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The Most Common Herbs to Cure the Most Common Oral Disease: Stomatitis Recurrent Aphthous Ulcer (RAU)

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Abstract

Context: Recurrent aphthous ulcer (RAU) is an oral disease and the most common oral lesion, with 2% to 66% of the world's population infected annually. Its prevalence is about 25% in Tehran and 27.6% in Mashhad. The etiology of RAU is multifactorial. Aphthous risk factors include: immunological factors, psychological factors, stress, trauma, sensitivity, family history, blood disorders, malnutrition, and use of certain medications, It should be noted that the best treatment for RAU is the topical application of drugs. The use of topical treatments is recommended not only because the drug can directly impact the source of the disease, but also systemic side effects of the drug are reduced. Treatment of RAU has been considered in Iranian traditional medicine (ITM), and is covered in therapeutic books. The use of herbs in RAU has a centuries-old history; accordingly, extensive research should be conducted for this treatment of the disease.

Evidence Acquisition: Iranian medical sources were reviewed and effective plants used in the traditional treatment of RAU were found and compared with new findings. Finally, we have created a table listing the plants that are part of the therapeutic protocol for RAU.

Results: Based on this article we can explain some of traditional pharmacological effects of plants and how these plants can be a source for a cure.

Conclusions: The plants listed can be used as a prediction of RAU management. Of course, there are is no evidence for curing RAU by some of these plants in allopathic medicine, and the further investigations in this area could lead to the discovery of a new drug

Keywords: Traditional Medicine, Aphthous, Medicinal Plants, Pharmacological Effects, Gholaa

1. Context

Aphthous is the most common oral lesion and the highest incidence occurs between the ages of 35 and 44 years old (1). Additionally, there is a direct relationship with the incidence of infection, associated with age, sex and socioeconomic status. The word "aphthous" comes from the Greek word "aphtha," which means ulcer. Aphthous ulcers are painful at first and after 24 hours appear as a grayish-yellow membrane with an erythematous halo. These ulcers occur on non-keratinized mucosa, for example, on the edge of the tongue, the buccal mucosa, and the lips. The etiology of RAU is unknown, and according to their clinical characteristics, these ulcers are divided into three types: the major, minor, and herpetic forms. The most common type is minor RAU, with a prevalence of 70% and lesion diameter of less than 1 cm. A minor RAU has a clear margin and heals within 10 - 14 days. In the major type, prevalence is 7% to 20%, the lesion diameter is more than 1 cm, and dysphagia may occur. The duration of treatment may be weeks. The herpetic form happens rarely and is associated with small and multiple ulcers, with healing may take 7 to 10 days. The appearance of this type is similar to herpetic lesions, but the herpes simplex virus is not seen with culture (1, 2).

RAU is more common among white women and usually occurs the first time in the second decade of life (1). The etiology of RAU is multi-factorial and factors such as immunologic factors, psychological factors, trauma, sensitivity, family history, blood disorders, malnutrition, use of certain drugs, such as antineoplastics and barbiturates can be a cause. Eating chocolate and nuts are risk factors for the disease. Deficiency of vitamin B, especially B12, folic acid, iron, and zinc are associated with susceptibility to RAU (1, 2).

Treatment of aphthous will usually be for three purposes:

1- Reduction of pain and inflammation.
2- Prevention of secondary infection.
3- Reduction of duration and repetition of aphthous.

The most common treatments, after oral hygiene, are:

1- Use of local and oral steroids that have effect on T-lymphocytes and reduce inflammation.

2- Use of local antibiotics, for example, chlorohexidine, benzidamine.

3- Solving vitamin and mineral deficiency, such as B12, iron, folic acid, and avoidance of food allergens.

4- Other treatments such as amelexanox, a potent inhibitor of inflammation due to mast cells and neutrophils. levamisol, talidomide are effective also (1, 2).

2. Evidence Acquisition

2.1. Viewpoints of Iranian Traditional Medicine (ITM) About Aphthous

Aphthous in traditional texts is very important, and a separate chapter is devoted to the topic of ulcers. We can search it as "Gholaa" (3). It is a kind of ulcer that affects the surface of the mouth and tongue, and it can even be exceeded inner layers of mouth tissue. In the definition of wounds, it is in the corrosive lesions groups and the deep infectious ulcers group (3).

2.2. Etiology of RAU in ITM

ITM divides RAU into three types based on the humors of the substance that created them: a) If the substance that causes aphthous is blood, there will be a warmth and inflammation around it; b) If the substance that causes aphthous is salty phlegm, the ulcer will be white with less pain compared with a bloody ulcer; c) If the substance that causes aphthous is burned black bile, the wound tends to be black. Based on these definitions and evidence, it seems that RAU can be of the phlegmatic type or the black bilotic type (3). Minor aphthous can be matched with the phlegmatic type. Of course, there is another type of oral ulcer, called corrosive lesions (Akele alfam), in which many ulcers are propagated. These can be herpetic aphthous and they are caused due to irritants, and pungent and erosive mucus (3, 4).

2.3. RAU Treatment Protocol in ITM

After review of traditional medicine books, the aphthous treatment protocol is as follows: First, maturation of the substances in the lesion, then dissolution and dissection of the lesion. After that, creation of astringency in the weak member, and finally, disposal of the matter from it (3, 5).

Based on these studies, that were conducted thousands of years ago, plants were used without a suitable, equipped, and modern laboratory to analyze these plants. This is an indication of the academic ability of the traditional physicians. Since traditional medicine is based on the humors and temperament, and we still cannot really define them based on laboratory criteria using modern science, we decided to compare the new findings with the traditional findings, and match them to take a step towards the vindication of the traditional medicine.

2.4. Methods

In this study, we evaluated traditional books (Akbari medicine book, Axir-e-Azam, Sharh Al-Asbab va Al-Alamat book, the Aghili treatments book, Kamel Al-Sanaat, Makhzan Al-Adviye and Al- Shamel fi Sanaate Tebbiye). We first studied the chapters on ulcers and oral diseases, and then searched the exact term of "gholaa" to describe the disease and learn of the medicinal plants that have been used in aphthous treatment for hundreds of years. After determination of the list of plants, we collected the temperament, usage, and mechanisms of these plants in the treatment of RAU from the herbal traditional books (Makhzan al-Adviye, Al-Shamel). Then we extracted the scientific names of these plants from botanical books. Finally, we collected new research, pharmacological mechanisms, and the effects of these plants by searching the scientific name of these plants in articles that were collected from databases such as Google Scholar, Science Direct, Scopus, Iranmedex, PubMed, and, with unlimited range. Then these plants were compared in a table.

3. Results

As can be seen in Table 1, the pharmacological effects of plants that are used in the treatment of RAU, consist of anti-inflammatory effects, analgesic, local anesthetic, antifungal, antibacterial, antiviral, and immunomodulatory (6). On the other hand, traditional effects that are mentioned in ITM books for these plants were tonic, astringent, cleansing, purified, resolvent, adsorbent, and diluting (4, 7)

Although there was not advanced equipment for identification of chemical components in plants, traditional physicians have explained their opinions about chemical components by the theory of the quadratic elements and confirmed the temperaments of plants. By comparing the traditional effects and modern pharmacological findings, some of these effects are matched to each other. For example, the term tonic in traditional medicine can be considered as an immunomodulatory effect (39), or the resolvent effect of the drugs in ITM may be the anti-inflammatory effect (40). Perhaps the maturation, purified, and cleansing effects of drugs in wound healing can be matched to the antibiotic effects. Based on the above explanations, for some plants in Table 1 there are no findings, and we can predict the anti-aphthous effect for them with research in this area.

Furthermore, some of these effects may be attributed to the compounds found in these plants, for example, the tannins in plants, due to their astringent effects, may strengthen organs and actually enhance the immunomodulatory effect (39). Or proanthocyanidins and saponins, which are found in plants, have anti-inflammatory and antioxidant properties. Therefore, they can be effective as a resolvent (40) in the healing of aphthous ulcers. Another important point in Table 1 is that based on temperament, these plants are divided into two groups: hot and dry, cold and dry.

Table 1. The Plants Used in the Treatment of RAU in ITM and Traditional Effects Associated with Their Pharmacological Effects

Name	Scientific Name	Use	Nature	Traditional Effects	Pharmacological Effects
Myrtle	*Myrtus communis* (8)	Leaf (4, 5)	composite powers, cold component is more (4, 5)	Desiccant, purified Resolvent inflammation (4, 7)	Anti-inflammatory, antioxidant, absorbing free radicals, antibacterial, anti-geneotoxic, analgesic, reducing aphthous (6)
Arnebia root	*Arnebia aucruma* (8)	Gargle juice with honey (4, 5)	Hot and dry (4)	Desiccant, resolvent of humors (4, 7)	Not found
Safflower	*Carthamus tinctorius* (8)	Scrubbing with honey (infant's aphthous) (4)	Hot dry (4, 5)	Maturative, resolvent (4)	Anti-inflammatory by histamine and carrageenan (triterpenoids), analgesic, anesthetic (serotonergic, monoaminergic) (9)
Purslane	*Portulaca oleraceae* (8)	Sprinkling powder (4)	Cool and wet with a little astringency (4)	Tonic, prevented the loss of pain stimulant, antihemorrhagic (4, 7)	Anti-inflammatory, antioxidant, analgesic, wound healing (10)
Oak	*Quercus ballota* (8)	Sprinkling burnt powder (4, 5)	Cool and dry (4, 5)	Desiccant, purified, detergent, severe astringency (4, 7)	Not found
Mulberry	*Morus alba* (8)	Gargle with juice, rob (4, 5)	Hot and wet (4, 5)	Restraint, resolvent of inflammation, prevented the loss of hot substances (4, 7)	Antibacterial, antioxidant, anti-inflammatory, analgesic (with central effect) (11)
Jambul	*Eugenia jambolana* (8)	Rinsing of fruit (4)	Cool and dry (4)	-	Antioxidant, anti-inflammatory (12)
Pomegranate flowers	*Punica granatum* (8)	Rinsing decoction with vinegar (4, 7)	Cool and dry (4, 7)	Desiccant, astringent, tonic, prevented the moisture flux, cicatrizant (4, 7)	Anti-inflammatory (COX-2 inhibitory and reduce PGE2) (13)
Small caltrops	*Tribulus terrestris* (8)	Rinsing juice with honey (4, 5, 7)	Combined strengths (4)	Cleansing, desiccant, purification with refrigeration (4, 7)	Anti-inflammatory, analgesic, antinociceptive (saponin), anti-oxidant (14)
Sour	*Vitis venifera* (8)	Dried extract (4)	Cool and dry (4)	Restraint, desiccant (4, 7)	Analgesic, anti-inflammatory, leukotrienes biosynthesis inhibitor, His antagonist, COX-2 inhibitor (proanthocyanidins) (15, 16)
Henna	*Lawsonia inermis* (8)	Rinsing decoction (4, 5)	Combined strengths willing to cold and drought (4)	Desiccant, cool, without pungency (4, 7)	Antiviral, antifungal, antibacterial, Anti-inflammatory, analgesic (Isoplumbagin, lawsaritol) (17)
Lettuce	*Lactuca sativa* (8)	Sprinkling burnt powder (4, 5)	Cool and dry (4)	Narcotic, hot steam rising toward mouth (4, 7)	Local analgesic, antinociceptive, anti-inflammatory (18)
Boxmyrtle, bayberry	*Myrica nagi* (8)	Rinsing decoction with wine (4, 8)	Hot and dry with cool power and astringent (4, 5, 7)	Desiccation of humidity ,purified, astringent, tonic of organs of body (4, 7)	Antioxidant, anti-inflammatory, central analgesic (proanthocyanidins and tannin) (11, 19)
Pomegranate	*Ponica granatum* (8)	Sprinkling powder of bark and rinsing decoction (4)	Cool and wet (4, 5)	Restraint, desiccant, purified, astringent, tonic, cleansing (4, 7)	Anti-inflammatory (Cox2- inhibitory and reduce PEG2 by polyphenoles and tannins) (13)
Lice-bane or stavesacre	*Delphinium staphsagria* (8)	Decoction with honey (4, 7)	Hot and dry (4, 5, 7)	High cleansing, purified of phlegm (4, 7)	Not found
Sumac	*Rhus coriaria* (8)	Tooth powder of fruit (4, 5)	Cool and dry (4)	Diluting, attenuant, penetration (sourness), restraint, organization contractor, condenser, antihemorrhagic (4, 7)	Antimicrobial, analgesic, antioxidant, anti-inflammatory, antiviral, astringent, cyclo-oxigenase inhibitor (tannin) (20)
Basil	*Ocimum basillicum* (8)	Rinsing and chewing (4, 5)	Hot and dry (4, 5)	Resolvent of inflammation (4, 7)	Antioxidant, antinociceptive, analgesic, antifungal, anti-inflammatory, antiviral (ursolic acid) (21)
Saatar	*Zataria multiflora* (8)	Extract of fresh flower (4)	Hot and dry (4, 5)	Exsiccation of septic humors ,astringent, resolvent of phlegm (4, 7)	Antibacterial, antifungal, analgesic, antioxidant, wound healing (20)
Sandals	*Pterocarpus santalinus* (8)	Timber with rosewater (4)	Cool and dry (4, 5)	Absorbent, tonic, refrigerant (4, 7)	Not found
Chalk	*Bambusa arundinacea* (8)	Sprinkling powder of stem and eating it (4, 5)	Cool and dry (4, 5)	Cool, dry, exsiccation, tonic, purified, resolving, absorbent of putrid humors (4, 7)	Anti-inflammatory, immunomodulatory (22)

Lentil	*Lens culinaris* (7)	Gargle with decoction (4, 5)	In the heat, mild and dry (4)	Polyearthiness, dry, desiccant with dissolution and cleansing (4, 7)	Antioxidant, anti-inflammatory (proanthocyanidins) (23)
Blackberry	*Rubus* sp.(8)	Chewing the leaves (4, 5)	Combined strengths with overcome coldness and dryness (4)	Astringent, tonic with resolvent, cleansing (4, 7)	Analgesic, anti-inflammatory, wound healing (24)
Jujube	*Zizyphus jujuba* (8)	Sprinkling powder of leaves and bark of stems (4, 7)	Hot and dry (4, 5)	Desiccant, purified, absorbent (4, 7)	Anti-inflammatory, wound healing, burn ulcer healing (25)
Bramble	*Lyceum* sp (8)	Chewing the leaves (4, 5)	Cool and dry (4, 5)	Astringent with resolvent, desiccant and tonic (4, 7)	Not found
Pistachio	*Pistacia vera* (8)	Mastication of pistachio kernel (4, 7)	Hot and dry (4, 5)	Deobstruent (opener), desiccant, cleansing, resolvent (4, 7)	Anti-inflammatory, antinociceptive, analgesic (alpha-pinen) (26)
Betel nut	*Areca catechu* (8)	Fruit (4, 5)	Cool and dry (4, 5)	Astringent, opener, tonic, reduced temperature and inflammatory (4, 7)	Antioxidant, analgesic, anti-inflammatory, antifungal, antimicrobial (tannin) (27)
Cardamom	*Elettaria cardamomum* (8)	Seed (4, 5)	Hot and dry (4, 5)	Resolvent, diluting (fieriness), cool astringent (earthiness), condenser, desiccant, absorbent of humors (4, 7)	Analgesic, anti-inflammatory, immunomodulatory (28)
Taro	*Colocasia antiquorum* (8)	Sprinkling burnt powder for union (leaves and root) (4, 5)	Hot and wet (4, 5)	Astringent, maturative swelling, union of ulcers and aphthous (4, 7)	Antifungal, COX1,COX2 inhibitory, anti-inflammatory (29)
Common centaury	*Centaurium erythraea* (8)	Root decoction with rosewater (4)	Hot and dry in the third degree (4, 5)	Desiccant without irritation, opener and cleansing and absorbent (4, 7)	Anti-inflammatory, analgesic, xantin oxidase, antipyretic (30)
Catechu	*Acacia catechu* (8)	Gum (odoritus-megma) (4)	Cool and dry (4, 5)	Astringent, desiccant, styptic, restraint (4, 7)	Oral pathogen against, anti-inflammatory (cyclooxignase and lipo-oxigenase inhibitor) (31)
Camphor	*Cinnamomum camphora* (8)	Gurgling of solution of gum plus rosewater (4, 5)	Cool and dry (4, 5)	Desiccant of humors that causes aphthous with overriding rising heat toward mouth (4, 7)	Anti-inflammatory, antioxidant, immunomodulatory, PGE2 suppressor (32)
Cubebs	*Piper cubeba* (8)	Chewing of fruit (4, 5)	Hot and dry (4, 5)	Desiccant, cleansing and purified of oral ulcers and aphthous (4, 7)	Anti-inflammatory, analgesic (33)
Grape vine (resin)	*Vitis venifera* (8)	Resin (4)	Cool and dry (4, 5)	Humors-breakers (4, 7)	Not found
Borage	*Echium amoenum* (8)	Sprinkling burnt powder of flower and leaves (4, 5)	Fresh: hot and wet Dried: hot and dry (4, 7)	Alterative of mouth temperament, annihilator of mouth inflammatory and aphthous (4, 7)	Anti-inflammatory, analgesic, antioxidant (34)
Plantain	*Plantago magor* (8)	Rinsing of root decoction or leaves decoction or mastication of leaves (4, 5)	Cool and dry (4, 5)	Astringent and tonic, restraint, cleansing with resolvent and opener, hurdle of flowing of excretions (4, 7)	Antifungal and oral antimicrobial, analgesic, antinociceptive, (tannin) (35)
Lemon	*Citrus* sp. (8)	Juice of lemon (4)	Cool and dry (4, 5)	Astringent, resolvent of oral excretions because of hot (skin), cleansing(inner and sour part of it), attenuant viscose humors (4, 7)	Anti-inflammatory, analgesic (hesperidins), immunomodulatory (vit C, mast-cells), decrease of release of histamines (glycoside- flavanon) (36)
Myrrh	*Commiphora myrrha* (8)	Gum (4, 5)	Hot and dry (4, 5)	Desiccant of infectious humors, tonic, purified, cleansing, high resolvent (fired parts and airy parts), wound healing (4, 7)	Anti-inflammatory, analgesic (decreasing of PGE2), anti-oral inflammatory, antiseptic, antifungal, decreasing of buccal bleeding, reduce duration of aphthous (37)
Rose	*Rosa damascene* (8)	Sprinkling powder of dry flower (4, 5)	Combined strengths (4, 5)	Dry, astringent, desiccant because there is earthiness. Corruption the flowing of substances (4, 7)	Antibacterial, anti-inflammatory, analgesic, reduce of duration of aphthous, antinociceptive (15, 38)

Dryness causes desiccation and astringency (4, 5), and hotness causes maturation, dilution and resolvation (4, 5), while coldness causes organ strengthening (4, 5).

4. Conclusions

Based on the actions of these plants, and based on their temperaments and this protocol, these plants are divided into two categories:

1- Plants that cure RAU by desiccation and purification, and maturation and resolvation (4, 5).

2- Plants that cure RAU by astringency power and preventing of falling down the substances and will strengthen the organ (4, 5).

From the above, it is found that astringent herbs used to treat RAU are due to the presence of tannins, and therefore, they have immunomodulatory properties (39) and resolvants in ITM may be antioxidant and anti-inflammatory compounds, for example anthocyanin components. Although some of pharmacological effects cannot be matched to traditional effects, treatment of RAU can be justified by traditional effects.

Eventually the plants listed in Table 1 can be used as a prediction of RAU management. Of course, there is no evidence for curing RAU by some of these plants in allopathic medicine, and further investigations in this area could lead to the discovery of a new drug.

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Footnotes

Authors' Contribution: Omid Sadeghpour and Mohammad Reza Shamsardekani were supervisors and developed the original idea and the protocol. Shokouhsadat Hamedi researched and collected matters and wrote the manuscript. Dawood Hajighasemali helped with collection. Zohreh Feyzabadi helped in changing the references to endnote format.

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