutations of active site residues and amino acids interacting with Ω loop on substrate activation of butyrylcholinesterase. Biochim. Biophys. Acta 2001, 1544, 166-176.
15. K.R. Dave, A.R. Syal, S.S. Katyare. Tissue cholinesterases. A comparative study of their kinetic properties. Z. Naturforsch 2000, 55c, 100-108.
16. C.A. Prody, D. Zevin-Sonkin, A. Gnatt, O. Goldberg, H Soreq. Isolation and characterization of full-length cDNA clones coding for cholinesterase from fetal human tissues. Proc. Natl. Acad. Sci. USA 1987, 84, 3555-3559.

17. D.J. Ecobichon, A.M Corneau. Pseudocholinesterase of mammalian plasma: Physiochemical properties and organophosphate inhibition in eleven species. *Toxicol. Appl. Pharmacol* 1973, 24, 92-100.

18. P.W. Allderdice, H.A.R. Garner, D. Galutira, O. Lockridge, B.N. LaDu, J. McAlpines. The cloned butyrylcholinesterase (BCHE) gene maps to a single chromosome site. *Genomics* 1991,11, 452-454.

19. D.M. Quin. Acetylcholinesterase: Enzyme structure, reaction dynamics, and virtual transition states. *Chem. Rev* 1987, 87, 955-979.

20. L. Raveh, E. Grauver, J. Grunwald, E. Cohen, Y. Ashani. The stoichiometry of protection against soman and VX toxicity in monkeys pretreated with human butyrylcholinesterase. *Toxicol. Appl. Pharm* 1997, 145, 43-53.

Authors Address for Communication:

^aDepartment of Chemistry, Ewha Womans University, Seoul, Republic of Korea

^bDepartment of Chemistry, Najran University, Najran, Kingdom of Saudi Arabia

^cDepartment of Chemical Engineering, Yonsei University, Seoul, Republic of Korea

^dInternational Center for Chemical and Biological Sciences, H.E.J. Research Institute of Chemistry, University of Karachi, Karachi-75270, Pakistan

Sher Bahadar Khan (Tel) +82-2-312-1417
(Fax) +82-2-312-6401

(E-mail) drkhanmarwat@gmail.com

JPRHC