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PREPARATION AND STANDARDIZATION OF NUTRACEUTICAL LOZENGES

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ABSTRACT

Nutraceuticals are food or part of food that provides health benefits including the prevention and/or treatment of a disease. This treats heart failure, cancer, hypertension and diabetis. The nutraceutical lozenges contain Antioxidants, Polyunsaturated fatty acids, Prebiotics, Probiotics, Omega-3-fatty acids and Dietary fibres. Nutraceutical lozenges are solid dosage forms provided the drug as well as absorbed through the buccal linings or when it is swallowed these medicated dosage form intended to be sucked and held in mouth or pharynx. Standardization of formulations is essential in order to assess the quality based on the concentration of their active principles. The present research work on standardization of Nutraceutical lozenges is used to sore throat. In this herbal formulation consists of *Zingiber officinalis, Glycyrrhiza glabra, Coriandrum sativum, Apis mellifera, Citrus limonsis, Ocimum sanctum*, *Curcuma Longa, Piper Nigrum,* The lozenges is one of the best remedy for sore throat etc. The quality of herbal formulations is assessing their acceptability in modern system of medicine against various throat diseases. In this study organoleptic, ash, extractive values, phytochemical screening, and physical characteristics like determination of Weight variation test, Friability test, Hardness test, *In vitro* mouth Dissolving Time, Drug Content.

KEYWORDS: Nutraceutical, Antioxidants, Lozenges , *Apis mellifera,* Drug Content, etc.

INTRODUCTION

Nutraceuticals are the chemical substances which can be considered as the food or its part, in addition to its nutritional value provides health benefits including prevention of disease or promotion of health. The major diseases for the prevention or treatment of which nutraceuticals have been associated are heart failure, cancer, hypertension and diabetis. The other diseases which related with role of nutraceuticals are osteoporosis, arthritis and neural tube defects.[1] The explosive demand growth for bioactive ingredients for nutraceuticals and functional foods is being driven by frequently cited health concerns: Cardiovascular disease, Breast, skin, colorectal, and brain cancers, Female health concerns, CNS disorders, Metabolism management, Gastrointestinal disorders and Immuno modulation.[2]

The quality of life in terms of income, spending and lifestyle has improved with economic development. However, it has also thrown up a major challenge in the form of `lifestyle diseases'. The first thing of this lifestyle change has been food habits. Consumption of junk food has increased manifold, which has led to a number of diseases related to nutritional deficiencies. Nutraceuticals can play an important role in controlling them. No wonder more and more people are turning to nutraceuticals.[3]

Increasing awareness levels about fitness and health, spurred by media coverage are prompting the majority of people to lead healthier lifestyles, exercise more, and eat healthy. The expanding nutraceutical market indicates that end users are seeking minimally processed food with extra nutritional benefits and organoleptic value. This development, in turn, is propelling expansion in the nutraceutical markets globally. The emerging nutraceuticals industry seems destined to occupy the landscape in the new millennium. Its tremendous growth has implications for the food, pharmaceutical, healthcare, and agricultural industries.[4]

Nutraceutical lozenges also possess nutritional value; this preparation can be considered as an alternative, cost effective, safer and potential medicine to treat many diseases. Due to the increasing popularity with health-conscious consumers, functional food science is becoming popular and creating new interest in marketing the products. It is hoped that serve to develop cost effective, safer and potential preparation for various chronic and sub chronic diseases. Designing a proper

food to maintain proper health has gained recognition and acceptance worldwide. Due to this, the food industry in many countries is modifying their products as responsible for consumer goods. The nutraceutical lozenges contain Antioxidants, Polyunsaturated fatty acids, Prebiotics probiotics, Omega-3-fatty acids and Dietary fibres.[5]

Antioxidant nutraceuticals contain vit-C, E, A and carotene. They are present in some fixed oils, fruits, vegetables, and fishes. Antioxidants present in such food materials which prevent the formation of free radicals or scavenging activity. Some of the naturally antioxidants are which c transferin, lactoferin, glutathione, carotenoids and their plant pigments. The oxidation of LDL cholesterol increases the chance of atherosclerosis, Tocopherols reduce platlet role in thrombous formation, Various plants like amla, myrobalan, lemon, prevent oxidation and scavenging of oxygen free radicals. Beta carotene and vit-A shown antioxidant effect.[6]

Polyunsaturared fatty acid**s** are present in various vegetable oils and marine animals. These source include safflower, corn oil, musturd oil, soyabean oil, they help reduce cholesterol formation.Vegetable oil contain PUFA belonging to Linolenic group.Some marine fishes contain PUFA belonging to omega-6 type, omega-3 type. These reduce thromboxane formation and hence useful as preventive measures of atherosclerosis.[7]

Probiotics are living microorganisms, which when taken with or without food, It improve the intestinal microbial balance and in turn functioning of large intestine. Probiotics include Bifidobacterium and lactobacilli species like *L. Acidophilus*. These microorganisms exert their effects by producing substances and conditions which inhibit the growth of harmful bacteria in the large intesine. The dairy products like sour milk, yoghurt containg probiotics.

Prebiotics are the food substances which reach to colon in intact form, without getting depleted by gastric pH. These are nutraceuticals which promote the flourishing the probiotics. Before reaching the colonic region, the probiotic microorganisms have to survive against the digestive enzymes and acids in the upper gut. To overcome this problem, nutraceuticals in the form of probiotics available. Example: inulin polyfructose obatained from raw chicory.[8]

Dietary fibres play a critical role in maintenance of health. They can be defined as such parts of plant stems, leaves and seeds. Which human body cannot digest and absorb. High fibre intake gives variety benefits to human body. Dietary fibres are generally categorized into two groups water soluble and water insoluble. Insoluble fibres mainly help in bulking of stools and their quick passage through digestive canal. Soluble fibres dissolve in water and forms that binds the stool. Insoluble fibres mainly present in brown rice, banana, cassoval, vegetables, whole grain , cereals, oats, barly, sorghum. Soluble fibres are present in oats, dried beans, legumes, chocory etc.[9]

The current trends in biodrugs indicate the commercial utility of omege-3-fatty acids, spirulina, soya, garlic, and royal jelly. Omega-3-fatty acids are Eicosapantaenoic acid and docosahexanoic acid DHA. They are polyunsaturated fatty acids mainly in the marine groups. They are found in the cold water fishes, cod, salmon, tuna, sardines, blue fish, mackerel and harring.[10]

Nutraceutical lozenges contain one or more medicaments in a flavoured and sweetened base and are intended to treat local irritation or infection of mouth or pharynx and may also be used for systemic drug absorption[11] Lozenges are intended to achieve local effect as soothing and pyrging the throat. Something they are used to relieve cough.

Nutraceutical lozenges are also for systemic effect provided the drug is well absorbed through the buccal linings or when it is swallowed these are flavoured medicated dosage form intended to be sucked and held in mouth or pharynx. They provide ease of administration for paediatric patients. The drugs having a large dose can be easily administered formulating as lozenges. Patient compliance is high with buccal delivery due to the accessibility of the cheek and lack of invasive measures.[12] Most of the illness is associated with high body temperature, fever, head ache and body ache. It is very difficult to manage these complications in pediatrics patients. The medicated lozenges are generally prepared by molding and compression techniques mostly in acacia or gelatin base- Pastilles and sugar as base- Troches. The oral or buccal cavity is highly vasculated which adds an advantage of maximum local activity thus minimizing systemic activity.[13]

Nutraceutical lozenges with antimicrobial and local anaesthetics as active ingredient are mostly advised for patients with swallowing problems, gastrointestinal blockade, paediatrics and geriatrics as they can be sucked easily into the saliva, providing localized drug delivery to the mouth, tongue and throat etc. Lozenges as the pharmaceutical dosage forms have several advantages than the oral administration as they can be manufactured with several excipients such as sweeteners for increasing solubility, colourants for elegant appearance, dyes to prevent photo degradation.[14]

MATERIALS AND METHODS

Plant material

This is a poly herbal formulation consisting of 7 ingredients *Spathodea Companulata, Zingiber Officinalalis, Pongamia Pinnata, Curcuma Longa, Aloe Barbadensis, Lawsonia Inermis, Piper Nigrum*. Procured from medicinal garden, Nellore, India. And these were authenticated by prof. P.Jayaraman, Director, National institute of herbal science,W.Tambaram, Chennai.

Extraction
About 1000 gm of powdered drug was successively extracted with suitable solvent, by using soxhlet apparatus. The extraction was carried out until the extract becomes colorless. The solvent is removed from extract by distillation under reduced pressure. The concentrated extract were kept in a desiccator and used for further experiment.[15]

Preliminary Phytochemical analysis
The poly-herbal formulation was subjected to preliminary phytochemical screening for the detection of various plant constituents present in the plant drugs. In this preliminary phytochemical analysis various tests like i.e. Test for alkaloids, test for glycosides, test for carbohydrates, Test for steroids, Test for flavonoids, Test for terpenoids, and Test for proteins.[16]

Physico-chemical evaluation
Physico-chemical investigations were carried out including determination of extractive values like Water soluble extractive, Alcohol soluble extractive, Ether soluble extractive and Hydro-alcoholic soluble extractive values were determined. Then Ash values like Total ash, Water soluble ash and Acid insoluble ash was determined. In Physico-chemical evaluation determined the moisture content of the poly-herbal formulation by Loss on drying method at 105°C.[17]

Preparation of Nutraceutical Lozenges
Required quantity of sugar syrup was prepared mixing sugar and water. Dextrose was dissolved in small quantity of water and heated it to 110^{o}C till dextrose dissolves completely forming as clear viscous syrup. Then the dextrose solution was poured into the sugar syrup and heated to 160^{o}C till the colour changes to golden yellow. The temperature was bought down to 90^{o}C and drug, polymer and other ingredients were added. The solution was poured into the mould having 2.8cm diameter and 6.5mm thickness. The prepared tablets were stored wrapped in aluminium foil and stored in desiccators to prevent moisture uptake. The final weight of each lozenge is 5gms.[18]

Organoleptic evaluation
Organoleptic evaluation means conclusions drawn from studies resulted due to impressions on organs of senses. It refers to evaluation of Nutraceutical Lozenges formulation by color, odour, taste, texture and touch.[19]

Evaluation tests for nutraceutical lozenges
Average weight and Weight variation test: 20 lozenges were selected and weighed collectively and individually on an electronic balance. From the collective weight, average weight was calculated. Each lozenge weight was then compared with average weight to assure whether it was within permissible limits or not. Not more than two of the individual weights deviated from the average weight by more than 7.5% for 300 mg tablets and none by more than double that percentage.

$$\text{Average weight} = \frac{\text{weight of 20 lozenges}}{20}$$

$$\%\ \text{weight variation} = \frac{\text{Average weight} - \text{weight of each tablet}}{\text{Average weight}}$$

Friability test: The friability of the 20 tablets from each batch was tested by a fribilator. At the speed of 25 rpm for 4 min. The lozenges were then dedusted, reweighed and percentage weight loss was calculated by the equation,

$$\%\ Friability = \frac{(initial\ Wt. - Wt.\ after\ friability)}{initial\ Wt.} X100$$

Hardness test: To evaluate the diametrical crushing strength, 3 tablets from each formulation were tested using a MAC hardness tester. The mean±SD values were calculated.

$$s = \sqrt{\frac{\sum(x - \bar{x})^2}{n - 1}}$$

***In vitro* mouth Dissolving Time**
Mouth Dissolving Time was determined by each batch formulation using USP disintegration apparatus, where lozenges were placed in each tube of the apparatus and time taken for the lozenges to dissolve completely was noted by using 100ml phosphate buffer of pH 6.8 at 37^{0}c. This test was done in triplicate. The average dissolving time for lozenges was calculated and presented with standard deviation.

Drug Content
Lozenges were powdered and dissolved in 5mL of methanol in 50 ml volumetric flask and volume made up to 50 ml with pH 6.8 Phosphate buffer. From this solution 1 ml taken and diluted with pH 6.8 Phosphate buffer in 50 ml volumetric flask then sonicated for 30 min then filtered using filter paper. The absorbance of this solution was measured at 280 nm using.

RESULT
The percentage yield of various extracts of the medicinal plants of *Zingiber officinalis, Glycyrrhiza glabra Coriandrum sativum, Apis mellifera, Citrus limonsis, Ocimum sanctum, Curcuma Longa, Piper Nigrum,* were presented in the following tables.

Table 1: Percentage yield of extract of various medicinal plants

Plant name	Part used	% yield of extractive (%w/w)			
		Methanol	Ethanol	Pet. ether	Water
***Coriandrum sativum* (Umbelliferae)**	**Leaves**	14.94	18.3	9.3	11.4
***Zingiber Officinalalis*(Zingiberaceae)**	Rhizome	20.15	29.20	12.34	10.4
***Glycyrrhiza glabra*, (Leguminoseae)**	Roots	23.4	20.3	12.34	9.8
***Curcuma Longa*. (Zingiberaceae)**	Rhizome	19.80	27.20	12.34	8.5
***Citrus limonsis*. (Rutaceae)**	Leaves	18.90	23.3	11.2	10.4
***Ocimum Sanctum*. (Laminaceae)**	Leaves	26.3	31.2	8.1	9.7
***Piper Nigrum*. (Piperaceae)**	Ripe fruits	24.3	33.2	15.1	9.7

Qualitative phytochemical examination[20]

Preliminary phytochemical screening of *Zingiber officinalis(Zo), Glycyrrhiza glabra(Gg), Coriandrum sativum(Cs), Apis mellifera(Am), Citrus limonsis(Cs), Ocimum sanctum(Os), Curcuma Longa(Cl), Piper Nigrum(Pn),* was carried out with different extracts and data represented in table.

Table 2: Phytochemical screening of the various plant extracts.

Tests	*Zo*	Gg	Cs	*Am*	Cl	Os	Cli	Pn
Alkaloids	_	–	–	_	_	+	_	+
Carbohydrates	+	+	+	+	+	+	+	+
Glycosides	+	+	+	+	+	+	+	_
Phytosterols	_	+	+	+	_	+	+	+
Lipids (Fats Fixed Oils& waxes)	+	+	–	+	+	+	+	+
Terpenoids	+	+	+	_	+	+	+	+
Phenolic & Tannins	+	+	+	+	+	+	+	+
Proteins & Amino acids	+	+	_	+	+	+	+	+
Gums & mucilage	+	+	+	+	+	+	+	+
Flavonoids	_	+	+	+	+	+	+	_

Table 3: Physicochemical parameters of various medicinal plants.

S.No	Physicochemical parameter	*Zo* (%w/w)	Gg (%w/w)	Cs (%w/w)	*Pn* (%w/w)	Cl (%w/w)	Os (%w/w)
5.	Total ash	13.2	18.5	13.8	11.4	21.2	13.7
6.	Acid insoluble ash	1.43	1.32	1.2	0.8	1.34	1.8
7.	Water soluble ash	14.7	8.2	6.4	2.1	11.3	3.4
8.	Carbonated ash	12.3	3.4	4.8	5.3	2.5	3.5
9.	Sulfated ash	7.4	2.4	3.2	6.5	3.5	2.5
10.	Nitrated ash	1.96	1.3	2.5	3.2	2.2	3.2

Table 4: Organoleptic characteristics of Nutraceutical lozenges.

S.No	Organoleptic characters	Nutraceutical lozenges
1.	Shape	Spherical
2.	Color	Brownish red
3.	Odour	Pleasant
4.	Texture	Smooth
5.	Taste	Sweet

Table 5: Results of Nutraceutical lozenges formulation.

S.No	Evaluation tests	Results
1.	Hardness kg/cm^2	10.16±0.002
2.	Weight variation	2.91±0.002
3.	Friability	2.90±0.008
4.	*In vitro* mouth dissolving time (min)	21±0.003
5.	Drug content	98.5±0.005
6.	Moisture content analysis	0.6±0.100

DISCUSSION AND CONCLUSION

In this research work the Nutraceutical lozenges was prepared and assesses the various characteristics for the standardization of Nutraceutical lozenges. In this standardization procedure Nutraceutical lozenges were tested for relevant organoleptic, preliminary phytochemical analysis, physicochemical evaluation and determination of physical characteristics like average weight, weight variation, friability, hardness, invitro mouth dissolving time and drug content.

The preliminary phytochemical analysis was conducted for various raw materials used in Nutraceutical lozenges and identified different active constituents which are responsible for treating sore throat and peptic ulcer given in the table. The physicochemical characteristics are determined and given in the table.

In these Physico-chemical characteristics like extractive values indicate the presence of acids, sugar and inorganic compounds. Less or more extractive values indicate addition of exhausted material, adulteration or incorrect processing during drying, storage or formulating. The ash values are like total ash indicates amount of minerals and earth materials present in the plant material. The deterioration time of Nutraceutical lozenges depends up on the amount of the water present in the plant material. If the water content is high the formulation easily undergoes to deteriorate due to microbial attacks.

The nutraceutical revolution will lead us into a new era of medicine and health, in which the food industry will become a research, oriented one similar to the pharmaceutical industry.[21] Although nutraceuticals have significant role in the promotion of human health and disease prevention, health professional, nutritionists and regulatory toxicologist should strategically work together to plan appropriate methodologies to provide the ultimate health and therapeutic benefit to human beings.[22]

The interaction of nutraceuticals with food and drugs is should be taken into consideration. The effect of different processing techniques on the biological availability and effectiveness of nutraceuticals to be determined. Since the ingredients used in nutraceutical lozenges also possess nutritional value, this preparation can be considered as an alternative, cost effective, safer and potential medicine to treat many diseases.

Due to the increasing popularity with health-conscious consumers, functional food science is becoming popular and creating new interest in marketing the products.[23] It is hoped that the study serve to develop cost effective, safer and potential formulation for various chronic and sub chronic diseases. Based on the literature survey these nutraceutical agents are *Zingiber officinalis, Glycyrrhiza glabra, Coriandrum sativum, Apis mellifera, Citrus limonsis, Ocimum sanctum, Curcuma Longa, Piper Nigrum*, having in addition to its normal nutritional value provides health benefits including are responsible for the prevention of sore throat and peptic ulcer in the body.

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