

## Effectiveness of Herbal Tinctures Formulated into Lozenges: A Current Stipulation in Pediatric Patients

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### Abstract

In the current scenario, herbal drugs have taken a jump up due to herbal ingredients (*Withania Somnifera*, *Azadirachta Indica*, and *Ocimum Sanctum*) having fewer side effects with high pharmacological action. Ingredients are chosen which are compatible with each other and have common target sites. Gastrointestinal and ingestion are the most common disorder which is followed by diabetes and these disorders risk weak immune systems and later cause bacterial and fungal infections, as these herbs have common antidiabetic, anti-inflammatory, and antimicrobial effects. At present, lozenges of these ingredients are not formulated till now for Pediatric patients in the market. As polyherbal lozenges ensure that all the phytochemicals give maximum therapeutic effect and provide broad-spectrum relief. Lozenges allow the medication to stay in a body for a longer period and increase the retention time of the drug which leads to an increase in the bioavailability of the active compounds present in the herbs. Multiple issues will be targeted with this combination therapy with single-dose intake. The focus of this study is on ayurvedic herbs which provide maximum pharmacological effect and can treat many diseases with a single dose with the demand of pediatric health psychology toward a developing attractive dosage form.

**Keywords:** Polyherbal lozenges, Antidiabetic, Anti-inflammatory, Antimicrobial effect, Pediatric health Psychology.

### Introduction

Medicinal conventional Indian ayurvedic system of medicine is meant for curing diseases and also preventing the occurrence of illnesses. Ayurveda provides a plethora of information on ethnic oral teaching practices and traditional aspects of therapeutically important medicines. It is based on the credence which justifies that health and wellness depend on a fragile balance between the mind, body, and spirit. The goal of Ayurveda is to develop good health and protect the health of the healthy and alleviate disorders in the diseased person. Herbal products are produced to maintain good health and to treat disease. (Mukherjee PK et al., 2017). Kapha, Vata, and pita are ayurvedic doshas. The Vata dosh symbolizes air and space elements. Pita dosh symbolizes the fire element. Kapha dosh symbolizes water and earth elements. Herbal products are specifically for internal and outer use as they have the least amount of side effects and are safer to use. Herbal medicine is a form of complementary medicine as a source of easily available effective therapy for diseases to the people. Medicinal plants are employed as a remedy for several diseases due to microbial infections. Herbal plants improve the stability and solubility of the dosage form. The traditional medicinal practice has employed medicinal plants as curatives for several diseases and microbial infections.

Ashwagandha, Neem, and Tulsi have been selected because of their uniqueness, they serve as multipurpose medicinal components and have common properties. The combination of these three herbs will enhance the property of the serving medicine. (Wilson rina et al., 2002).

*Withania somnifera* which is commonly known as ashwagandha and Indian ginseng belong to the family, Solanaceae (Singh N et al., 2011). The active constituents present in ashwagandha are steroidal lactones withaferin-A, withanone, alkaloids such as isopelletierine, cuseohygrine, anaferine, anahygrine, saponins, sitoindosides, and acylsteryl glucosides. (Yadav Shobhnath, et al., 2014). Ashwagandha is used to increase energy, improve overall health, reduce inflammation, Stress, anxiety, fatigue, pain, skin conditions, diabetes, arthritis, epilepsy increase energy, improve overall health, reduce inflammation, Stress, anxiety, fatigue, pain, skin conditions, diabetes, arthritis, epilepsy in Ayurvedic medicine (Singh Narendra, et al., 2011).

*Azadirachta indica* known as neem belongs to the family, Meliaceae (Singh N et al., 2013) and the active chemical constituents are azadirachtins, nimbinolin, gedunin, Nimbin, salannin, nimbidin, nimbidol, sodium nomainate, and quercetin responsible in the treatment of leprosy, diabetes, eye disorders, gingivitis, fever, intestinal worms, skin ulcers, diseases of the heart and blood, loss of appetite and liver problems (Jose Francisco Islas et al., 2020 & Mohammad A. Alzohairy et al., 2016). *Ocimum sanctum*, known as holy basil or Tulsi, belongs to the family, Lamiaceae. Its leaves and roots are used in various medicinal solutions to heal the body and mind. (Gowthami.R, Sharma, et al., 2021). The chemical constituents present in tulsi are linalool,  $\beta$ -caryophyllene, carvacrol, oleanolic acid, eugenol, ursolic acid, and rosmarinic acid. (Felix bast et al., 2014). Tulsi is a Natural Immunity Booster, Reduces Fever, Pain, and Blood Pressure to lower glucose levels in Diabetes patients. (Verma S. et al., 2016). There are different types of the dosage form of Ashwagandha, Neem, and Tulsi which is present in the market as shown in given Table 1. (Gupta SK et al., 2002).

**Table 1: Marketed dosage form of natural herbs**

Herb	Type of dosage form	Application
Ashwagandha	Caplets, Gumies, Capsules, Powders.	Stress, anxiety, fatigue, pain, skin conditions, diabetes, epilepsy.

Neem	Powders, Capsules, Oils, Tablet,	leprosy, eye disorders, bloody nose, stomach upset, loss of appetite, skin ulcers, fever, diabetes, gum disease, liver problems
Tulsi	Tablets, Capsules, Powders, Drops.	Supporting, liver health, fighting cancer, reducing high blood sugar levels, boosting mental health, reduce inflammation and swelling.

### Antimicrobial activity of Ashwagandha, Neem, and Tulsi

The extracts of the stem, leaf, and roots of *Withania somnifera* and *calotropis procera* were evaluated for the presence of phytochemical constituents and their antimicrobial activity. (Velu. S et al., 2012). The phytochemical analysis shows the presence of secondary metabolites such as alkaloids, glycosides, flavonoids, saponins, tannins, steroids, and anthraquinone revealing that chloroform extracts show a high no. of secondary metabolites. (Ugwu Celestina et al., 2019). Ethanol shows average extracted secondary metabolites. (Devmurari V. P et al., 2010). Thus, the preliminary screening analysis is useful in the direction of bioactive components in the discovery and development of the latest drug. (Autade, R.H et al., 2015 & Benbelaid F et al., 2013). *Withania* leaf and *Withania* root extract show inhibitory effects against multi-drug resistant strains *Pseudomonas aeruginosa*, *Salmonella typhi*, *Bacillus thuringiensis*, *Bacillus anthracis*, *Aspergillus fumigatus*, *Cryptococcus neoformans*, *Candida albicans*, and *Blastomyces dermatitidis* and average effects against *Chlamydia pneumoniae* (bacterial cell). (Devmurari V. P. et al., 2010). In the Neem plant, the presence of alkaloids, tannins, volatile oils, terpenoids, and glycosides was scrutinized by water and ethanol extract. (Kumar Vipul et al., 2011). The leaf extract at all the concentrations exhibited strong antimicrobial activity against bacteria and ethanol extract of the neem plant had a noticeable effect on the test organisms. (Alzohairy MA. et al., 2016). The leaf extract of *O. Sanctum* shows antimicrobial activity against *Escherichia coli* and *Staphylococcus aureus* and minimum inhibitory concentration was more effective against *Escherichia coli*. (Krishnan Y et al 2015 & Yamani, H. A., et al., 2016). The herbal products of Tulsi, ashwagandha, and neem available in the market are shown in Table 2.

**Table 2: Marketed herbal products of Tulsi, Ashwagandha, and Neem**

Tulsi products	Ashwagandha products	Neem products
Jolly Tulsi 51 drops	Sri Sri tattva ashwagandha tablet.	Morpheme remedies organic neem cold and pressed oil
Nature's velvet tulsi pure extract 500mg capsule	Dabur ashwagandha lehya.	Apex neem leaves powder
Sri Sri tattva tulsi arka	Organic ashwagandha capsule. India	Unjha neem tail
Dabur honitus adalsa cough syrup	Baidyanath ashwagandharishta.	Jiva neem tablet
Charak extramune tablet	Dabur ashwagandha churna.	Baidyanath ayurvedant neem tablet
Kudos tulsi gold green tea	Dr. morepen ashwagandha softgel.	Hapdco clodent neem dental cream

### The effective delivery system of natural medicine by lozenges dosage form

Lozenges are preparations that are solid and contain multiple ingredients. They are medicated and increase the retention time of drugs. (Allen LV et al., 2001). They are soft and hard formulations and are considered a novel method for delivering a drug into the human body. Some beneficial aspect is that they disintegrate haltingly in the mouth and this leads to their increased bioavailability as they maintain a consistent level of drug. (Chandrashekar J. Patil et al., 2019).

Lozenges are formed for patients who cannot swallow due to several reasons. They are also called troches and are of two types compressed and molded. Lozenges are acquired for local and systematic therapy. (Trofimiuk et al., 2019). Lozenges are tablets that are prepared by different methods like cutting, moulding, and compression. The purpose of formulating lozenges is that they dissolve very slowly in the mouth and medicate the throat for a long period. (Stephen O. Majekodunmi. et al., 2015). The excepted time of dissolving the lozenges in the mouth lies between 10 to 15 minutes. Lozenges are referred to as "medicated lozenges" as they carry an antimicrobial agent or an anesthetic that produces a local effect on the mouth. (Pundir Suchrita et al., 2014 & Avalaskar A et al., 2019).

There are mainly two types of herbal lozenges which are medicated lozenges and non-medicated lozenges as shown in given Figure 1. (Surbhi choursiya et al., 2020).

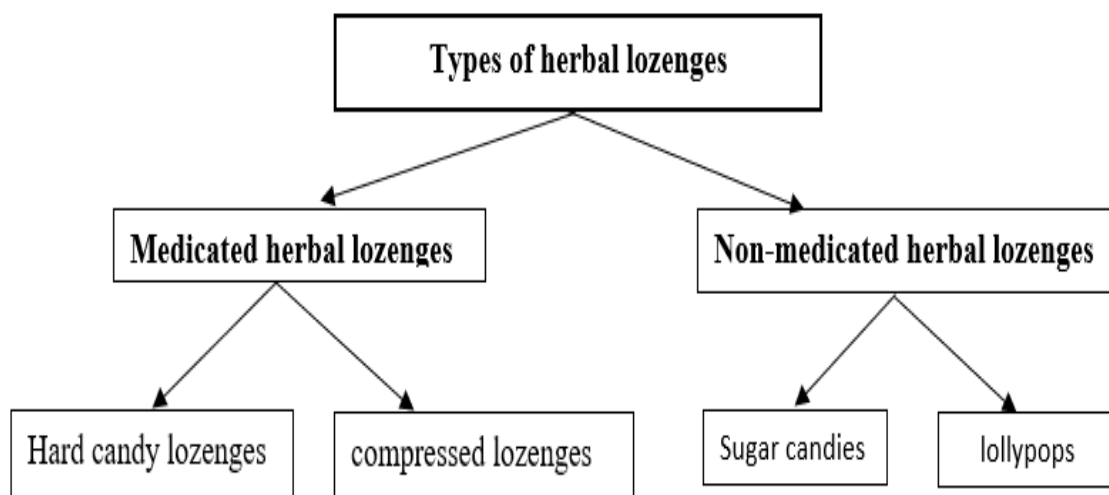


Figure 1: Types of herbal lozenges

### Polyherbal lozenges

Polyherbal lozenges are medicated lozenges that contain more than one herb to give the maximum therapeutic effect of the dosage form. The lozenges provide a convenient, affordable, and ready-to-use delivery system that allows the drug to remain in a body for a long period. (Rehman, Hina et al., 2011 & Pundir Suchrita et al., 2016).

Lozenges increase the bioavailability of the active ingredient present in the drug. Herbal drugs are used in several ayurvedic preparations like powder, syrup, tablet, syrup, or decoction for the treatment of several diseases, a new and innovative way of drug delivery is lozenges which are beneficial over other medicated formulations. (Choursiya, S. et al., 2019). Lozenges are medicated and flavored dosage form which is held in the mouth for giving their therapeutic effect on the pharynx. (Chandrashekhar J. Patil et al., 2019).

The benefit of lozenges is the retention time of the dosage form is increased in the cavity of the mouth which increases bioavailability and reduces gastric irritation. (Singh N et al., 2011). They avoid first-pass metabolism and increase in bioavailability which is used for purpose of both local and systemic effects. (Jose Francisco Islas et al., 2020). They gave better patient compliance is often given to those patients who have difficulty swallowing. Some polyherbal lozenges available in the market are shown in table 3.

The common applications of ashwagandha, Tulsi, and neem are they lower the blood glucose level in the body in diabetic patients, help in cold and cough, are used in inflammation, boost immunity, lower blood pressure, and also have antimicrobial action. Diabetes is a condition that results from insulin deficiency in the body or malfunction. (Bast, Felix, et al., 2014).

As herbal medicines have no or very least side effects and high pharmacological effects if taken appropriately, they treat diabetes too. (Modak M et al., 2007). The blood glucose level decrease by taking these herbs due to the ability of these herbs to improve the performance of pancreatic tissues by increasing the insulin secretions and by reducing the intestinal absorption of glucose. (Dey L et al., 2002)

In a previous study, the antidiabetic effect of these herbs was observed, according to that, the leaf extract and seed oil of neem were administered for 4 weeks in alloxan diabetic rabbits. (Yikna BB et al., 2021). The blood glucose level was reduced and neem extract helped in preventing and delaying the onset of diabetes. This extract also shows a similar effect to the antidiabetic drug glibenclamide. (Kooti W et al., 2016).

It was also observed that single-dose administration of aqueous extract of bark and root (250mg/kg) can reduce urea (13%), triglycerides (32%), cholesterol (15%), glucose (18%), lipids (15%), and creatinine (23%) in diabetic rats for 24 hours. (Khosla P et al., 2000).

Tulsi leaves are also found to treat diabetes when 2gr/kg leaf was consumed for 30 days in the group of albino rabbits and there was a sharp reduction in the blood glucose level of antioxidant enzyme, glutathione increased and lipid peroxidation decreased by consuming this leaf. (Kooti, Wet al., 2016). The ethanolic extract of tulsi leaves causes a reduction in blood glucose levels in normal and alloxan-induced diabetic rats.

These herbs also have anti-inflammatory action. Inflammation is reduced when the active constituents of the herbs show their effect, cells that induce pro-inflammation (Kashif, M., Hwang, Y., et al., 2019). change their phenotype which leads to the blocking of the release of pro-inflammatory mediators while releasing anti-inflammatory mediators, and blocks the neuron's chronic electrical activity. (Sethi J, Sood S & Seth S et al., 2004).

The antimicrobial effect is also shown by these herbs, they relieve pain, reduce fever, and protect from microbial infection caused by environmental conditions and hygiene. (Vats V et al., 2002). Antimicrobial herbs act against bacteria and viruses. (Salehi, B. et al., 2019). They prevent the human body from infectious diseases. The biomaterials act as a scavenger and block the production of ROS so that it doesn't cause any toxic effect (A. Nirmala et al., 2018, Remenapp, K et al., 2022 & Antosh Kumar et al., 2022).

**Table 3: Marketed Polyherbal lozenges**

Type	Ingredient	Effect produced	Applications	References
Garlic and ginger lozenges	Sucrose, sodium chloride, polyvinylpyrrolidone, NaCMC	Taste masking good release matrix lozenges	Inhibitory activity against non-resistant C. Albicans infection, non-resistant oral thrush	Charles O. Esimone 2010
Liquorice and catechu lozenges	Galen IQ 990, liquid glucose, liquorice powder extract, black catechu powder extract	Combination of both drugs produced synergistic effect	Recurrent aphthous stomatitis	Kasha D., 2016
Polyherbal extract based links lozenges	Adhatodavasica, glycyrrhiza labra, piper longum, viola odorata, hyssopusofficinalis, cordialatifolia, Alpinia galanga	The suitable dosage form for symptomatic relief	Sore throat and cough	Hina R., 2017
Eucalyptus oil and coleus aromatics oil lozenges	Magnesium stearate, lactose, mannitol, gelatine, sucrose	Inhibitory activity against non-resistanceC. Albicans infection	Antimicrobial activity	Binu A., 2018

### Psychology of Pediatric patients toward the attractive dosage form

According to the psychology of pediatric patients, the traditional form of medication such as tablets (Gopale, O. et al., 2022), capsules and oral liquids are difficult and unsuitable for children due to swallowing conditions that lead to vomiting and nausea situation (Carisa Parrish et al., 2020). To overcome these problems of traditional dosage form, the most attractive dosage form is in demand for new approach development has been promoting nowadays to attract the pediatric patients and also for their convenience with focusing on their behavior, developing process and finally psychological demand of children and their families in the health care system. Lozenges are attractive dosage form and more convenient as per pediatric psychology deliberated for the gulpy holding in the buccal cavity and also provided easy to use for administration by pediatric patients. (Duryodhan et al., 2015) They are more preferable to children as per their variety of availability is to be formulated in different types such as hard, soft, chewable, compressed tablet, candies, and lollypop types of lozenges are intended to treat local irritation or infection of the mouth and also used for the systemic delivery system with one or more medicaments, some of the ingredients enlisted in table 4 (Pattanayak et al., 2012).

**Table 4: Ingredients use for the Preparation of Medicated Lozenges:**

S. No.	Ingredients Name	Examples	Role
1.	Sugar	Dextrose, sucrose, maltose, lactose etc.	Use as a sweetening agent and for sweet taste
2.	Binder	Acacia, corn syrup, sugar syrup, gelatin, tragacanth	Use to hold the particle
3.	Lubricants	Magnesium stearate, calcium stearate, vegetable oil, fat oil.	Use to avoid sticking and chipping.
4.	Colorant	Water-soluble dye, orange color past, red color cube.	Use for the appearance of color in lozenges
5.	Acidulants	Citric acid, tartaric acid, fumaric	Use to strengthen the flavor profile

		acid	
6.	Flavoring agents	Methanol, spearmint, cherry flavor	Use to give the flavor and taste.

### Pediatric Health Psychology

Lozenges which are under the solid dosage form help for the various preparation and are easy to dissolve as well as disintegrate slowly into the mouth. However, in the case of the pediatric patient, it is easy to administer and put in between cheeks and gum which results in the drug absorption starting due to the dissolution and disintegration of the drug it increases its uncontrollable swallowing and that may lead to unexpected changes in the pharmacokinetics of the drug. (Buckley, L.A.; et al., 2018).

On the other hand, pediatric psychology is the combination of various medical disciplinary fields such as child behavior, child development and growth, child emotions, and psychological needs. Whereas medical practitioners, scientist, and pediatric psychologist plays an important role to support the healthcare needs of children and their families. (Stancin, T., & Perrin, E. C. et al., 2014). They provide various services which include the proper screening related to their quality of life, assessment, interventions, and consult with the various medical fields of hospitals to ensure the absence of disease in a well-being manner. (WHO et al., 2019)

### Future prospective and conclusion

As discussed above, Ashwagandha, Tulsi and Neem herbs exhibit the common applications of lowering blood glucose levels, anti-inflammatory action, antimicrobial effect, and polyherbal lozenges are unique formulations with low harmful effects. A previous study shows that these three have antidiabetic action which was experimented on rats. The combination of these herbs is not formulated yet when these herbs are formulated into a single dosage form like lozenges they will provide several health benefits, treat many diseases, useful for diabetic patients, and relieve patients from inflammation and infection. Herbal lozenges are attractive and easy to use for Pediatric patients without any harmful effects on children in a single dosage form.

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