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DESIGN AND DEVELOPMENT OF POLY HERBAL LOZENGES FOR NOOTROPIC ACTIVITY

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ABSTRACT

The present study states that the traditional medicinal plant *clitoriaternatea* which is having the nootropic activity by formulating as a lozenges. The present study states the design and development of poly herbal lozenges. It is the advanced method of medication delivery which has the excellent future for both local and systemic effect. A lozenge does not pass through the digestive system and they should be released in controlled manner which releases over extended time period. Hard boiled lozenges are most frequently used and popularly known among the customers to promote patient compliance which ensuring the patient safety and efficacy. Lozenges are the OTC (over the counter) medication that does not requires prescription. Some drugs require a prescription, while others are given by a doctor. The *clitoria ternatea* has prominent effect on CNS which have indegious character of enhancing nervous system activities like person's speech, mood, ability to grassing and remembering, intellectual behavior and recall information. The *clitoria ternatea* is used in the alzheimer's disease instead of using conventional medicine because of the adverse effects in addition to their pharmacological activity. In our present study we have developed a novel formulation to lozenges and evaluated the final product which was obtained at the end of formulation. The herbal powders of *Clitoria ternatea*, *Curcuma longa* and *Glycyrrhiza glabra* are used in the present formulation. The herbal powders were done for Preformulation

studies. Corn syrup (Binder) and sugar (candy base) used in the formulation as excipients. The lozenges were formulated by using the heating and congealing method. The formulated lozenges were evaluated by tests like Weight variation, Hardness, Thickness, Diameter, Friability, pH and *In-Vitro* Dissolution studies.

Keywords: Hard Boiled Lozenges (HBL), *Clitoria ternatea*, *Curcuma longa, Glycyrrhzia glabra*, Nootropic, Alzheimer's, CNS, OTC, In-Vitro Dissolution Studies

INTRODUCTION:

As an advanced method of medication delivery for both local and systemic effects, lozenges have an excellent future. Both adults and children accept lozenges as an effective dose form. Typically designed to be held in the oral cavity and moistened with saliva before being completely dissolved. Lozenges can be categorized according to their texture and makeup, including chewy, caramel, compressed tablet lozenges, soft lozenges, and hard boiled lozenges. The most frequent and popular items among customers are hard boiled lozenges (HBL), also known as hard boiled candies (HBC). In a flavoured and sweetened base, and when sucked, are meant to gently dissolve or disintegrate in the buccal cavity. Lozenges are used for patients who have trouble swallowing solid oral dosage forms and for medications that need to be given gradually to maintain a steady level of medication in the oral cavity. Lozenges can also be utilized for systemic effects if the medication is effectively absorbed when ingested or through the buccal mucosa. These are the over-the-counter (OTC) drugs that do not require a prescription. Pastilles are a term occasionally used to describe molded lozenges, whereas troches are a term sometimes used to describe compressed lozenges **[1 - 4]**.

MATERIALS AND METHODS:

Materials: Shankhpushpi was purchased from Madhav Herbals-India, Liquorice was purchased from Yucca Enterprises Pvt Ltd, Turmeric was purchased from Herbal products-India, Sugar powder was purchased from Delta sugars Ltd-Vijayawada, Corn syrup was purchased from Health genix and Magnesium Stearate was purchased from Merk Specialities Pvt Ltd-Mumbai.

Methods:

Preformulation studies: Preformulation tests were performed for the identification of the possible drug-excipients incompatibility. The compatibility studies were performed for the development of dosage form, preformulation studies is carried out to confirm that there was no interaction between the drug and excipients

[5]. Preformulation studies are the initial phases of development, which the psychochemical property of the drug substance is determined. These are designed to provide information that will assist the formulator in producing stable and bioavailable dosage forms that can be mass manufactured **[6]**.

Method of preparation of lozenges:

Formulation 1: The lozenges base were prepared by mixing sugar powder and distilled water with the aid of heating until the base mixture is turns into thick yellow colored consistency. Binding agent corn syrup is added to the prepared base by continuous heating. Shankhpushpi and turmeric powders are added to the base and binding agent mixture. The prepared mixtures were poured into the moulds with required dimensions. The lozenges are cooled at the room temperature and allowed to evaluation studies.

Formulation 2: Base was prepared by heating and congealing method. Binding agent corn syrup was added. Required quantities of the herbal powders shankhpushpi, turmeric and ant diabetic agent liquorice were added. Mixture was poured into the moulds, cooled and dried at the room temperature and evaluation tests were performed.

Formulation 3: In this formulation the hard candy herbal lozenges was prepared by adding magnesium stearate as a lubricating agent after the addition of the herbal powders.

Formulation 4: In the last trail we are formulating the lozenges with different concentrations of herbal powders. The base was prepared by adding sugar powder and distilled water by applying heat. The binding agent corn syrup is added to the thick base consistency. Increased concentrations of the shankhpushpi powder and turmeric, liquorice were added to the mixture. Lubricating agent is added to the final mixture. Mixture was poured into the moulds for specific dimensions. Cooled and dried at room temperature. Perform the evaluation studies of lozenges.

Figure 1: Formulation 1 Lozenges

Figure 2: Formulation 2 Lozenges

Figure 3: Formulation 3 Lozenges

Figure 4: Formulation 4 Lozenges

Identification Tests for *Clitoria ternatia*:

Identification tests for clitoria ternatea gives negative results for Biuret test, molisch test and bontragers test which indicates the absence of proteins, carbohydrates and glycosides. It gives the positive results for millions test, hagers test, salkowski test and shinoda test which indicates presence of amino acids, alkaloids, triterpinoids, flavonoids.

Post Formulation Studies:

Partition Coefficient: It is also known as Distribution Coefficient. The drug is added to a mixture of immiscible liquids, drug is distributed between two phases, which each phase becomes saturated. It is calculated by concentration of drug in a mixture of immiscible liquids at equilibrium **[7]**.

$$K_{O/W} = C_{Organic}/C_{Aqueous}$$

These liquids are usually water and organic solvents like n-octanol, benzene and chloroform etc. The drugs having partition coefficient value >2 can easily cross the blood brain barrier. Partition coefficient is calculated by following formula:

$$N_1V_1=N_2V_2$$

Weight variation: Weight variation ten lozenges were chosen at a random rate from each batch and weighed one by one. Ten lozenges were weighed, and the average weight and standard deviation were obtained. If no more than two of the individual lozenges depart from the average weight, the batch passes the weight variation test.

Thickness: Thickness consistency, Vernier calipers were used to measure the thickness of the six lozenges that were randomly chosen from each batch.

Hardness: The force needed to shatter a lozenge in a diametric compression using the Monsanto Hardness tester is known as hardness or crushing strength (Fo). Six lozenges were tested for hardness for each batch. The tester's two jaws were used to hold the lozenges between them along their oblong axis. Reading should be 0 kg/cm^2 at this

moment. After then, the knob was rotated continuously until the lozenges broke. At this stage, the value was indicated as kg/cm^2.

Moisture content: A sample weighing 1 g was kept in a desiccator at room temperature for 24 hours. After specified period of time, weigh the sample and moisture content is calculated by substraction of final weight from initial weight. The moisture content and the weight of hard boiled lozenges should range in between 0.5 – 1.5% and 1.5 – 4.5g respectively.

$$\boldsymbol{MC = \frac{W1 - W2}{W1} \times 100}$$

Friability: The friablity was tested using Roche Friabilator. The apparatus treats the tablet to abrasion and shock in a plastic chamber that rotates at 25rpm and drops a tablet from a height of six inches with each rotation. In the friabilator, a pre-weighted sample of tablets were put and subjected to hundred rotations. The tablets were reweighed after being dusted with a white muslin towel. The USP limit is 0.5% to 1% the formula for friability (F) is as follows:

$$\% \boldsymbol{F = \frac{Wi - Wf}{Wi} \times 100}$$

pH Determination: It is defined as negative logarithm of H^+ ion concentration, in which saliva is slightly acidic in nature (pH: 6 – 7). Buccal lozenges are meant to reach the saliva pH to known the dissolution in the buccal mucosa and avoid the buccal irritation. The pH of the hard bolied lozenges are ranges from 5 – 6, in which they are adjusted by the adding acidulents and calcium carbonates, sodium bicarbonates and magnesium trisilicate **[8]**.

Compatibility Studies:

FT-IR: FTIR spectroscopy tests were used to examine the compatibility of the herbal powder with the specified excipients using a physical mixture of various excipients in a 1:1 ratio. The KBr pellet method was used to study the spectroscopic properties of the physical mixture samples. The primary interactions were discovered by analyzing the herbal powder and excipient spectra.

In-vitro **Dissolution studies:** USP apparatus II (paddle type) was employed for the studies in *in-vitro* dissolution tests. Shankhpushpi lozenge formulations were precisely weighed and added to a 900 ml phosphate buffer solution with a pH of 6.8. A 37°C constant temperature and a 50 rpm mixing speed were used. A 5 ml aliquot of the material was removed after 5 minutes and replaced with an equal volume of plaine buffer held at 37°C. The collected samples were filtered and the UV visible spectro-photometer was used to analyze them at 222 nm.

RESULTS AND DISCUSSION:

Pre formulation studies: (Table 1)

Table 1: Results of flow properties

Test	Obtained value	Observation
Angle of repose	29.68°	Good
Bulk density	0.4972g/cm^3	-
Tapped density	0.6215g/cm^3	-
Carr's index	20 %	Fair
Hausner's ratio	1.25	Fair

Identification Tests for *Clitorea Ternatea:* (Table 2)

Table 2: Results for identification tests

S. No.	Test Name	Inference
1	Molisch test	Absence of carbohydrates
2	Biuret test	Absence of proteins
3	Millons test	Presence of aminoacids
4	Hagers test	Presence of alkaloids
5	Salkowski test	Presence of triterpinoids
6	Bontragers test	Absence of glycosides
7	Shinoda test	Presence of flavonoids

Post Formulation Studies:

Partition coefficient:

Trial 1:

a) Aqueous phase:

$$N_1V_1=N_2V_2$$

N_1= Normality of sodium hydroxide = 0.1N

V_1 = Volume of sodium hydroxide consumed

N_2 = Normality of unknown concentration = ?

V_2 = Volume of unknown concentration = 10ml

$$V_1=0.8ml$$

$$N_2=\frac{0.1x0.8}{10}=0.008N$$

b) Organic phase:

$$V_1 = 2ml$$

$$N_2=\frac{0.1x2}{10}=0.02N$$

$$K_{O/W}=\frac{\text{Organic phase}}{\text{Aqueous phase}}=\frac{0.02}{0.008}=2.5 \longrightarrow X$$

Trial 2:

a) Aqueous phase:

$$V_1= 0.9ml$$

$$N_2=\frac{0.1x0.9}{10}=0.009N$$

b) Organic phase:

$$V_1 = 2.2ml$$

$$N_2=\frac{0.1x2.2}{10}=0.022N$$

$$K_{O/W} = \frac{\text{Organic phase}}{\text{Aqueous phase}} = \frac{0.022}{0.009} = 2.44 \qquad Y \longrightarrow$$

Average: $$\frac{X+Y}{2} = \frac{2.5+2.44}{2} = \frac{4.94}{2} = 2.47$$

Weight variation: (Table 3)

Table 3: Results for weight variation Test

S. No.	Weight (gm) (W_1)	Average Weight (W_2) (gm)	Difference (W_1-W_2) (gm)	% Difference
1.	2.1	2.06	0.04	1.94
2.	2.0	2.06	-0.06	-2.91
3.	2.0	2.06	-0.06	-2.91
4.	2.1	2.06	0.04	1.94
5.	2.1	2.06	0.04	1.94
6.	2.0	2.06	-0.06	-2.91
7.	2.0	2.06	-0.06	-2.91
8.	2.1	2.06	0.04	1.94
9.	2.0	2.06	-0.06	-2.91
10.	2.2	2.06	0.14	6.79

All the lozenges obtained were within the percentage criteria of ±5%. Hence batch passes the test

Thickness and diameter: (Table 4)

Table 4: Results for Thickness and Diameter

S. No.	Thickness (mm)	Diameter (mm)
1.	0.6	1.33
2.	0.6	1.31
3.	0.7	1. 31
4.	0.5	1.32
5.	0.6	1.33
Average	0.6 mm	1.32 mm

The average thickness and diameter is 0.6 mm and 1.32mm

Hardness: (Table 5)

Table 5: Results for Hardness Test

S. No.	Hardness Kg/cm^2
1.	4.2
2.	4.4
3.	4.4
4.	4.6
5.	4.2
Average	4.36 Kg/cm^2

The average hardness values of the lozenges were in the range of 4 – 4.4 kg/cm^2. Hence the batch passes the test for hardness

Moisture content:

$$MC = \frac{W1 - W2}{W1} \times 100$$

W_1 = Weight of sample before drying (34.40g)

W_2 = Weight of sample after drying (33.37g)

$$MC = \frac{34.40 - 33.37}{34.40} \times 100$$

$$MC = \frac{0.28}{34.40} \times 100$$

$$= 0.81\%$$

Friability: (Table 6)

Table 6: Results for Friability Test

Weight (W_1)	Weight (W_2)	(W_1-W_2)gm	% Friability
12.19gm	12.11gm	0.02	0.16 %

The percent friability of the lozenges was within the % criteria of 0.8. Hence the batch passes the friability test.

pH Determination: (Table 7)

Table 7: Results for pH

Trail	Ph
1	5.98
2	6.12
3	5.92
4	6.09
Average	6.02

Compatibility Studies:

FTIR: (Table 8)

Table 8: Results for IR Spectroscopy

Fuctional Group	C=O	O-H	C-O	C-H	C=C	C-C
Drug	1322.68	3409.24	1246.30	2860.29	1639.98	1032.30
Formulation	1319.87	3399.33	1263.51	2933.70	1641.17	1052.88

In-Vitro Dissolution Studies: (Table 9)

Table 9: Results for *in-vitro* studies

Time (min)	Absorbance	Dilution factor	Conc π/ml	Amt in mg/ml	Amt in 5 mg/ml	Amt mg/900 ml	Cumulative	% Drug release
10	0.28	2	16.666	0.0333	0.1666	30	30	30
20	0.41	2	24.404	0.0488	0.2440	43.928	44.095	44.095
30	0.549	2	32.678	0.0653	0.3267	58.821	59.232	59.232
40	0.68	2	40.476	0.0809	0.4047	72.857	73.594	73.594
50	0.758	2	45.119	0.0902	0.4511	81.214	82.807	82.807
60	0.898	2	53.452	0.1069	0.5345	96.214	97.807	97.807

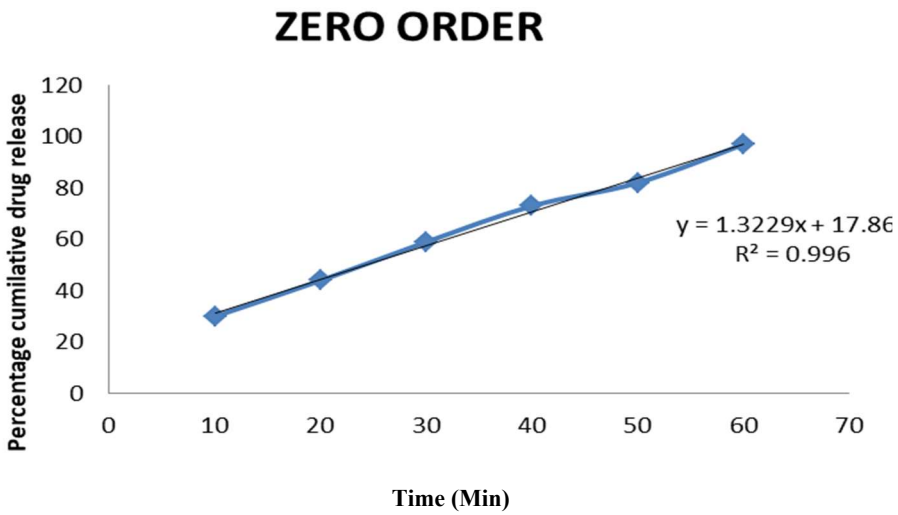

Figure 5: Zero order

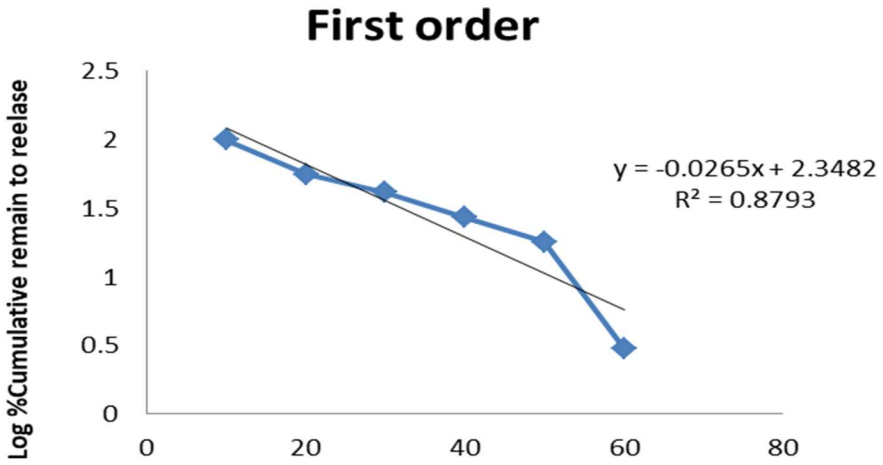

Figure 6: First order

INTERPRETATION:

The best fit model from the kinetic study was found to peppas. The n-value was found to be n=0.77 which indicate to non-flickian diffusion controlled mechanism.

CONCLUSION:

We came up with a novel idea of formulating herbal medical powder into lozenges. The medicinal herbal powders used were *Clitoria Ternatea, Glycyrrhiza glabra and Curcuma longa.* The herbal powders were characterized by preformulation studies like physicochemical properties and bulk characteristics. The compatibility of herbal powders with excipients is done by using IR spectroscopy. The stability of formulated lozenges were determined by moisture analysis. The lozenges passed all evaluation testes like weight variation, friability, hardness, pH, thickness and diameter. To add the future scope to polyherbal lozenges *in-vitro* studies are being performed for its nootropic activity.

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