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Original Research

Slippery elm, its biochemistry, and use as a complementary and alternative treatment for laryngeal irritation

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Abstract

Slippery elm is an herbal medicine derived from the inner bark of the slippery elm (Ulmusrubra - also known as Red Elm or Indian Elm) tree. It has been used to treat edema and inflammation as an alternative/complimentary form of medicine for many years. In the United States, slippery elm is marketed commercially to treat upper airway inflammatory conditions, and its reported benefits in treating these conditions are ubiquitous in anecdotal contexts. Individuals with voice disorders and other inflammatory conditions of the upper airway (e.g., laryngitis) are increasingly seeking information related to the use of herbal medications such as slippery elm, although most clinicians are unfamiliar with these medications and do not understand their biological actions and purported benefits. Furthermore, no scientific evidence is available to support the validity of slippery elm's use in treating upper airway inflammatory conditions. The purpose of this manuscript is to review the biochemical composition, biological actions, and purported societal use of slippery elm as a complementary or alternative medicine specific to upper airway inflammatory conditions, present results from a pilot study investigating the soothing effects of slippery elm on the tissue of the upper airway, and present a framework for potential scientific investigation of slippery elm and related herbal medications.

INTRODUCTION

For thousands of years, humans have utilized the medicinal properties of vegetation, or herbal medicines, to treat ailments. In this context, herbal medicines fall under contemporary classifications as a type of complementary (used along with conventional medical treatments) and/or alternative (used in place of conventional medical treatments) medicine [1]. Between 1990 and 1997, the use of these treatments among United States residents significantly increased to a level of approximately 629 million annual visits to practitioners of alternative medicine, which exceeded the number of annual visits of U.S. residents to primary care physicians [2]. By 2002, this number had stabilized, with the most common form of alternative medicine utilized being herbal medicines by over 38 million U.S. Adults [3].

One herbal medicine which has historic relevance to the treatment of laryngeal and pharyngeal (upper airway) conditions is slippery elm. Slippery elm is a substance produced from the ground and dried bark of the slippery elm tree, Ulmusrubra. It is considered a dietary supplement by the US Food and Drug Administration (FDA), and as such it is not regulated. However, the FDA has recognized slippery elm as a safe and effective oral demulcent. Historically, slippery elm has been used to treat irritation and inflammation in mucosa via application of a poultice, tincture, or tea [4].

According to the Natural Medicines Comprehensive Database, slippery elm is used for the treatment of coughs, sore throat, colic, diarrhea, constipation, hemorrhoids, irritable bowel syndrome (IBS), cystitis, urinary inflammation, urinary tract infections, syphilis, herpes, expelling tapeworms, protecting against stomach and duodenal ulcers, for colitis, diverticulitis, GI inflammation, and acidity [5]. It has been used to treat inflammatory conditions of mucous membranes, including as a component of recipes in traditional Oriental medicine and use as a poultice by Native Americans. In traditional Oriental medicine, elm bark has been used for edema, inflammation, and cancer [6]. Today, it can be found commercially in products marketed to treat throat irritation such as herbal teas and lozenges, but also in concentrated pill and liquid forms.

Table 1. Examples of anecdotally reported uses for slippery elm, specific to upper airway conditions.

Upper Airway Condition	Purported Action	Source Examples
Inflammation & Edema	Soothes inflammation, reduces swelling, heals damaged tissue	Van Wyk, B., & Wink, M. (2004) [8]
Mucosal Irritation	Relives soreness and irritation in mouth and throat tissues	Law, D. (1972) [9]
Singing Difficulty	Aid to singing voice by relieving dry or sore throat	Peirce, A. (1999) [10] Boon, H., & Smith, M. (2004) [12]
Laryngitis	Coats and soothes mucous membranes	Skidmore-Roth, L. (2005) [13]
Acid Reflux	Aids in the management of reflux symptoms	Vemulapalli, R. (2008) [14]

It is also used as a dietary supplement. It's reported anecdotal benefits are considerable and societal use ubiquitous, suggesting that society perceives this substance as beneficial for upper airway mucosal irritation and/or inflammatory conditions, even though scientific evidence supporting this belief is virtually non-existent. Table 1 illustrates some of the reported uses for slippery elm specific to upper airway complaints and conditions.

Products containing slippery elm are frequently championed by professional and non-professional voice users as beneficial for alleviating adverse throat sensations. Companies often market their products specifically to these populations, with well known examples including Thayer's Slippery Elm Throat Lozenges® and Throat Coat®. Clinical voice specialists including otolaryngologists and speech-language pathologists might occasionally be presented with patients who use and purport the benefits of these types of products. This is supported by a report in 1995 which indicated that 41% of a treatment seeking population at a major voice center made inquiries regarding the use of alternative treatments [7]. Information regarding the use of herbal medications as complimentary or alternative form of treatment is sparse in the communication disorders literature. In addition, few if any graduate programs offer courses which educate clinicians on this topic. As such, most practicing clinicians will be unfamiliar with a product such as slippery elm when its use is reported or questioned by a patient.

While the popularity and use of slippery elm among individuals who use alternative medicines is clear, there is no objective, empirical research available that investigates the effectiveness of this herb for reducing inflammation and/or soothing epithelial tissue. However, it would benefit health professionals to have at least an elementary understanding of this substance's chemical makeup, known biological actions, and recommended uses in order to (1) be able to understand why a patient might be utilizing it, and (2) to better counsel patients who question its application for their throat/voice condition. The purpose of this paper is to present this information by reviewing the biochemical composition, biological actions, and purported societal use of slippery elm as a complementary or alternative medicine specific to upper airway inflammatory conditions. In addition, results from a pilot study investigating the perceived soothing effects of slippery elm in a non-treatment seeking population are reported, along with a framework for potential scientific investigation of slippery elm and related herbal medications used for the treatment of voice or laryngeal conditions will be presented.

Chemical Composition and Biological Actions

The slippery elm tree is a member of the elm family, with a geographic distribution ranging along the eastern and central United States. Its name is derived from the viscous, slimy liquid created when the inner bark is chewed, which was common among Native Americans and early pioneers as a relief to dehydration and hunger. The inner bark is the only part of the tree known to be used for medicinal purposes, and the remainder of the tree has no significant commercial value. The inner bark is thin, tough, and flexible with a fibrous texture. The hue of the natural bark is a reddish-yellow or reddish-brown color, although when dried and in powder form (as is commonly used in medicinal applications) the color is grayish [9-15].

A number of early investigations have shed light on the biochemistry of slippery elm. The most abundant, and medicinally important, biochemical components of slippery elm are mucilage and tannins. Mucilage, which forms the bulk of chemical compounds in slippery elm, is composed of carbohydrates which, when added to water, swell to form a viscous, sticky substance [11]. Pharmacologically, viscous gel-like substances increase the retention time of polymers over mucosal surfaces and facilitates adhesion. This has the effect of coating mucous membranes and helping to ameliorate adverse sensations and the involuntary reflexes (e.g., coughing, throat clearing) triggered in response.

Mucous membranes are lined with mucus, a product of mucins and inorganic salts suspended in water. Mucins comprise a family of glycosylated proteins made up of oligosaccharide chains attached to a protein core. They contain a dense sugar coating providing substantial hygroscopic properties and increased resistance to enzymatic protein degradation [11]. Mucosal saliva contains a high molecular weight mucin capable of binding to the oral mucosal surface, an important mechanism for providing lubrication and maintenance of hydration [11]. The affinity of saliva and salivary mucin also contributes to host defense.

The bioadhesive nature of mucilage provides favorable properties for drug delivery when solute bioavailability is diminished by absorption or increased mucociliary clearance. The mucilage components of slippery elm are displayed in table 2. Mucilage constituents include monosaccharides (e.g.,hexose, pentose), methylpentose (a monosaccharide with an added methyl group) and uronic acids [16-17]. These compounds are structured as to prevent them from being dissolved, thus preserving their ability to retain water. As a result, powder preparations of slippery elm can be used as a demulcent (forms a film, or coating, over tissue) by mixing the preparation with water to form a thick gel, which can be applied to mucous membranes of the mouth and throat. Thus, indications of mucilage in medicine include palliative care and reducing discomfort from tissue irritation via emollient (soothing) and demulcent (coating) effects [18].

Table 2.Chemical composition of slippery elm.Information from Kemper (1999) [7], Anderson (1933) [15], and Hough, Jones, &Hirst (1950) [16].

Biochemical Component
Mucilage
Uronic acid (36%)
Pentose (6.5%)
Hexose
Methylpentose (rhamnose, galactose) (25%)
Other
Tannins
Oxalate acid
Flavanoids
Phytosterols
Salicyclic Acid
Capric Acid
Caprylic acid
Decanoic acid

Tannins are water soluble polyphenolic constituents capable of binding and precipitating proteins by way of hydroxyl and carboxyl moieties. Carboxyl groups contain a single carbon atom attached to an oxygen atom by double covalent bond and to a hydroxyl group by single covalent bond (e.g., -COOH). The binding and precipitation properties of tannins allow for them to bind with protein-rich structures of the skin such as collagen. Tannins have also been proposed to interact with the plasma glycoproteins fibronectin and fibrinogen [19]. Tannin phytochemicals possess potent astringent properties. In medicine, tannins have been used for the treatment of inflamed superficial skin diseases, and as a desiccant in the treatment of weeping skin inflammations such as shingles and acute eczema [19]. The mechanism of action is thought to be related to the cross-linking of structural proteins [19]. The precipitation of proteins and sealing of cell membranes reduces tissue exudate, allowing for dessication of the affected area and expedited healing. Contraction of the skin and wound closure is mechanistically important to prevent pathogen invasion. Thus, tannins exert antimicrobial properties via their ability to expedite tissue contraction. The fully closed wound prevents bacteria and other substances from entering the wound bed.

Tannins also display strong antioxidant activity and protection against reactive oxygen species. Several cellular processes, including lipid peroxidation, protein denaturation, carbohydrate and nucleic acid formation can be influenced by free radicals generated during oxidative stress. The accumulation of reaction oxygen species during oxidative stress can interrupt normal physiologic cellular processes. Phenolic compounds such as tannins are capable of inhibiting these processes [20]. For example, the phytochemical constituents of slippery elm have been shown to display antiradical and radical scavenging properties by inhibiting the formation of cytotoxic reactive species, such as peroxynitrite ($ONOO^{-}$) [21].

Tannin phytochemicals are found naturally in many foods, including wine, tea, and fruits, and are responsible for the taste of bitterness in these products. Witch hazel, derived from the plant of the same name, is a familiar medicinal product which contains many tannins, where it is used as an astringent for inflammatory skin conditions such as acne and eczema. Tannins comprise no more than 3% of the chemical composition of slippery elm, though their presence certainly could have a local effect on pharyngeal/laryngeal tissue if applied topically, such as with teas or lozenges.

Extracts from elm bark have been investigated scientifically with regards to the anti-inflammatory and anti-oxidant properties of this substance. It has been demonstrated that elm bark has systemic anti-inflammatory effects in the stomach and intestines of a porcine animal model [22]. Elm bark has also been shown to influence immune system activity through increased production of cytokines in a murine animal model [6]. The potential anti-inflammatory properties of slippery elm have definite relevance to voice and other upper airway inflammatory conditions. If it can be demonstrated that slippery elm is effective in reducing inflammation in the upper airway, these findings may have significant clinical value related to management options of these conditions.

METHODS OF DELIVERY AND DOSAGE

A review of the preferred delivery method and dosage level suggested by various herbal medicine texts and sources of information on the internet revealed a large degree of heterogeneity in both areas. Delivery methods fall into three categories: liquid preparations, lozenges and capsules. Liquid preparation forms of delivery are made by the production of a decoction (boiling the bark or bark derivative in water), tea (dried, ground bark steeped in hot liquid), or liquid extract [9-10, 12]. These may be swallowed directly and/or gargled. Formula content, directions, and additions of other herbal ingredients in these liquid preparations vary widely from source to source. Lozenges containing slippery elm are consumed similar to cough lozenges, with the herbal contents of the lozenge mixing with saliva and then swallowed. Slippery elm capsules are typically marketed towards the treatment of digestive ailments. These are taken orally and believed to soothe the lower gastrointestinal tract once the outer capsule is dissolved [10]. Oral capsules are marketed by some vendors as alleviating upper airway irritation, although no scientific evidence exists, and many questions remain, regarding the systemic effects of slippery elm in the upper airway after oral ingestion in pill form.

Various anecdotal “recipes” for teas and decoctions exist, available for viewing on the internet and in the numerous volumes of herbal medicine textbooks [9-13]. Because slippery elm is not a regulated substance, there are no official guidelines or recommendations for its use, and no empirical investigations for dosage effects on upper airway inflammatory conditions have been published. The University of Maryland publishes a Complementary and Alternative Medicine Index online whose dosage recommendations are consistent with many of the information sources identified. These include: (1) as a decoction, one part bark to eight parts water, (2) as a tea (infusion), 4 grams of powder steeped in 2 cups of water, and (3) as a capsule, 200mg-500mg three times a day [11]. While these levels are commonly identified as recommended amounts, a large degree of heterogeneity exists in dosage recommendations among vendors of slippery elm and sources of information for its use [9-13]. A review of vendor sources marketing slippery elm capsules on the internet found dose level ranges between 200mg-600mg per capsule, with varying recommendations for the number of doses per day. There are no reported side effects of slippery elm, and no known correlation exists between dose amount and the presence of adverse events from slippery elm ingestion. It has been reported that slippery elm has abortive effects, and its use by females who are pregnant is not recommended.

Pilot Study

Purpose: The purpose of the study was to determine if slippery elm effects a change in laryngeal/pharyngeal sensation of "soothing" compared to a control treatment when measured at one, five, and ten minutes after receiving treatment.

Design: Randomized control (single blind) treatment design with alternative treatment as the control. The study was approved by a university Institutional Review Board.

Participants: 24 graduate speech-language pathology students (22 females, 2 males) were recruited via a convenience sample and randomly allocated (based on order in which they volunteered, 12 participants in each group) to the treatment or control group. To be included in the study, it was required that participants reported no current pharyngeal or laryngeal complaints including irritation or soreness, upper respiratory infection, or voice problems. Due to the report of potential abortive effects of slippery elm, female participants were asked if they were currently pregnant, think they may be pregnant, or are planning to become pregnant, and if they indicated "yes" to either of those questions they were excluded from the study.

Procedures: Testing for each participant was completed in one day. After consent procedures, participants were seated in front of a desk, and served a warm 6*oz* beverage in an unlabeled white Styrofoam cup, so that they were blind to group. Participants were asked to consume the 6*oz* within 3 minutes. Participants received one of two possible warm liquid stimuli (liquid was boiled in a commercial electric kettle and allowed to sit for 45 seconds before pouring into cup), depending on their group allocation. Participants allocated to the experimental group received a tea consisting of water mixed with 2 tsp (3g) of pure slippery elm powder (Now Foods, Bloomingdale, IL). The slippery elm tea was flavored with 2 drops of orange flavoring (Frontier Natural Products Co-op, Norway, IA.). The orange flavoring contained organic orange oil and organic sunflower oil, and was used to flavor beverages in each group. Participants randomly allocated to the control group received a warm tea consisting of water steeped with Decaffeinated Lipton's orange pekoe tea (Unilever PLC, London, U.K.). This tea was also flavored with 2 drops of the orange flavoring.

Once all the beverage was consumed (confirmed by the PI looking into the cup), a timer was started. After 1, 5, and 10 minutes, each participant was asked to rate the degree to which pharyngeal sensations changed from baseline (prior to drinking beverage), if at all, in response to the following sentence & question: "**Tissue is soothed when the surface feels as if it were coated with something, such as a layer of protective covering. To what degree does your throat feel soothed compared to before you had a drink?**"

Participants responded to this prompt at each measurement interval using a 5-point equal appearing interval (EAI) where 0 corresponded to no change from baseline (before consuming beverage) and 4 corresponded to strong, very noticeable change. A total of 3 measurements from each participant were obtained (one measurement at each temporal interval – 1, 5, and 10 minutes).

Data Analysis: This study was comprised of two independent variables: group (slippery elm vs. control) and time (one, five, and ten minutes post consumption of beverage). As ordinal data was used to measure perceptions of "soothing", non-parametric statistics were applied to the data, including separate Friedman Anova's applied to the time data separately for each group and a Mann-Whitney U test comparing the effect of slippery elm vs. control across the three levels of time. Post-hoc testing, when appropriate, utilized Wilcoxen sign-ranked tests, and a Bonferonni correction (adjusting down from an initial value of 0.05) were used when statistical tests involved more than one comparison to protect against Type 1 error. All statistical calculations were obtained using SPSS Statistics ver. 19 (IBM).

Results: Means and standard deviations of perceived "soothing" ratings are reported in Table 3. At each measurement time, the slippery elm group rated perceptions of "soothing" greater than those of the control group. These ratings were highest for both groups at the 1-minute interval (slippery elm = 2.17; control = 1.75) compared to the later time intervals, which appeared to decrease proportionally.

Table 3. Means and standard deviations (sd) of perceptual ratings of "soothing" in groups receiving slippery elm and the control tea in the three different levels of time.

Group	Time	Mean	SD
Slippery Elm	1-minute	2.17	1.12
	5- minute	1.75	0.86
	10-minute	1.42	1.24
Control	1-minute	1.75	1.22
	5- minute	1.42	1.08
	10-minute	1.17	1.19

To investigate an effect of measurement time on perceptions of "soothing" separately for each group, Friedman Anova's were applied to the data. Results indicated a significant effect of time in the measures of the slippery elm group (F_r =9.941;

p = 0.007) but not the control group (F_r = 7.280; p > 0.025) when alpha level was adjusted to 0.025 using the Bonferonni correction. Post-hoc tests on the three levels of time for the slippery elm data utilized a Wilcoxon sign-rank test with alpha level adjusted using the Bonferonni correction. Results revealed a significant difference between ratings of soothing measured at one and ten minutes (z = -2.714; p = 0.007), but not the remaining two time comparisons.

Data from Table 3 were applied to statistical testing as a function of group. To investigate the effect of slippery elm vs. control on perceived "soothing" separate Mann-Whitney U tests were applied to the group data at each measurement time interval, with alpha level adjusted down appropriately using the Bonferonni correction. Results revealed no difference between perceived "soothing" at either the one minute (U = 59.0; p > 0.017), five minute (U = 53.5; p > 0.017), or ten minute (U = 62.5; p > 0.017) measurement intervals.

Discussion and Framework for Future Scientific Investigation

The use of alternative and complimentary medicines in the United States is widespread [2]. Treatment-seeking populations with voice problems frequently request information from clinicians regarding the use of these substances, and also report their current use in managing symptoms associated with upper airway complaints [7]. Nevertheless, clinical training programs typically do not incorporate education in alternative medical treatments as part of the curriculum, and the scientifically-validated evidence for their use in upper airway conditions which affect the pharynx and larynx is non-existent. It would benefit clinicians to be aware of the different alternative and complementary substances that might be used by a specific treatment-seeking population (e.g., those with voice disorders) and their scientifically validated effectiveness, as speech-language pathologists are increasingly being asked for information relative to their use in treating related conditions.

The results of the pilot study presented in this manuscript revealed a significant influence of slippery elm on ratings of laryngeal/pharyngeal "soothing" when measured at one minute after treatment compared to ten minutes. There was also a trend for ratings of "soothing" to be greater in participants consuming slippery elm compared to those consuming Lipton tea at each measurement interval, although the difference did not reach the level of statistical significance. A number of factors limited the power of the current study, most notably sample size, which should be addressed in future research focused on measuring clinical outcomes of alternative medicine application in voice and laryngeal conditions. Although the descriptive statistics showed ratings of "soothing" in the slippery elm group being greater at each measurement interval, it is likely that statistical power was not large enough to detect a difference it if actually existed. The definition we used to guide the perceptual rating process may also have influenced outcomes and should be addressed in future research. A framework for building an evidence-based line of research to acquire greater knowledge in this area is presented below.

Clinical outcome research is warranted with regards to the effects of herbal alternative/complimentary medicines in the treatment of voice disorders and upper airway inflammatory conditions. An emphasis in clinical decision making based on evidence-based information from clinical research has been on the upsurge for decades, supporting the need for studies that investigate the effectiveness of slippery elm and other herbal medications in the treatment of laryngeal & pharyngeal inflammatory conditions. These clinically-oriented investigations should be planned with the strictest possible scientific standards, as studies designed to eliminate bias (as much as possible) are more likely to influence clinical practice [23]. In addition to methodological rigor, it is suggested that these investigations should follow a phased process (e.g., initial small scale exploratory studies leading to larger randomized controlled trials) designed to identify (1) the activity induced by a treatment and (2) the subsequent treatment effect and efficacy [23].

Phased clinical research is typically initiated as small scale pre-clinical studies designed to assess treatment activity/effect in laboratory models or exploratory studies designed to measure activity/effect in a defined population. This initial phase to clinical outcome research is the model used by numerous private and public health-related organizations, including the National Institutes of Health in the U.S. As scientifically validated treatment activity and effect are unknown for the use of slippery elm in treating upper airway inflammatory conditions, it is recommended that future programmatic research investigating this topic begin as initial phase exploratory designs. Such designs could include investigations of the cellular and molecular activity induced by slippery elm in upper airway tissue (e.g., pharyngeal or laryngeal tissue) in animal models, and/or identification of a possible soothing effect of slippery elm in normal control populations.

Slippery elm is used as an emollient, demulcent, or anti-inflammatory. The basic perceived effect of an emollient or demulcent is to soothe irritated tissue, although with a demulcent the perceived outcome is due to a surface coating of protective mucilage while the perceived outcome of an emollient is due to an increase in tissue surface hydration (e.g., it moisturizes). The deposition of mucilage on the surface of tissue and the hydration levels of tissue can be measured via laboratory procedures. These measurements can elucidate the chemical activity induced by treatment (e.g., changes within the tissue which occur at a cellular and molecular level). However, to measure the treatment effect (the degree of benefit to an individual) of an emollient or demulcent, subjective measures must be utilized as any changes in the degree of "soothing" induced by a treatment is an obligatory perceptual experience which cannot be measured with objective means. Thus, studies investigating the soothing effect of slippery elm and/or other herbal medications should include some perceptual scale or measurement designed to assess this self-perceived factor.Inflammation is a chemical reaction of tissue due to some irritant or damage. Inflammatory responses can result in perceptual experiences (e.g., pain in a sore throat), but the process underlying inflammation occurs within the affected tissue, due to changes in cellular and molecular activity. The activity that is the inflammatory response can be objectively measured, as can the change in this activity secondary to some medical treatment. This means that the changes in chemical activity that occur in an inflammatory process relate directly to the effects of an anti-inflammatory medication given to treat it. This differs from the relationship between the activity induced by an emollient or demulcent and the indirect perceptual experience of "soothing". As such, anti-inflammatory effects of medicines can be quantified objectively, without relying on perceptual judgments. If the purported effects of slippery elm are to soothe and reduce inflammation, clinical research focusing on the effectiveness of this herb should take into account the perceptual response to its administration (in its capacity to soothe tissue) as well as changes in the activity within tissue at the cellular and molecular level (in its capacity to reduce inflammation), the latter of which can be assessed via histochemical methods in animal models.

SUMMARY

Herbal alternative/complimentary medications are being used by and are of interest to populations with upper airway inflammatory conditions which affect voice production and/or adverse sensations in the throat. The anecdotally reported benefits of slippery elm use in treating these conditions are ubiquitous. However, no scientific evidence exists to support these claims. There is evidence which supports anti-inflammatory effects of elm bark in the lower digestive tract. Research is needed to investigate the validity of slippery elm's use in managing upper airway inflammatory conditions. Results from a small pilot study revealed trends of perceived "soothing" being rated greater by those receiving slippery elm compared to a control substance, although the effect did not reach statistical significance. It is recommended that initial exploratory pre-clinical or phase 1 trials be implemented to study the perceptual soothing effects related to the emollient and demulcent properties of slippery elm, and the cellular and molecular activity related to the anti-inflammatory properties of this herb. If the benefits of slippery elm are scientifically validated, these findings could have a significant impact on clinical decision making and management options.

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REFERENCES

1. What Is Complementary and Alternative Medicine? In: National Center for Complementary and Alternative Medicine Available via http://nccam.nih.gov/health/whatiscam (Accessed 12 March 2012).

2. Eisenberg DM, Davis RB, Ettner SL, Appel S, Wilkey S, Van Rompay M, Kessler R. Trends in alternative medicine use in the United States.JAMA 1998; 280: 1569-75.

3. Tindle HA, Davis RB, Phillips RS, Eisenberg DM. Trends in use of complementary and alternative medicine by US adults. AlternTher Health Med 2005; 11: 42-49.

4. Kemper KJ. Slippery elm (Ulmusrubra or U. fulva). In: The Longwood Herbal Task Center for Holistic Pediatric Education and Research Force Available via http://www.longwoodherbal.org/slipperyelm/slipperyelm.pdf (Accessed 4 April 2012).

5. Jellin JM, Gregory P, Batz F, Hitchen K, Burson S, Shaver K, Palacioz K (eds). Natural Medicines Comprehensive Database. Therapeutic Research, Stockton, 2000.

6. Yousuk L, Hyunjin P, Ryu H, Chun M, Kang S, Kim HS. Effects of elm bark (Ulmusdavidiana var. japonica) extracts on the modulation of immunocompetence in mice. Journal of Medicinal Food, 2007: 10:118-125.

7. D'Antoni ML, Harvey PL, Fried MP. Alternative medicine: Does it play a role in the management of voice disorders? J Voice 1995; 9: 308-311.

8. Van Wyk, B., &Wink, M. Medicinal Plants of the World. Timber Press, Portland, Timber Press, pp. 329-430, 2004.

9. Law, D. The Concise Herbal Encyclopedia.St. Martin's Press, New York, pp. 220-238, 1972.

10. Peirce, A. The American Pharmaceutical Association: Practical guide to natural medicines. Stonesong Press, New York, pp/601-602, 1999.

11. University of Maryland. (2002). Slippery Elm. Complementary and Alternative Medicine Index (CAM). Retrieved October 5, 2007, from http://www.umm.edu/altmed/articles/slippery-elm-000274.htm

11. The Columbia Encyclopedia. 6th ed., Columbia University Press, New York, 2005.

12. Boon, H., & Smith, M. The complete natural medicine guide to the 50 most common medicinal herbs. Robert Rose, Toronto, 2004.

13. Skidmore-Roth, L. Mosby's Handbook of Herbs & Natural Supplements. 2nd ed., Mosby Elsevier, St. Louis, 2005.

14. Vemulapalli, R. Diet and lifestyle modifications in the management of gastroesophageal reflux disease. NutrClinPract 2008; 23: 293-298

15. Sudhakar Y, Kuotsu K, Bandyopadhyay AK. Buccalbioadhesive drug delivery--a promising option for orally less efficient drugs. J Control Release 2006; 114: 15-40.

16. Anderson E. The mucilage from slippery elm bark.J BiolChem 1933; 104:163-170.

17. Hough L, Jones J, Hirst E. Chemical constitution of slippery elm mucilage: Isolation of 3-methyl d-galactose from the hyrodolysis products. Nature 1950; 165:34-35.

18. Boon H, Smith M. 50 Most Common Medicinal Herbs. Robert Rose, Toronto, 2004.

19. Folster-Holst R, Latussek E. Synthetic tannins in dermatology--a therapeutic option in a variety of pediatric dermatoses. *PediatrDermatol* 2007; 24: 296-301.

20. Blokhina O, Virolainen E, Fagerstedt KV. Antioxidants,

oxidative damage and oxygen deprivation stress: a review. *Ann Bot (Lond)* 2003; 91: 179-194.

21. Choi HR, Choi JS, Han YN, Bae SJ, Chung HY. Peroxynitrite scavenging activity of herb extracts. *Phytother Res* 2002; 16: 364-367.

22. Cho SK, Lee SG, Kim CJ. Anti-inflammatory and analgesic activities of water extract of root bark ofUlmusparvifolia. Kor J Pharmacognosy 1996; 27: 274–281.

23. Robey, R. & Schultz, M. A model for conducting clinical-outcome research: an adaptation of the standard protocol for use in aphasiology. Aphasiology 1998; 12: 787-810.