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Review Article

LAUQ KHAYAR SHAMBAR: A POLYHERBAL UNANI FORMULATION FOR THE MANAGEMENT OF COUGH

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ABSTRACT

Cough is a physiological reflex, experienced by every human, is an important protective and defensive mechanism whose action secures the removal of foreign materials and secretions from the airways (larynx, trachea and bronchi). In various circumstances, such as respiratory tract inflammation, viral infections, allergic rhinitis, or inhalation of various irritants, it is unintentionally stimulated and a cough suppressant may be needed to relieve the cough. The currently available cough suppressants (opiates, dextromethorphan, etc.) limit their use in humans due to significant side effects such as constipation, respiratory depression, drowsiness. *Lauq Khayar Shambar* (LKS) is used as an antitussive in Unani medicine for centuries and is also used to treat various upper respiratory tract ailments such as asthma, dyspnoea, catarrh, productive and dry cough, pharyngitis and laryngitis. So, this review aims to explore the role of LKS in the management of cough.

Keywords: Antitussive, Lauq, Munaffis-ī-balgham, Expectorant, Unani medicine

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INTRODUCTION

Cough is a physiological reflex, experienced by every human, is an important protective and defensive mechanism whose action secures the removal of foreign materials and secretions from the airways (larynx, trachea and bronchi). It can be considered to be an inbuilt defence mechanism [1, 2]. In various scenarios, such as respiratory tract inflammation, viral infections, allergic rhinitis, or inhalation of various irritants, it is unintentionally stimulated due to stimulation of receptors presents in the throat, respiratory passage or the lungs. In these cases, the cough has a pathological nature and a cough suppressant may be needed to relieve the cough [3, 4]. According to severity, cough can be divided into three categories: acute<three weeks; subacute>three to<eight weeks; chronic>eight weeks [5]. It is also classified as productive (producing mucus or phlegm) and non-productive (dry) cough [4]. A productive cough can require therapy to either correct the abnormality that triggers sputum development or to alter the consistency of the secretions to make it less difficult to expectorate. A non-productive cough will require drugs to mitigate the cause or minimise the frequency of the cough [6]. The currently available cough suppressants (opiates, dextromethorphan, etc.) limit their use in humans due to significant side effects such as constipation, respiratory depression, and drowsiness [7]. Medicinal plants are a potential source of drugs with high-antitussive efficiency with limited adverse effects. There are so many single and compound drugs in Unani medicine which are used to suppress the cough [8]. *Lauq* is a classical semisolid dosage form in Unani medicine that has been used primarily to treat various respiratory disorders. The Arabic word '*Lauq*' means 'licking'. It was firstly prepared by *Jalinoos*, (Galen; 129-200 CE). It is thick and sticky in nature and prepared by mixing the powdered or decoction of the natural drug(s) with honey or sugar syrup. It is given orally and advised to lick [9]. LKS is one of them. It contains *magz-ī-khayar shambar* (Pulp of the fruit of Cassia fistula L.) as the main ingredient along with *sapistan* (Cordia myxa L.), *aslussoos* (Glycyrrhiza glabra L.) and *katira* (Cochlospermum religiosum (L.) Alston). It is used as an antitussive in Unani medicine for centuries and is also used to treat various upper respiratory tract ailments such as asthma, dyspnoea, catarrh, productive and dry cough, pharyngitis and laryngitis [10, 11].

A literature search was carried out to collect all relevant information on cough, antitussive, *Lauq Khayar Shambar,* and its ingredients. Publicly available electronic databases, including PubMed, Scopus, Google Scholar and ScienceDirect, have been scanned. A large number of literature articles published up to 2020 were reviewed. The keyword used for the search included "antitussive", "Cassia fistula", "Cordia myxa", "Glycyrrhiza glabra", "Cochlospermum religiosum", *"su'āl" "lauq", "lauq khayar shambar", "magz-ī-khayar shambar", "sapistan", "aslussoos"* and *"katira".* The name of species has been validated by using 'World Flora Online (http://www.worldfloraonline.org/). "Standard Unani Medical Terminology" published by CCRUM has been used to describe the proper Unani terminologies (http://namstp.ayush.gov.in/#/Unani).

Table 1: Ingredient of LKS

Name	Botanical name	Family	Part used	Quantity (Ratio)	References
Sapistan	*Cordia myxa* L.	Boraginaceae	Fruit	1.5	[10, 11]
Aslussoos	*Glycyrrhiza glabra* L.	Fabaceae	Root	1.5	
Magz-ī-khayar Shambar	*Cassia fistula* L.	Leguminosae	Pulp of fruit	2	
Katira	*Cochlospermum religiosum* (L.) Alston	Bixaceae	Gum	1	
Qand safaid (Sugar)				18	

Method of preparation

Firstly, *aslussoos* (Glycyrrhiza glabra) is crushed to small pieces in an iron mortar and softened, then *sapistan* (Cordia myxa) and *aslussoos* (Glycyrrhiza glabra) are immersed in water (18 L) at night. In the morning, boil these infusion tills remain half. After that, Mesh it well and filter it, then mix *floos-ī-khayar shamber* in the filtrate and filter it again. Add Sugar to the filtrate of these drugs and boiled it on low fire till it acquired *qiwam* (consistency) of two tar. Lastly, mix the powder of *katira* in *qiwam* [10].

Important points regarding the preparation of LKS

- The *qiwam* (Consistency) of *lauq* is tested by pressing the drop of *qiwan* in between the thumb and index finger and observed for two Tar
- *Sapistan* should be mixed cautiously as these drugs are mucilaginous in nature and on mixing with *qiwam* form a viscous mass
- *Floos-ī-khayar shamber* (Pulp of the fruit of Cassia fistula L.) should not be boiled as it loses its property on boiling. It should not always be first rubbed with hands and squeezed out through a fine cotton cloth and then be used along with other decoctions for mixing in the *qiwam* [10, 11].

Dose: 7 g

Action and Uses (*Af'āl wa Mawaqe istemal*)

It possesses *munaffis-ī-balgham* (expectorant), *musakkin-ī-Su'āl* (Antitussive), *munzij* (concoctive), *mulayyan* (Laxative) properties. It is used in *nazla* (catarrhs), *zukam* (coryza), *su'āl* (cough), *su'āl Balghamī* (Phlegmatic Cough) and *qabz* (constipation) [10–14].

Table 2: Physicochemical standards of LKS

Properties	Result	References
Appearance	Semi-solid	[10, 11]
Colour	Light chocolate	
Smell	Pleasant	
Taste	Sweet	
Alcohol soluble matter	19.80-20%	
Water-soluble matter	91.90-92.40	
Successive extractive value		
Pet ether	0.02-0.04%	
Chloroform	0.05-0.08%	
Ethyl alcohol	37.29-38.53	
pH		
pH of 1%solution	4.77-4.85	
pH of 10%solution	4.37-4.54	

Table 3: Properties of ingredient of LKS in Unani medicine

Name	Temperament	Pharmacological action	Therapeutic uses	References
Sapistan	Moderate (in hot and cold) and wet in 1°	*Munaffis-ī-balgham* (expectorant), *Musakkin* (sedative), *Mulattif* (demulcent), *Mulayyin-ī-sadr* (emollient of the chest)	*Nazla-o-Zukām Ḥārr* (acute Coryza and catarrh), *Khushūnat-ī-Ḥalaq wa Ṣadr* (Irritation of throat and chest), *Su'āl* (cough), *Ḥummā Ṣafrāwī wa Damawī* (Bilious and haemolytic Fevers)	[15–17]
Aslussoos	Hot 2 and dry in 1°	*Munaffis-ī-balgham* (expectorant), *Musakkin* (sedative), *Munzij-i-akhlat-i-ghalizah* (Concoctive of viscous humour), *Muqawwi-ī-'asāb* (nervine tonic), *Muhallil-ī-warm* (anti-inflammatory), *Daf-ī-humma* (Antipyretic)	*Su'āl* (cough), *Su'āl Balghamī* (Phlegmatic Cough), *Ḍīq al-Nafas/Dama* (Bronchial asthma), *Waram-i-Ḥalaq* (Pharyngitis), *amrad-ī-'asāb* (Nervine disordes)	[18–20]
Magz-ī-khayar Shambar	Hot and wet in 1°	*Munaffis-ī-balgham* (expectorant), *Muhallil-ī-warm* (anti-inflammatory), *Mushil-ī-Balgham* (Purgative of Phlegm)	*Waram-i-Ḥalaq* (Pharyngitis), *Su'āl* (cough), *Ḍīq al-Nafas/Dama* (Bronchial asthma)	[17, 19, 21, 22]
Katira	Cold and dry in 2°	*Munaffis-ī-balgham* (expectorant), *Mushil-ī-Balgham* (Purgative of Phlegm) *Musakkin* (sedative), *Mulattif* (demulcent), *Habis-ī-dam* (Haemostatic)	*Su'āl* (cough), *Amrāḍ-i-Ḥalaq* (Diseases of Throat), *Nafs ud dam* (haemoptysis), *Bawl al-Dam* (Haematuria)	[17, 20, 23, 24]

Table 4: Important identified chemical constituents and scientific studies on ingredients of LKS

Botanical name	Important chemical constituent	Pharmacological studies
Cordia myxa L.	Flavonoids, terpenoids, saponins, tannins, sterols, steroids, coumarin, resins, gums, mucilage, phenolic acids, stearic acid, palmitic acid, rutin, hesperidin, caffeic acid, d-arabinose, l-fructose, d-glucose, d-xylose, polysaccharides [25–27]	Antitussive [28], Smooth Muscle Relaxant [29] Analgesic [30], Anti-inflammatory [30], Immunomodulatory [31], Antiparasitic [32] Antimicrobial [25], Antioxidant [30]
Glycyrrhiza glabra L.	Glycyrrhizin, glabrene, formononetin, glabrol, liquiritigenin, liquirtin isoliquertin, glucoliquiritin apioside [33–35]	Immunomodulatory [36], Antitussive [37], Anti-inflammatory [38], Antinociceptive [39] Antiulcer [40], Antioxidant [41] Antiviral [42], Antimicrobial [43]
Cassia fistula L.	1,8-dihydroxy-3-anthraquinone derivative, ziganein, rhein, methyl ester, scopoletin, vanillic acid, aspartic acid, glutamic acid and lysine [44–46].	Antioxidant [47] Antimicrobial [48] Anti-inflammatory [49] Anti-rheumatic [50] Immunomodulation [51]
Cochlospermum religiosum (L.) Alston	L-rhamnose, D-galactose, α-cochlospermic acid, alanine, glutamic acid, methionine, stearic acid, palmitic acid, erucic acid [52, 53]	Anti-inflammatory [54] Catalytic [55] Antibacterial [56] Insecticidal [57] Antioxidant [57]

Table 5: Antitussive and relaxant activity of ingredient of LKS

Drug	Activity	Dose form	Positive control	Model/Method	Result	References
Cordia myxa L.	Smooth Muscle Relaxant Activity	Alcoholic extract	---------	*In vitro*/Isolated tracheal smooth muscle of sheep	Relaxed the trachea muscles contracted by acetylcholine	[29]
	Antitussive activity	hydro-alcoholic extract	Dextromethorphan	Ammonia induced cough in mice	Significantly inhibit the frequency of cough	[28]
Glycyrrhiza glabra L.	Broncho relaxant effect	Powder	Prednisolone	54 patients with chronic bronchial asthma	Licorice has a similar effect as a standard drug but is more potent due to the presence of glycyrrhizin which shows corticosteroid like activity	[58]
	Antitussive activity	water-extracted polymeric fraction	Codeine	Citric acid-induced cough in guinea-pigs	Significantly suppress the cough compared to codeine	[37]
	Antitussive activity	Hydroalcoholic extract	Codeine sulphate	SO_2-induced cough in mice	At a dose of 800 mg/kg the extract significantly inhibits the cough reflex	[59]
Cassia fistula L.	Antitussive activity	Methanol extract	Codeine phosphate	SO_2-induced cough in mice	At a dose of 600 mg/kg the extract significantly inhibits the cough reflex	[60]

A well-recognized LKS has been commonly used for respiratory complications, especially in the case of cough. The researches prove the relevant pharmacological effects of their ingredients and prescribed in asthma, chronic bronchitis, influenza and recurrent upper respiratory tract infections. Due to expectorant and demulcent properties, *Cordia myxa* brings up the phlegm, suppress cough and enhances respiratory system secretions [61, 62]. It significantly inhibits the frequency of cough by affecting the cough centre in the brain [28]. It also relaxed the Tracheal Smooth Muscle of sheep due to the expression and activation of Ca^{2+}-dependent NOS isoforms [29].

The ethanol extracts of *Glycyrrhiza glabra* inhibit the SO_2-induced cough reflex in experimental animals [59]. At a dose of 50 mg/kg orally, the aqueous extract of *Glycyrrhiza glabra* decreases the frequency of cough induced by citric acid in guinea pigs more effectively than codeine due to spasmolytic and protective effects on mucous [37]. The broncho relaxant effect of *Glycyrrhiza glabra* is due to the presence of glycyrrhizin which has corticosteroid-like activity [58]. Glycyrrhizic acid, which is the major active compound of *Glycyrrhiza glabra*, effectively ameliorate the progression of ovalbumin-induced asthmatic features in the experimental animal by suppressing IL-4, IL-5 and IL-13. It also prevented the reduction of IFN-γ and inhibit the overproduction of eosinophils and mucus [63–65]. The anti-allergic effect of *Glycyrrhiza glabra* is mainly due to glycyrrhizin, 18β-glycyrrhetinic acid and liquiritigenin, which is useful for asthma and allergic disease [66]. The leaf extract of *Cassia fistula* showed significant antitussive activity in experimentally induced cough reflex in mice, same as codeine phosphate [60].

In Unani medicine, a cough is an act by which *tabiyat* (internal power of the body) removes irritating substances from the lungs and adjacent structures. According to *Ismail Jurjani* there are three causes of cough: (1) When an *asbabe badiyah* (extrinsic factors) i.e., smoke, dust, fumes cold air enters into the respiratory system; (2) *asbabe wasila* (intrinsic factors) i.e., any type of *su'-i mizaj* (impaired temperament); (3) Inflammation in lungs [67]. *Asbabe badiyah* causes inflammation in the airways and produces *ratoobat* (mucus hyper-secretion) that result in a narrowing of the airways. Dry cough occurs due to *su'-i mizaj har sada* (impaired hot temperament) and *su'-i mizaj barid sada* (impaired cold temperament) and wet cough occur due to *su'-i mizaj har maddi* (impaired hot temperament with humoural involvement) and *su'-i mizaj barid maddi* (impaired cold temperament with humoural involvement). *Su'-i mizaj maddi* is more prevalent in the persons of *balghamī mizaj* (phlegmatic temperament) [68, 69]. According to the nature of the cause, *su'āl har maddi* (cough of hot humours) and *su'āl barid maddi* (cough of cold humours) are collectively known as *su'āl ratab* (productive cough) [70, 71]. *Su'āl Ratab* (productive cough) is caused by the fluids (*ratubat*) of the lungs and chest. It is mainly found in elderly people and people with wet temperaments. The symptoms are hoarseness of voice, and excessive discharge of phlegm during sleep and after waking [67, 68].

In Unani medicine, the principle of treatment of cough is *ta'dil-i su'-i mizaj* (correction of impaired temperament) through *taltif* (rarefaction), *taskhin* (warming), *tartib* (moistening), *tajfif o tanshif* (Drying) or *taghriya* (Soothing) as required.

In *su'āl ratab* (productive cough), treatment should be started with the drugs having the property of *mulattif* (demulcent), *munaffis-ī-balgham* (expectorant) and *musakkin* (sedative) properties [72–74]. In the compound formulation of LKS, all the four ingredients are *munaffis-ī-balgham* (expectorant) and *musakkin* (sedative) properties, and due to its expectorant properties, it helps in clearing the airways by eliminating phlegm [10, 75, 76].

As described above, LKS is a dense, sticky dosage form and is used as a licking. The physicochemical properties and method of administration increase the transit time of the drug from the oesophagus and therefore increase the absorption of the drug into the trachea. It also induces the persistent and prolonged release of drugs to the respiratory tract [14, 77–79].

CONCLUSION

Based on the information amassed above, it can be concluded that LKS is a semisolid dosage form that has been effectively used in traditional medicines for centuries to manage cough. The physicochemical and experimental studies on the ingredient of LKS indicate that it possesses an Antitussive effect. However, to establish the efficacy, safety and mechanism of action, more experimental and clinical studies are needed.

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CONFLICT OF INTERESTS

There is no conflict of interest to declare.

AUTHORS CONTRIBUTIONS

All authors contributed equally.

REFERENCES

1. Chung KF. The Clinical and Pathophysiological Challenge of Cough. In: Cough: Causes, Mechanisms and Therapy [Internet]. Malden, Massachusetts, USA: Blackwell Publishing Ltd; 2008. p. 1–10. Available from: http://doi.wiley.com/10.1002/9780470755846.ch1. [Last accessed on 30 Mar 2022]
2. Kuang Y, Li B, Fan J, Qiao X, Ye M. Antitussive and expectorant activities of licorice and its major compounds. Bioorg Med Chem. 2018;26(1):278-84. doi: 10.1016/j.bmc.2017.11.046, PMID 29224994.

3. Saraswathy GR, Sathiya R, Anbu J, Maheswari E. Antitussive medicinal herbs-an update review. Int J Pharm Sci Drug Res. 2014;6(1):12-9.
4. Meher A. Antitussive evaluation of formulated polyherbal cough syrup. J Drug Delivery Ther. 2012;2(5):61-4. doi: 10.22270/jddt.v2i5.238.
5. Irwin RS, Rosen MJ, Braman SS. Cough. A comprehensive review. Arch Intern Med. 1977 Sep 1;137(9):1186-91. doi: 10.1001/archinte.137.9.1186, PMID 901087.
6. Ziment I. Herbal antitussives. Pulm Pharmacol Ther. 2002;15(3):327-33. doi: 10.1006/pupt.2002.0343, PMID 12099787.
7. Jahan Y, Mahmood T, Bagga P, Kumar A, Singh K, Mujahid M. Future prospects of cough treatment; Herbal medicines v/s modern drugs. Int J Pharm Sci Res. 2015;6(9):3689-97.
8. Gairola S, Gupta V, Bansal P, Singh R, Maithani M. Herbal antitussives and expectorants-a review. Int J Pharm Sci Rev Res. 2010;5(2):5-9.
9. Karegar Borzi H, Salehi M, Rahimi R. Lauq: a sustained-release dosage form for respiratory disorders in traditional persian medicine. J Evid Based Complementary Altern Med. 2016;21(1):63-70. doi: 10.1177/2156587215587417. PMID 26008751.
10. Anonymous. National Formulary of Una ni Medicine part 1. First. New Delhi (India): Central Council for research in Una ni Medicine. Ministry of Health and Family Welfare, Government of India; 2006. p. 1-337.
11. Anonymous. Physicochemical standards of Una ni formulation, Part 2. New Delhi (India): Central Council for research in Una ni Medicine. Ministry of Health and Family Welfare, Government of India; 1987.
12. Qarabadeen-e-Qadri AA. Urdu translation by CCRUM. New Delhi (India): Central council for research in Una ni Medicine. Ministry of Health and Family Welfare, Government of India; 2009.
13. Anonymous, Majeedi Q. New Delhi (India): (waqf Hamdard) all India Una ni Tibbi conference. 9th ed; 1986.
14. Al-Qarabadeen KM. New Delhi (India): Central Council for research in Una ni Medicine. Ministry of Health and Family Welfare, Government of India; 2006.
15. Muheet-e-Azam KA. New Delhi (India): Central Council for research in Una ni Medicine. Vol. 3. Ministry of Health and Family Welfare, Government of India; 2014.
16. Ghani N. Khazain al-Advia Vol. I and IV. Khazainul Advia. New Delhi: Idara Kitab al Shifa; 2011. p. 1–1260.
17. Makhzanul Mufradat KM. New Delhi: Aijaz Publication; 2014. p. 392.
18. Khan A. Muheet-i Azam. Vol 1. New Delhi (India): Central Council for research in Una ni Medicine. Ministry of Health and Family Welfare, Government of India; 2011.
19. Khazainul GM, Advia (Urdu). New Delhi, India: Idara Kitab al Shifa; 2011.
20. Al-Razi Z, Abdal KAl. Third edit. New Delhi (India): Central Council for research in Una ni Medicine. Ministry of Health and Family Welfare, Government of India; 2000.
21. Khan A. Muheet-e-Azam vol-2. New Delhi (India): Central Council for research in Una ni Medicine. Ministry of Health and Family Welfare, Government of India; 2013.
22. Mufradat Azizi HA. New Delhi (India): Central Council for research in Una ni Medicine. Ministry of Health and Family Welfare, Government of India; 2009.
23. Khan A, Muhit Azam. Vol 4. (Urdu Translation: CCRUM) [internet]. Ministry of Health and Family Welfare, Government of India; 2018. p. 1. Available from: http://ccrum.res.in. [Last accessed on 30 Mar 2022].
24. Maghrabi AS. Kitab al Fatah fi al tawdi (Urdu). 1st editio. New Delhi, India: Jamia Hamdard (Hamdard University); 2007.
25. Jasiem TM, Al-Mugdadi SFH, Aljubory IS, Latef QN. Phytochemical study and antibacterial activity of crude alkaloids and mucilage of cordia myxa in Iraq. Int J Pharm Sci Rev Res. 2016;39(1):232-6.
26. Al-Snafi PDAE. The pharmacological and therapeutic importance of Cordia myxa-a review. IOSR J Pharm. 2017;7(3):72-91.
27. Hojjati M, Beirami Serizkani F. Structural characterization, antioxidant and antibacterial activities of a novel water-soluble polysaccharide from Cordia myxa fruits. Food Measure. 2020 Dec 1;14(6):3417-25. doi: 10.1007/s11694-020-00586-y.
28. Salimimoghadam S, Ashrafi A, Kianidehkordi F, Najafzadehvarzi H. Hypoglycemic, antitussive and analgesic effects of nanoparticles of cordia myxa fruits extract. Int J Pharm Investig. 2019;9(4):205-9. doi: 10.5530/ijpi.2019.4.38.
29. AlBayaty MAA. Mechanism of the tracheal smooth muscle relaxant activity of the cordia myxa plant extract in sheep. Iraqi J Vet Med. 2008;32(2):214-26. doi: 10.30539/iraqijvm.v32i2.755.
30. Abdel-Aleem ER, Attia EZ, Farag FF, Samy MN, Desoukey SY. Total phenolic and flavonoid contents and antioxidant, anti-inflammatory, analgesic, antipyretic and antidiabetic activities of Cordia myxa L. Leaves. Clin Phytosci. 2019 Dec 9;5(1):29. doi: 10.1186/s40816-019-0125-z.
31. Rashid Ali W, Al-Asady ZT, Ibrahim AJ. Immunomodulatory of cordia myxa (L.) aqueous extract fruit in immunized mice with hydatid cyst fluid. J Nat Sci Res. 2015;5(10).
32. Saki J, Khademvatan S, Pazyar N, Eskandari A, Tamoradi A, Nazari P. *In vitro* activity of cordia myxa mucilage extract against leishmania major and l. infantum promastigotes. Jundishapur J Microbiol. 2015 Mar 21;8(3):e19640. doi: 10.5812/jjm.19640, PMID 25861436
33. Fenwick GR, Lutomski J, Nieman C. Liquorice, glycyrrhiza glabra L.—composition, uses and analysis. Food Chem. 1990 Jan;38(2):119-43. doi: 10.1016/0308-8146(90)90159-2.
34. Farag MA, Porzel A, Wessjohann LA. Comparative metabolite profiling and fingerprinting of medicinal licorice roots using a multiplex approach of GC–MS, LC–MS and 1D NMR techniques. Phytochemistry. 2012 Apr;76:60-72. doi: 10.1016/j.phytochem.2011.12.010, PMID 22336263.
35. Li G, Nikolic D, van Breemen RB. Identification and chemical standardization of licorice raw materials and dietary supplements using UHPLC-MS/MS. J Agric Food Chem. 2016 Oct 26;64(42):8062-70. doi: 10.1021/acs.jafc.6b02954, PMID 27696846.
36. Mitra Mazumder P, Pattnayak S, Parvani H, Sasmal D, Rathinavelusamy P. Evaluation of immunomodulatory activity of glycyrhiza glabra L roots in combination with zing. Asian Pac J Trop Biomed. 2012 Jan;2(1):S15-20. doi: 10.1016/S2221-1691(12)60122-1.
37. Saha S, NosAlova G, Ghosh D, Fleskova D, Capek P, Ray B. Structural features and in vivo antitussive activity of the water extracted polymer from glycyrrhiza glabra. Int J Biol Macromol. 2011;48(4):634-8. doi: 10.1016/j.ijbiomac.2011.02.003, PMID 21329720.
38. Siracusa L, Saija A, Cristani M, Cimino F, D'Arrigo M, Trombetta D. Phytocomplexes from liquorice (Glycyrrhiza glabra L.) leaves — chemical characterization and evaluation of their antioxidant, anti-genotoxic and anti-inflammatory activity. Fitoterapia. 2011 Jun;82(4):546-56. doi: 10.1016/j.fitote.2011.01.009, PMID 21281704.
39. Maione F, Minosi P, Di Giannuario A, Raucci F, Chini MG, De Vita S. Long-lasting anti-inflammatory and antinociceptive effects of acute ammonium Glycyrrhizinate administration: pharmacological, biochemical, and docking studies. Molecules. 2019 Jul 4;24(13):2453. doi: 10.3390/molecules24132453, PMID 31277398.
40. Jalilzadeh Amin G, Najarnezhad V, Anassori E, Mostafavi M, Keshipour H. Antiulcer properties of glycyrrhiza glabra L. extract on experimental models of gastric ulcer in mice. Iran J Pharm Res. 2015;14(4):1163-70. PMID 26664383.
41. Tohma HS, Gulçin I. Antioxidant and radical scavenging activity of aerial parts and roots of Turkish liquorice (Glycyrrhiza glabra L.). Int J Food Prop. 2010 Jun 30;13(4):657-71. doi: /full/10.1080/10942911003773916.
42. Ashfaq UA, Masoud MS, Nawaz Z, Riazuddin S. Glycyrrhizin as an antiviral agent against hepatitis C virus. J Transl Med. 2011 Dec 18;9(1):112. doi: 10.1186/1479-5876-9-112, PMID 21762538.
43. Gupta VK, Fatima A, Faridi U, Negi AS, Shanker K, Kumar JK. Antimicrobial potential of glycyrrhiza glabra roots. J Ethnopharmacol. 2008 Mar;116(2):377-80. doi: 10.1016/j.jep.2007.11.037, PMID 18182260.

44. Sharma A, Kumar A, Jaitak V. Pharmacological and chemical potential of Cassia fistula L-a critical review. J Herb Med. 2021 Apr 1;26. doi: 10.1016/j.hermed.2020.100407, PMID 100407.
45. Rahmani AH. Cassia fistula Linn: potential candidate in the health management. Pharmacogn Res. 2015;7(3):217-24. doi: 10.4103/0974-8490.157956, PMID 26130932.
46. Barthakur NN, Arnold NP, Alli I. The Indian laburnum (Cassia fistula L.) fruit: an analysis of its chemical constituents. Plant Foods Hum Nutr. 1995 Jan;47(1):55-62. doi: 10.1007/ BF01088167, PMID 7784398.
47. Kaur S, Kumar A, Thakur S, Kumar K, Sharma R, Sharma A. Antioxidant, antiproliferative and apoptosis-inducing efficacy of fractions from cassia fistula L. Leaves. Antioxidants (Basel). 2020 Feb 20;9(2):173. Available from: https://www.mdpi.com/2076-3921/9/2/173. doi: 10.3390/antiox9020173, PMID 32093300.
48. Singh I, Gupta S, Gautam HK, Dhawan G, Kumar P. Antimicrobial, radical scavenging, and dye degradation potential of nontoxic biogenic silver nanoparticles using cassia fistula pods. Chem Pap. 2021 Mar 22;75(3):979-91. doi: 10.1007/s11696-020-01355-3.
49. Jyoti K, Arora D, Fekete G, Lendvai L, Dogossy G, Singh T. Antibacterial and anti-inflammatory activities of cassia fistula fungal broth-capped silver nanoparticles. Materials Technology. 2021;36(14):883-93. doi: 10.1080/10667857.2020.1802841.
50. Farooq H, Piracha MI, Usman M, Tariq R, Alam SS. Radiological analysis of hind paw joint in murine rheumatoid arthritis model treated prophylactically or therapeutically with cassia fistula versus naproxen. Proceedings. Proceedings of the Shaikh Zayed Med Complex Lahore. 2020 Nov 11;34(4):58-63. doi: 10.47489/p000s344z772mc.org.pk/index.php/szmc/article/view/11/11.
51. Laxmi V. Investigating the immunomodulatory effect of cassia fistula on albino rats. Adv Pharm Ethnomedicines. 2015;3(1):1-5. doi: 10.14737/journal.ape/2015/3.1.1.5.
52. AS, M LR, NS. Quantification of primary and secondary metabolites from leaves and stem bark of cochlospermum religiosum (l) alston. Int Res J Pharm. 2013 Sep 9;4(8):228-31. Available from: doi: 10.7897/2230-8407.04845/php/uploads/1969_pdf.
53. Ojha AK, Maiti D, Chandra K, Mondal S, Das Sadhan K, Roy DDSK, Ghosh K. Structural assignment of a heteropolysaccharide isolated from the gum of Cochlospermum religiosum (Katira gum). Carbohydr Res. 2008 May;343(7):1222-31. doi: 10.1016/j.carres.2008.03.010, PMID 18374321.
54. Bernela M, Ahuja M, Thakur R. Enhancement of anti-inflammatory activity of bromelain by its encapsulation in katira gum nanoparticles. Carbohydr Polym. 2016 Jun;143:18-24. doi: 10.1016/j.carbpol.2016.01.055, PMID 27083339.
55. Maity S, Kumar Sen I, Sirajul Islam SS. Green synthesis of gold nanoparticles using gum polysaccharide of cochlospermum religiosum (katira gum) and study of catalytic activity. Physica E: Low-dimensional Systems and Nanostructures. 2012 Aug;45:130-4. doi: 10.1016/j.physe.2012.07.020.
56. Mahendra C, Murali M, Manasa G, Ponnamma P, Abhilash MR, Lakshmeesha TR. Antibacterial and antimitotic potential of bio-fabricated zinc oxide nanoparticles of cochlospermum religiosum (L.). Microb Pathog. 2017 Sep;110:620-9. doi: 10.1016/j.micpath.2017.07.051, PMID 28778822.
57. Ponnamma P, Manasa G, Sudarshana MS, Murali M, Mahendra C. *In vitro* antioxidant, antibacterial and phytochemical screening of cochlospermum religiosum (L.) alston- A potent medicinal plant. Trop Plant Res. 2017 Jan 31;4(1):13-9. Available from: doi: 10.22271/tpr.2017.v4.i1.003/archives/2017/vol4issue1/3.pdf.
58. Al-Jawad F, Al-Razzuqi R, Hashim H, Al-Bayati N. Glycyrrhiza glabra versus Boswellia carterii in chronic bronchial asthma: A comparative study of efficacy. Indian J Allergy Asthma Immunol. 2012;26(1):6. doi: 10.4103/0972-6691.104437.
59. Jahan Y, Siddiqui HH. Study of antitussive potential of glycyrrhiza glabra and adhatoda vasica using a cough model induced by sulphur dioxide gas in mice. Int J Pharm Sci Res. 2012;3(6):1668-74.
60. Bhakta T, Mukherjee PK, Saha K, Pal M, Saha BP. Studies on the antitussive activity of Cassia fistula (Leguminosae) leaf extract. Pharm Biol. 1998;36(2):140-3. doi: 10.1076/ phbi.36.2.140.4598.
61. Abdallah IZA, Khattaba HAH, Heebab GH. Gastroprotective effect of cordia Myxa L. Fruit extracts against indomethacin-induced gastric ulceration in rats. Life Sci J. 2011;8(3):433-45.
62. Gupta GK, Tejas Joshi, Keshu Madhudiya, Arijit Chaudhuri. Therapeutic properties and nutritive values of some fruit bearing medicinal plants of rajasthan State in India. Pharmaceutical and Biosciences Journal. 2017;5(5):18. doi: 10.20510/ukjpb/5/i5/166552.
63. Ma C, Ma Z, Liao XL, Liu J, Fu Q, Ma S. Immunoregulatory effects of glycyrrhizic acid exerts anti-asthmatic effects via modulation of Th1/Th2 cytokines and enhancement of CD4(+)CD25(+)Foxp3+ regulatory T cells in ovalbumin-sensitized mice. J Ethnopharmacol. 2013;148(3):755-62. doi: 10.1016/j.jep.2013.04.021, PMID 23632310.
64. Ram A, Mabalirajan U, Das M, Bhattacharya I, Dinda AK, Gangal SV, Ghosh B. Glycyrrhizin alleviates experimental allergic asthma in mice. Int Immunopharmacol. 2006;6(9):1468-77. doi: 10.1016/j.intimp.2006.04.020, PMID 16846841.
65. Hocaoglu AB, Karaman O, Erge DO, Erbil G, Yilmaz O, Bagriyanik A, Uzuner N. Glycyrrhizin and long-term histopathologic changes in a murine model of asthma. Curr Ther Res Clin Exp. 2011 Dec 1;72(6):250-61. doi: 10.1016/j.curtheres.2011.11.002, PMID 24648593.
66. Shin YW, Bae EA, Lee B, Lee SH, Kim JA, Kim YS. *In vitro* and *in vivo* antiallergic effects of glycyrrhiza glabra and its components. Planta Med. 2007 Mar;73(3):257-61. doi: 10.1055/s-2007-967126, PMID 17327992.
67. Ikseer Azam KA. Urdu translation by Kabeeruddin. New Delhi, India: Idara Kitabus Shifa; 2011.
68. Sina I. Al-Qanun Fit-Tibb. Vol. I-V (Urdu translation by Ghulam husain Kantoori). New Delhi, India: Idara Kitabu-us-Shifa; 2007. p. 1-960.
69. Kulliyat-e-Nafeesi NB (Urdu translation by Kabeeruddin). 1st ed. New Delhi, India: Idara Kitabus Shifa; 1954. p. 1-528.
70. Kulliyat-e-Qanoon SI (Urdu translation by Kabiruddin). 2nd ed. New Delhi, India: Idara Kitabus Shifa; 2015. p. 1-383.
71. Kitab Al-Kulliyat RI (Urdu). Lahore: Maktaba Daniyal; 1987. p. 1-456.
72. Majoosi A bin A. Kamil-us-sana (Urdu translation by Hkm. Ghulam Hussain Kantoori. New Delhi, India: Idara Kitab-us-Shifa; 2010. p. 1-820.
73. Firdous Al-Hikmat TA. (Urdu translation by Hakeem Muhammad Shah). 2nd ed. New Delhi, India: Idara Kitabus Shifa; 2017. p. 1-484.
74. Kitab al Hawi Razi Z. New Delhi, India: CCRUM; 2004.
75. Khan MS, Khas BE. Urdu translation. New Delhi, India: Ejaz publishing house; 2006.
76. Bayaz-e-Kabeer KM. New Delhi: Idara Kitabu-us-Shifa-Part II; 2010.
77. Sherazi MMBK. Qarabadeen-e-masoomi. New Delhi (India): national mission for manuscripts; 2017.
78. Qarabadeen-e-Qadri AA. New Delhi: (Urdu translation) CCRUM, Govt. of India. Ministry of Health and F.W. Department of AYUSH; 2009. p. 26-7.
79. Ghani HN. Qarabadeen-e-najmul ghani. New Delhi, India: CCRUM; 2010.