WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 7, 1996-2010. Review Article ISSN 2277– 7105

A REVIEW ON HERBAL APPROACH TOWARDS URTICARIA AN ALLERGIC SKIN DISORDER

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Article Received on
19 Feb. 2018,

Revised on 12 March 2018,
Accepted on 02 March 2018,

DOI: 10.20959/wjpr20187-11806

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ABSTRACT

Urticaria is either acute or chronic condition, characterized by a rash of wheals and surrounding erythema which is very itchy and associated with swelling, especially of the mouth and round the eyes; to an individual rarely last longer than 48 hours or are often very short-lived. It is mainly the result of excessive release of histamine, bradykinin, leukotriene C4, prostaglandin D2, and other vasoactive substances from mast cells and basophils in the dermis, occurs to 20% demographic of the world. The modern allopathic preparations though available for the management of utricaria come along with considerable adverse effects. Traditional herbal medicines have found to be very active in the treatment of urticaria. This review covers such plants as a panacea for such inflammatory diseases.

KEYWORDS: Urticaria, Plants, Traditional medicine, Herbal approach, Vasoactive substances, Erythema.

INTRODUCTION

Urticaria (hives) is a vascular reaction of the skin marked by the transient appearance of smooth, slightly elevated papules or plaques (wheals) that are erythematous and that are often attended by severe pruritus. Individual lesions resolve without scarring in several hours. Most cases of urticaria are self-limited and of short duration; the eruption rarely lasts more than several days, it but may be recurrent over weeks. Chronic urticaria is defined as urticaria with recurrent episodes lasting longer than 6 weeks).[1]

The word 'Urticaria' is derived from the plant, '*The stinging nettle'*. This plant commonly known as *Urtica diocia* found all over the world. Nettle is the latin word, which means "urtica." The root word is "urere" in Latin, means to burn and signifies the inflammatory, type I hypersensitivity reaction. Urticaria the disease condition highly resembles with disease named Angioedema. Urticaria is the situation, which occur mainly in superficial epidermis layer of skin where angioedema occur in the deep dermis and subcutaneous tissue. Combination of both is known as Urticarial Angioedema Syndrome (UA). Prevalence of UA in general population is very high up to 10-20% and children prevalence up to 2-6%. In urticaria person should suffer from red, raised, itchy areas of dermal edema that usually in multiple and vary in size and form. Where angioedema it occurs in deep dermis that persist for minimum 72 hours. Both diseases contain similar pathophysiological mechanisms, which associated with release of histamine and other mediators from mast cells and basophils. The major difference between two conditions is whether mast cells in superficial dermis that results urticaria or in deeper epidermis that results in angioedema. Urticaria either acute or chronic may takes place by release of bio active mediators such as histamines, leukotrienes etc. by activation of mast cells or basophils. Activation of mast cells can be done by specific IgE, IgM or IgG antibody activating the classical complement pathway (However, the exact mechanism of action and significance of these antibodies remain unclear), also done by other mediators (neuropeptides, such as substance P, calcitonin gene related peptide and neurokinin A) and medications such as opiates which directly activates mast cells or basophils through specific receptors to induced hives by non-IgE mediated pathway. In pediatric studies investigating the cause for most common etiology of acute urticaria there is still unclear.

Restorative plants have been utilized remedially all around the world, being an imperative part of different conventional pharmaceutical frameworks. From Ayurveda to Chinese, from Unani to Tibetan Medicine, from Amazonian to African Medicine, all frameworks of customary pharmaceutical, embrace the phytotherapy in their doctrine. Phytotherapy is on the rise as one of the leading scenarios of the health industry. Major research is being conducted on incorporating the phytochemicals and phytoactive constituents into pharmaceutical formulations that can reach the demographic having scarcity of allopathic medicines. In this review we have referenced such plants which can be exploited for the treatment of urticaria without having any deplorable adverse effects on patients.[2-7]

Fig 1

Fig 2

Fig 3

Fig 4

Fig 1-4: indicates symtoms of patients suffering from acute and chronic urticaria.

Epidemiology

The worldwide incidence is 0.1%–3% of the population with women affected twice more likely than men. It is estimated that about 1 in 5 people will have urticaria once in their lifetime and this seems to be the case across all age groups. Up to 1% of the population suffers from chronic urticaria (CU) and all age groups appear to be affected, although the peak incidence is between 20 and 40 years of age. In most cases, the disease lasts between 1 or 5 years, but the duration can be longer for those with severe urticarial. Urticaria affects 15% to 25% of the population at some point in their lifetime. The prevalence in preschool children is 6% to 7%.[5,8]

ETIOLOGY

Various Atmospheric and Host factors are responsible to develop this particular disease are characterized into 3 categories listed in to Table 1 and there specific examples are given below.[6]

Table 1: Causative factors of urticarial.

Immunoglobulin E mediated	Non-immunoglobulin E mediated	Non-immunologically mediated
Aeroallergens	Autoimmune disease	Elevation of core body temperature, Food pseudoallergens, Light, Medications (direct mast cell degranulation)
Contact allergen	Cryoglobulinemia	Physical stimuli (cold, local heat, pressure, vibration),
Foodallergens	Infections (bacterial, fungal, viral),	Water
Insect venom	Lymphoma	
Medications (allergic reaction)	Vasculitis	
Parasitic infections		

1. **Drugs:** Antibiotics (penicillin, cephalosporin, macrolides, vancomycin), NSAIDs, opiates, narcotics can cause acute urticaria with or without angioedema.
2. **Food allergens:** Milk, eggs, wheat, soy and peanuts. Other food allergens involved in causing urticaria in older children are peanuts, tree nuts, seafood and shellfish.
3. **Environmental allergens:** Dust mites, moulds and animal dander can also trigger hives.
4. **Insects:** It can occur by insect bite or sting mainly by mosquitoes, bees and spiders.
5. **Systemic diseases:** It mainly include infectious, autoimmune diseases and malignancies. In children, viral infections are considered to be the most common cause of acute urticaria.
6. **Physical urticaria:** Physical stimuli such as cold, heat, scratch, pressure, vibration. Dermatographism is the most common physical urticaria.
7. **Idiopathic causes:** Most chronic urticaria are idiopathic.(5)

Classification

Urticaria is mainly divided into three categorized shown into Fig.5

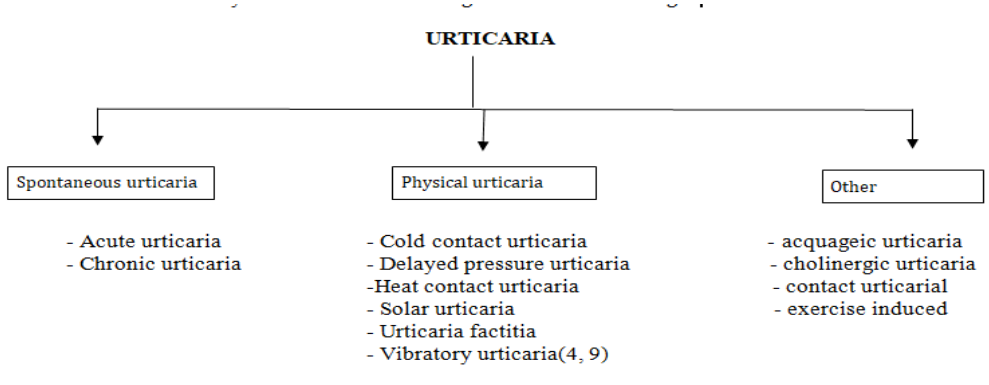


Fig 5 Classification of Urticaria

Pathophysiology

Pathophysiology of urticaria is mainly associate with the release of histamine. Along with it some other mediators like tryptase, proteoglicans, heparin and chondroitin sulphate A and B, leukotriens (LTB4 and LTC4) which are also responsible. Theses mediators is secretes from the cells include mast cells and basophils. Both cells are paly important role in pathogenesis of urticaria. Mast cells mainly located in tissue where basophils mainly found in tissue as well as circulation too. Both the cells can produce such mediators like chondroitin sulphate A and B, leukotriens, IL-1, IL-3, IL-4; where in addition mast cells secretes prostaglandin D2 (PGD2) as well as IL-5, IL-6, TNF-alfa. Several soluble serum factors, cytokines and other factors that causes release of histamine from basophils, which plays absolute role in pathogenesis. Sometimes it causes sudden raise in procalcitonin level also. Autoimmune urticaria mainly occurs by IgG autoantibody directing to alpha subunit of high affinity IgE receptor, but still the pathophysiology of mast cells and basophils is remains unproven.[4,8]

Treatment

The main focus in treatment for urticaria with or without angioedema is to obtain complete relief. First step in management of urticaria is to identify triggers and eliminate it, and the second step is medical treatment to relieve symptoms. Acute urticaria with angioedema may develop life-threatening airway obstruction. If angioedema affects the respiratory tract, the first step should be securing airway. To reduce edema subcutaneous or intramuscular adrenaline is incorporated.

Specific treatment (first) approaches involve the use of non-sedating long acting antihistamine (anti-H1).

The second approach is lowering or inhibiting mast cell mediator release are corticosteroids.

Table 2: Provides a list (not comprehensive) of antihistamine medications available in India.

Medications

Table 2: Treatment of urticarial.

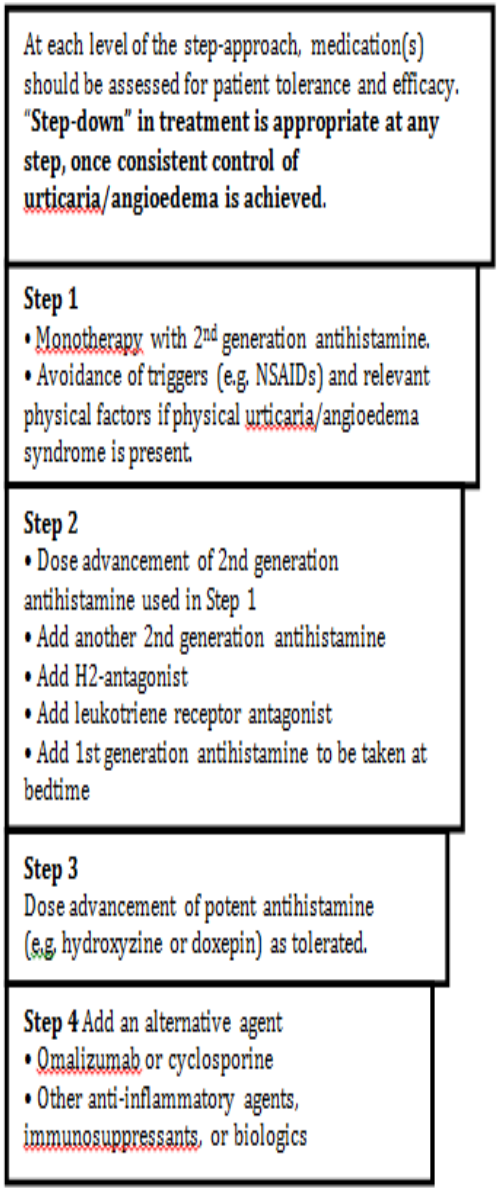
Class	Drugs	MOA	Comments
H1 antagonists	levocetirizine, desloratadine, loratadine and fexofenadine	as inhibition of cytokines release from basophiles and mast cells as well as reduction of chemotactic activity of eosinophils	considered as first-line treatment of urticaria
Corticosteroids		relieve symptoms such as swelling and inflammation	Short-term corticosteroid therapy may reduce urticaria, reduce the likelihood of relapse
leukotriene receptor antagonist (LTRA)	Montelukast or zafirleukast	It reduces the bronchoconstrictive and inflammatory effects of LTD4 in the airways	effective in controlling the urticaria in about 50% of the patient

Other agents

In patients with autoimmune chronic urticaria Cyclosporine therapy is introduced to treat high dose antihistamines. The patients with severe diseases intravenous immunoglobulins (IVIG), plasmapheresis and antagonists of tumor necrosis factor α (TNFα) are recommended only by specialists. For patients with chronic spontaneous urticaria, cholinergic urticaria, cold urticaria and solar urticaria Omalizumab is used as a therapeutic alternative.[5]

Therapy

Two guidelines European Academy of Allergy and Clinical Immunology(EAACI) and Practice Parameters and Other Guidelines consists of American Academy of Allergy, Asthma & Immunology(AAAAI), Joint Task Force(JTF) are adapted these three line therapy for diagnosis and management of acute and chronic urticaria shown in fig 6&7. (7)



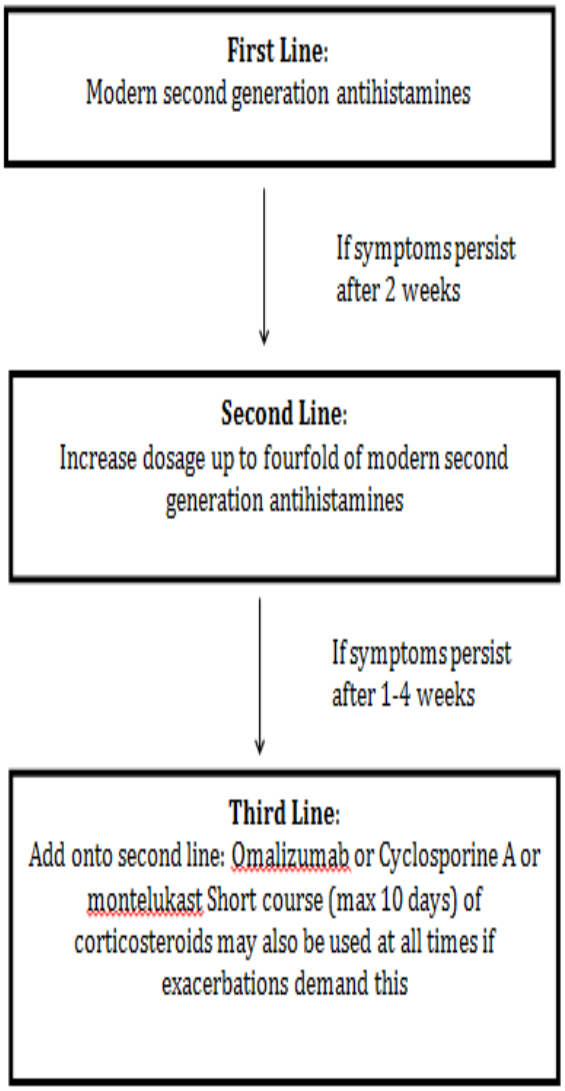


Fig 6 Adapted from JTF Practice Parameters "The diagnosis and management of acute and chronic urticaria: 2014 update".	**Fig 7 Adapted from EAACI Urticaria Guideline for the definition, classification, diagnosis and management of urticaria: the 2013 revision and update.**

Herbal Approach on Urticaria

Literature survey of ancient texts like Shushtrut Samhita, Chinese matria medica, Handbook of Unani medicines and others provided a compendium of plants specifically categorized to show action for these conditions. These complications are prepared by the Vaidyas and Monks who tried a combination of plants before they were classified. The plants included in these texts are safe without having profound side effects on the patients.{Kokate, 2008 #52} List of such plants have been included in the Table 3 below:

Table 3: List of plants used in urticarial.

Sr. no.	Plants	Family	Local Name	Part used	Application	Reference
1.	*Adansonia digitataLinn.*	Bombacaceae	Gorakshi	Fruit	Fruit pulp is used in urticaria.	[10,11]
2.	*Adeniumobesum (Forssk.) Roem. &Schult.*	Anysophylacae	Loukhoure, Djindjipete, Bouloukourane	Leaf	Maceration form used in Urticaria.	[12]
3.	*Aegle marmelos*			Stem, Root, bark,	The aqueous extracts of the stem and root bark are used to treat urticaria.	[13]
4.	*Albizzialebbeck (L.) Benth*	Fabaceae	Shirisha	Bark	Decoction is used in all allergic conditions. Shirisha acts as an antidote to animal poisons which are histaminic in nature and are also responsible for the production of urticaria. Its acts as anti-histaminic.	[10,14,15]
5.	*Allium cepaL.*	Liliaceae	Bassanle	Fruit	Maceration is used in Urticaria	[12]
6.	*Anisochilus Carnosus Wall*	Lamiaceae	Karpuravalli	Whole plant, Leaves	Juice of fresh leaves is used in urticaria.	[10,11]
7.	*Basella alba Linn.var. rubra Stewart.*	Basellaceae.	Upodikaa	Leaves	Leaves are used as poultice in urticarial.	[10,11,16,17]
8.	*Bergia odorata Edgew.*	Elatinaceae	Gangharan	Whole Plant	Plant paste is used.	[10]
9.	*C. asiatica(L.) Urb.*	Apiaceae	Brahmi	Leaf	Leaf paste used in urticaria.	[18]
10.	*Cassia fistula L.*	Caesalpiniaceae	Aaragwadha	Flowers	aurantiamide acetate, *alpfa*-Sitosterol and its alpfa- D – glucoside major chemical constituent which is used to treat urticaria.	[19]
11.	*C. oppositifoliaSm.*	Lamiaceae	Gadoosa	Leaf	Leaf paste used.	[18]
12.	*C. reflexaRoxb*	Convolvulaceae	Akashbel	Whole Plant	Plant paste can be used in urticaria.	[18]
13.	*C. sativa L.*	Cannabaceae	Bhaang, bhangolu, Vijaya	Leaves	Leaves paste used in urticaria.	[18]

14.	*Cedrus deodara*	Pinaceae	Deodar	Resin	Resin is used for the treatment of urticaria.	[10]
15.	*Cordia dichotoma G. Forst.*	Ehretiaceae	Shleshmataka	Seed, Leavev, Fruit	Paste used in urticaria.	[10]
16.	*Curcuma Domestica Valeton*	Zingiberaceae	Turmeric	Rhizome	Leaves and taken orally in the treatment of urticarial	[10,20]
17.	*Curcuma longa L.*	Zingiberaceae	Turmeric	Rhizome	Paste of fresh turmeric with leaves of neem and paste of turmeric and Durva (Cynodondactylon) helps in the healing of itches, boil, rheumatism, urticaria, etc.	[10,21]
18.	*D. falcatum (Nees) Keng f.*	Poaceae	Dhadhanj, nigaal, Gohra	Leaves	Leaves are boiled with leaves of P. mollissimaand extract is used to take bath	[18]
19.	*Dictamnus dasycarpusTurcz.,*	Rutaceae	Bai Xian Pi	Root Bark	In Korea, the root bark used for the treatment of skin diseases	[10,22]
20.	*Heliotropium indicumLinn.*	Boraginaceae	Hastishundi	Leaves	Decoction of leaves used for urticaria	[10,11,23]
21.	*Hibiscus tiliaceus*L. /*Hibiscus rosa-sinensis L.*	Malvaceae		Young leaves	Young leaves are crushed and squeezed into a small amount of water, juice prepared is used in to treat urticaria.	[20,24]
22.	*Impatiens balsamina Linn.*	Balsaminaceae	Tarini	Petals	In japan juice obtained from white petal is used to treat urticaria.	[11]
23.	*Ipomoea nil (L.) Roth*	Convolvulaceae	Sulkairi	Seed	Seed paste is applied in urticaria	[10,25,26]
24.	*Kaempferia galangaL.*	Zingiberaceae	Kercur	Rhizome	Used in urticaria.	[10,27]
25.	*Lagerstgroemia Parviflora Roxb.*	Lythraceae	Sinamara	Bark	Used in urticaria.	[10]
26.	*Mentha piperata Linn.*	Lamiaceae	Pudinaa.	Leaves	Take a few leaves of pudina by mashing it with a few pieces of black	(10,11,28,29){Maurya, 2014 #19;Maurya,

					pepper and a pinch of ajwain.	2014 #20}
27.	*Mirabilis jalapa Linn.*	Nyctaginaceae	Trisandhi Gulambasa	Leaves, Root, Stem	Leaf juice Externally applied for cure the urticaria.	[10,11,30,31]
28.	*Musa sapientum var. paradisiaca*	Musaceae	Banana	Fruit	Used in urticaria	[10]
29.	*Ocimum Americanum L.*	Lamiaceae	Hoary Basil	Leaves	The fresh leaves are used in urticaria in Mahi communities.	[10]
30.	*Ocimum sanctum L.*	Lamiaceae	Tulasi	Leaves	Fresh leaf juice mixed with the juice of Curcuma domesticaValeton rhizome is taken orally for treatment of urticaria.	[10, 20]
31.	*Piper betel L.*	Piperaceae		Leaves	Mostly act as anthelmintic agent & antibacterial agent	[32,33]
32.	*Piper. nigrum L.*	Piperaceae	Kali mirch	Fruit	Fruit powder is given with clarified butter	[18]
33.	*Pongamia pinnata Linn. Merr.*	Fabaceae	Karanja	Seed	Seed oil/powder is used in urticaria.	[14]
34.	*Premna Integrifolia Linn.*	Verbenaceae	Agnimantha	Root	Root rubbed into a paste with water is recommended to be taken with clarified butter in Urticaria.	[10,34]
35.	*R. campanulatum D. Don.*	Ericaceae	Shargar	Leaf	Leaf paste can be used in urticaria.	(18)
36.	*Rubusfruticosus L.*	Rosaceae	Blackberry Karwara	Fruit	Used in urticaria	[10]
37.	*Terminalia Chebula Retz.*	Combretaceae	Haritaki	Bark	Fresh bark decoction is taken orally for the treatment of urticaria.	[10,20,35
38.	*Trachyspermum Ammi L.*	Apiaceae (Umbelliferae)	Ajowan	Fruit	Ajowan daily intake is said to cure urticarial within a week	[10,36]
39.	*Tylophora tenuis Bl.*	Asclepiadaceae		Whole plant	Used.	[11]
40.	*S. americanum Mill.*	Solanaceae	Pattghaien	Leaf	Leaf paste used.	[18]

41.	*Saccharum officinarumL.*	Poaceae	Aakh	Stem juice	Urticaria (nettle-rash). 1 teaspoon juice of Zingiberofficinaleis mixed with 10 g molasses prepared from juice of Saccharumofficinarum. It is taken daily in the morning for 1 month.	[37,38
42.	*Urtica diocia*			Leaf	Leaf is mainly used to treat urticaria.	[3]
43.	*Vernonia colorata (Willd.) Drake*	Asteraceae	Starry Bitter-Tea	Leaves	The fresh leaves are used in urticaria1	[10]
44.	*Xeromphisspinosa (Thumb.) Keay*	Rubiaceae	Maindal	Leaves	Leaf juice is applied in urticaria.	[25]
45.	*Xylopiaaethiopica (Dunal) A. Rich*	Annonaceae	Simingni, Guile, Kani	Fruit	Maceration/decoction is used in urticarial	[12]
46.	*Zingiber officinaleRoscoe*	Zingiberaceae	Ada	Rhizome	Urticaria (nettle-rash). 1 teaspoon juice of Zingiberofficinaleis mixed with 10 g molasses prepared from juice of Saccharumofficinarum. It is taken daily in the morning for 1 month.	[37,38]

Formulations (Unani/Ayurvedic)

1. **Pitkirya:** Basically Pitkirya is the poly-herbal Unani formulation, which combination of six herbs. *Rauwolfiaserpentina, Acrouscalamus, Achilleamillefolium, fumalian officinalis, Nardostachysjatamansi, Lavandulastoechas*the powder of all six herbs taken in equal amount 500 mg in each capsule is preferred in urticaria.[39]
2. **AdrakaKhanda:** It is the poly-herbal Ayurvedic formulation.AdrakaKhandawas prepared as per the procedure given in the Bhaishjyaratnavali, where more than 12 plants are incorporated in powder form and pass through 40# sieve and used as dry granule form.[40]
3. **Unani formulation:** It's a decoction formulation in which 4 herbs in various proportion incorporated which named as *Iris ensata, Zingiber officinalis, Eugenia caryophyllata, Cassia fistula.*[41]

CONCLUSION

Urticaria is characterized as autoimmune disorders in which various neurotransmitters like histamine, leukotrienes, TNF-alfa are released and causes inflammation. The widely prevalent treatment forms are non-sedative anti histamines and corticosteroids. The allopathic formulations contain leukotrine and other histamine receptor antagonist that shows higher structural affinity. A complementary approach for Urticaria is the application of various single or combination of herbs and extracts that have shown to present lesser adverse effects than the allopathic approach. The various herbal phyto constituents have grater SAR than these drugs. Curcumin (active constituent of Turmuric), Gingerol (active constituent of Ginger), Aaragawdha, Shirish and few other plants have actively been used for urticaria since ages. Some poly-herbal Unani and Ayurvedic formulations are available which shows potential effect on Urticaria. The current requirement implores the clinical attestation of these drugs. Modern medicine can incorporate these herbal preparations so as to provide much needed comfort to the population at large.

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