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Design, Development and Evaluation of Oral Herbal Formulations of *Piper nigrum* and *Nyctanthes arbortristis*

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ABSTRACT: In the present investigation, three orally administrable dosage forms of fruits of *Piper nigrum* (Maricha) and leaves of *Nyctanthes arbortristis* (Parijataka), in combination, were developed. Tablet form of drugs from solid dosage form and two formulations from liquid class were designed and developed. By considering difficulty of solubility of herbal drugs in a vehicle, in one of the liquid class, decoction form of drugs in specific vehicle was used. This form of drugs hereafter considered as Liquid Oral Dosage Form of drugs. To prepare a liquid form with suspended particles of drugs, Suspension form was also designed. Formulated dosage forms then subjected to evaluation of production quality by different methods stated as per official compendia. Such evaluation has unique position in development of new formulations.

KEY WORDS: *Piper nigrum* (Maricha), *Nyctanthes arbortristis* (Parijataka), herbal formulations, Evaluation, Production Quality.

INTRODUCTION

The oral route of drug administration is the most important method of administrating drugs for systemic effects. Except in few cases, parenteral route is not routinely used for self administration of medications. The topical route of administration is limited in its ability to allow effective drug absorption for systemic drug action. It is probable that most of drugs used to produce systemic effects are administered by the oral route[1]. Ayurvedic herbal formulations were also administered preferentially by oral route.

Oral solutions, syrups, elixirs etc., are prepared and used for the specific effects of the medicinal agents present. In these preparations, the medicinal agents are intended to provide systemic effects. The fact that they are administered in solution form usually means that their absorption from the GI tract into the systemic circulation may be expected to occur more rapidly than other oral dosage forms of the same medicinal agent.

Solid oral dosage forms represent the preferred class of product for orally administered drugs. Advantage beings unit dosage forms, easy to handle and transport, convenient and safe. Liquid forms of drugs have certain limitation, but public demand or expectations are very high for such formulations. Moreover, some products are more effective in a liquid form and are used commonly by young children's or the elderly to over come problem of swallowing the solid oral dosage forms[2]. Most of the orally administered Ayurvedic formulations belong to liquid form of drug or drug combination[3].

Designing of oral herbal formulations is till date a challenge in modern pharmaceutics. There are number of medicinal herbs in traditional system of medicine which are time tested, useful for the number of aliment. There are many medicinal plants mentioned in Ayurvedic Texts/*Nighantu*s from *Jwaraghna* group like *P. nigrum* (Maricha)[4,5], *N.*

arbortristis (Parijataka)[5,6,7], *H. antidysentrica* (Kutaja), *T. chebula* (Hirda), etc., which have application in different types of fever and in Malaria. In present study the two Ayurvedic medicinal plants parts such as *Piper nigrum* (Maricha) fruits and *Nyctanthes arbortristis* (Parijataka) leaves were selected for designing the possible modern formulations.

MATERIAL & METHODS

Materials:

Piper nigrum (Maricha) fruits and *Nyctanthes arbortristis* (Parijataka) leaves obtained from local market and authenticated by taxonomist. Sorbitol, tragacanth, glycerin, methyl and Propyl Paraben, Starch and Talc were purchased from Loba chemicals Ltd. Mumbai. All other chemicals used were of analytical grade.

Methods:

The three dosage forms, in combination, of *Piper nigrum* fruits and *Nyctanthes arbortristis* leaves planned to formulate that are

- Solid dosage form i.e. Tablet
- Liquid dosage form i.e. Liquid Oral and Suspension

I) Preparation of Solid dosage form i.e. Tablet

General Procedure:-

A 50:50 mixture of fine powder of Maricha fruits and Parijataka leaves were used for the manufacture of tablet. Tablets were prepared by wet granulation method, by using starch mucilage with varying concentration (5% w/v, 10% w/v and 12% w/v) as binder and Disintegrant. Talc was used as lubricant. For preparing tablets by wet granulation method[8], following steps were carried out- milling of drugs and excipients, mixing of milled powders, preparation of binder solution, mixing of binder solution with powder mixture to form a wet mass, using 6 to l2 mesh screen drying the moist granules, screening of dry granules through 14 to 20 mesh screen, mixing of dry granules with lubricants, and lastly tablet compression. Three possible formulations of Tablets viz. T_1, T_2 and T_3 were prepared by single punch tablet compression machine (Kevin Engineering Pvt. Ltd.). Suitable numbers of tablet were prepared only once so as to avoid bias of the second batch. The three possible formulations were formulated with varying concentrations of starch paste with drugs as shown in **Table 1**. All the formulations were checked for efficiency by its preliminary tests and all formulations were extensively studied for its quality control parameters.

II) Preparation of Liquid dosage form:

A} Preparation of Liquid Oral:-

To prepare Liquid Oral form of fruits of Maricha and leaves of Parijataka, following steps were carried out-

a) Method of Preparation of Decoction[9]-

500 g each of powder of dried unripe fruits of Maricha and shade dried leaves of Parijataka was taken. Powder was mixed with 4000ml (4 liter) of water. The powdered material was boiled until total volume become one fourth of previous. After boiling liquid was cooled and filtered. Filtrate was taken to prepare final Liquid Oral form.

b) Method of Preparation of Simple Syrup –

850 g. of sucrose was dissolved in sufficient water to get 1000 ml of concentrated simple syrup. Then the solution was filtered. This simple syrup was used as vehicle.

c) Method of preparation of final Liquid Oral form-

To prepare final Liquid Oral of Maricha and Parijataka, One part of decoction was mixed with Five parts of Simple Syrup **(1: 5)**. Solubility was checked by observing the clarity of solution visually. The final Liquid Oral form of Maricha and Parijataka was then subjected to evaluation of production quality as per official standards.

B} Preparation of Herbal Suspension dosage form:-

The formulae for preparing 1000 ml of suspension of *Piper nigrum* and *Nyctanthes arbortristis* was as shown in **Table 2**. The 120 mesh size fine particles of both the drugs are properly mixed by triturating. 5 ml of sorbital solution was mixed with 25 ml of glycerin. The powdered form of drugs was wetted thoroughly with Sorbital and Glycerin solution to reduce liquid–air interfacial tension[8]. The suspending agent, tragacanth in the aqueous medium containing selected preservatives was then added in to the wetted mass slowly, with continuous triturating. Three possible formulations of Suspension viz. S_1, S_2 and S_3 were prepared by using 5ml, 7ml and 10ml of 1.25% aqueous tragacanth solution respectively. Finally suspension brought up to the final volume with purified water by continuous trituration so as to get uniform product. All three possible forms of suspension of Maricha and Parijataka were then subjected to evaluation of production quality as per official standards.

III) Evaluation of Production Quality:

1. **Evaluation of Tablets**

The three forms of Tablets (T_1, T_2 and T_3) were evaluated for general appearance, friability test, hardness test, weight variation test, disintegration test and dissolution test[10,11].

2. **Evaluation of Liquid Dosage Forms**

a. Evaluation of Liquid Oral

The different parameters of decoction and final Liquid Oral were assessed such as pH, specific gravity and density[12]. Stability study of final Liquid Oral was carried out at different temperature and at relative humidity[11,13].

b. Evaluation of Suspension

The three forms of Suspension (S_1, S_2 and S_3) were evaluated for rate of sedimentation. Stability study of the final suspension was carried out[11,13].

RESULT AND DISCUSSION

The primary objective of this work was to develop combinational oral herbal dosage form of *Piper nigrum* (Maricha) and *Nyctanthes arbortristis* (Parijataka). The development of such formulations will mark an important advancement in the area of phytopharmaceuticals. The present investigation examines design & development of solid and liquid oral herbal dosage form. The solid dosage form, Tablets were prepared using starch as binder and disintegrant in varying concentration & talc as lubricant. The two liquid dosage forms such as Liquid Oral & Suspension were also prepared.

The prepared three possible forms of tablets (T_1, T_2 and T_3) were evaluated for various evaluation parameters such as general appearance, hardness, friability, weight variation, disintegration & dissolution (**Table no. 3**). The prepared tablets were spherical puffy green colour with smooth surface having acceptable elegance. T_2 form of tablets was of good quality with regard to hardness, friability & weight variation. T_2 form of the tablets formulated with starch paste (10% w/v) as disintegrating agent & binder show disintegration within 42 min.

The liquid oral herbal dosage forms like Liquid Oral & Suspension prepared showed good elegance. The Liquid Oral evaluated for measurement of p^H, specific gravity & stability. The final formulation found to have p^H 4.3 and specific gravity 1.17 g/ml (**Table 4**). The results of stability study of final Liquid Oral form of drugs indicate the homogeneity of syrup without turbidity at storage temperature (**Table 5**).

The suspension dosage form showed good palatability. The final formulation has pH 4.3 and specific gravity 1.34 g/ml. Three possible forms of suspension were evaluated for sedimentation ratio. S_3 form of suspension shows sedimentation ratio 2.1 after 270 min. (**Table 6**), which is better than S1 and S2 form of suspension (**Figure 1**). All forms of suspension although shows easily dispersible pattern. The stability study of S_3 form of suspension indicates retaining stability at room temperature (**Table 7**).

CONCLUSION

Oral herbal dosage forms of *Piper nigrum* (Maricha) fruits and *Nyctanthes arbortristis* (Parijataka) leaves in combination like Tablets, Liquid Oral & Suspension showed good elegance & palatability. Tablet dosage forms are of good quality with regards to characteristics like hardness, friability, weight variation and disintegration time. Liquid dosage forms like Liquid Oral & Suspension having good stability on storage. Thus it can be concluded that these combined oral herbal dosage forms could be suitable dosage form for *Piper nigrum* (Maricha) fruits and *Nyctanthes arbortristis* (Parijataka) leaves.

Table 1: Formulae for preparing Tablet Dosage Forms

Sr. No	Ingredients	Formulations		
		T_1	T_2	T_3
1	*Piper nigrum* (Maricha) fruits	250 mg	250 mg	250 mg
2	*Nyctanthes arbortristis* (Parijataka) leaves	250 mg	250 mg	250 mg
3	Starch Paste	5% w/v	10% w/v	12% w/v
4	Talc	5 mg	5 mg	5 mg

Table 2: Formulae for preparing Suspension of *P. nigrum* and *N. arbortristis*

Sr. No	Ingredients	Formulations		
		S_1	S_2	S_3
1.	*Piper nigrum* (Maricha) fruits	50 gm	50 gm	50 gm
2.	*Nyctanthes arbortristis* (Parijataka) leaves	50 gm	50 gm	50 gm
3.	Sorbitol Solution {0.5 %}	5 ml	5 ml	5 ml
4.	Glycerin	25 ml	25 ml	25 ml
5.	Aqueous Tragacanth Solution {1.25 %}	5 ml	7 ml	10 ml
6.	Methyl Paraben	0.9 gm	0.9 gm	0.9 gm
7.	Propyl Paraben	0.3 gm	0.3 gm	0.3 gm
8.	Purified Water	Up to 1000 ml	Up to 1000 ml	Up to 1000 ml

Table 3: Quantitative Evaluation of Tablet Form of Drugs

Sr.No.	Parameters	*Observed Data For Formulations*		
		T1	**T2**	***T3***
1	Disintegration Time	51min.	42 min.	*39min.*
2	Dissolution Time	*110min.	*90 min.	**90min.*
3	Hardness	1.7kg/cm	2.5kg/cm	*3.2kg/cm*
4	Friability	0.93%	0.86%	*0.72%*
5	*Weight Variation*	*0.41%*	*0.42%*	*0.42%*

*Complete dissolution was not observed

Table 4: Quantitative Evaluation of Liquid Oral Form of Drugs

Sr.No.	Parameters	*Observed Values*
1	pH of Decoction	*4.4*
2	Specific Gravity of Decoction	*1.34g/ml*
3	Density of Decoction	*1.29 g/cm^3*
4	pH of Final Liquid Oral	*4.3*
5	Specific Gravity of Liquid Oral	*1.17 g/ml*
6	*Density of Liquid Oral*	*1.13 g/cm^3*

Table 5: Results of Stability Testing of Liquid Oral Form of Drugs

Sr.No.	Sample No.	Time Duration (Hrs.)	Temperature (^{0}C)	Turbidity/ Homogeneity	Colour / Odour
1	P-1	24	4^{0}c	No Turbidity	No change
2	Q-1	24	R.T.	×	No change
3	R-1	24	47^{0}c	Homogeneity	No change
4	P-2	48	4^{0}c	No Turbidity	No change
5	Q-2	48	R.T.	×	No change
6	R-2	48	47^{0}c.	Homogeneity	No change
7	P-3	72	4^{0}c	No Turbidity	No change
8	Q-3	72	R.T.	×	No change
9	R-3	72	47^{0}c	No Homogeneity	Change in both Colour, Odour

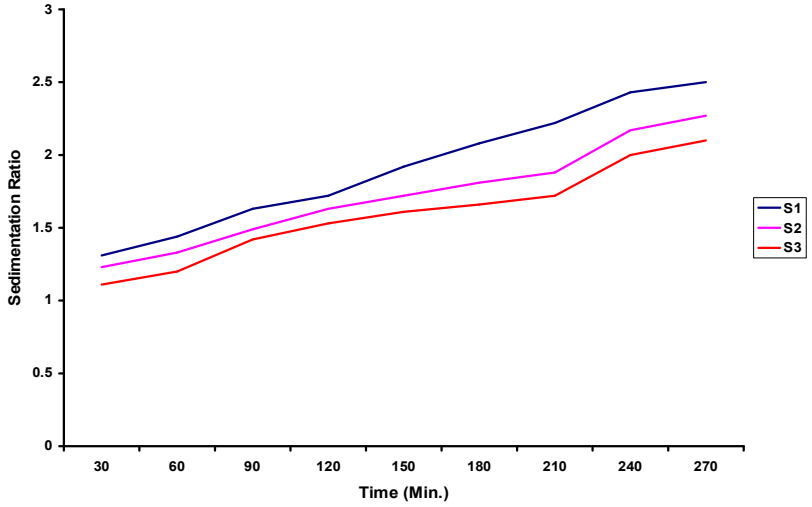
Table 6: Results of Rate of Sedimentation of Suspension Form of Drugs

Sr. No.	Time (min.)	Ultimate Height (Hu) (ml)	S1		S2		S3	
			Final Height (Ho)(ml)	Sedimentation Ratio (Hu/Ho)	Final Height (Ho)(ml)	Sedimentation Ratio (Hu/Ho)	Final Height (Ho)(ml)	Sedimentation Ratio (Hu/Ho)
1	30	100	76	1.31	81	1.23	90	1.11
2	60	100	69	1.44	75	1.33	83	1.2
3	90	100	61	1.63	67	1.49	70	1.42
4	120	100	56	1.72	61	1.63	65	1.53
5	150	100	52	1.92	58	1.72	62	1.61
6	180	100	48	2.08	55	1.81	60	1.66
7	210	100	45	2.22	53	1.88	58	1.72
8	240	100	41	2.43	46	2.17	50	2.0
9	270	100	40	2.50	44	2.27	48	2.1

Table 7: Results of Stability Test of Suspension Form of Drugs

Sr.No.	Sample No.	Time Duration (Hrs.)	Temperature (^{0}C)	Crystal Formation	General Appearance
1	A-1	24	4^0c	×	Good
2	B-1	24	R.T.	×	Good
3	C-1	24	47^0c	×	Good
4	A-2	48	4^0c	×	Good
5	B-2	48	R.T.	×	Good
6	C-2	48	47^0c.	×	Good
7	A-3	72	4^0c	×	Good
8	B-3	72	R.T.	×	Good
9	C-3	72	47^0c	✓ (Crystal formation was seen)	Colour was changed

Figure 1: Comparative Rate of Sedimentation of three forms of Suspension Form of Drugs



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