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Research Article

Development and Evaluation of Standardized Solid Dosage Formulations of *Trikatu*

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ABSTRACT

Aim of the study: Development of standardized, safe and effective traditional herbal formulations with robust scientific evidence can offer faster and more economical alternatives for desired therapeutic actions. The main objective was to develop the method of preparation and evaluation of *Trikatu* tablets.

Materials & Methods: The study involved chromatographic fingerprinting of three drug extracts; black pepper (*Piper nigrum*, Linn.) long pepper (*Piper longum*, Linn.) and ginger (*Zingiber officinalis*, Rosc.) for standardization followed by preparation of tablets by wet granulation and direct compression methods. The tablets were evaluated for performance tests like weight variation, disintegration and hardness etc.

Results: The results revealed that the developed dosage forms have good flow properties with zero drug-excipient incompatibility, less disintegration time and better release rate thus provide a reasonable solution to the problem associated with powder formulations.

Conclusion: The standardised solid dosage formulations of *Trikatu* developed in the present provide several advantages over traditional form and thus have immense potential to be adopted at industrial scale.

Keywords: Ayurveda, *Trikatu* tablets, HPTLC, piperine, 6-shoagaol, standardisation

INTRODUCTION

Trikatu, a Sanskrit word meaning 'three acrids' is an Ayurvedic formulation consisting of powders of three drugs black pepper (*Piper nigrum*, Linn.) long pepper (*Piper longum*, Linn.) and ginger (*Zingiber officinalis*, Rosc.) in equal proportions. For improving shelf life, churnas (powders) are converted into gutikas (tablets). *Trikatu* has gained importance in the traditional system of medicine due to its chief alkaloidal constituent, viz. piperine. Literature has revealed a number of pharmacological properties of piperine, one of them being its anti-inflammatory activity[1] .

Apart from its indigenous uses, *Trikatu* has also gained importance in modern medicine due to piperine[2]. Documented reports indicates the importance of piperine (one of the most important constituent of *Trikatu)* in enhancing the bioavailability of drugs, like phenytoin[3], theophylline[4], vasicine[5], oxyphenylbutazone[6] and indomethacin[7] etc. Improved oral bioavailability of poorly absorbed drugs can help in altering the therapeutic dosage of such drugs or even routes of drug administration.

Tablets can be manufactured by the methods of wet granulation, dry granulation or direct compression[8]. Manufacturing of tablets should be followed by quality control tests such as weight variation tests or the disintegration test[9]. Factors affecting the disintegration of tablets[10] are physiochemical properties of drugs (Solubility, particle size, solid phase characteristic, polymorphism), formulation factors (effect of excipients such as binder, disintegrant, diluents and lubricant), the test apparatus (pH and surface tension of the medium, temperature of the medium and its viscosity), the tablet manufacturing process (method of granulation and compression). The advantages of direct compression includes uniformity of blend, few

manufacturing steps involved, elimination of heat, moisture and physical stability[11].

There are very few attempts on systematic studies for the development and evaluation of Ayurvedic dosage forms. The main objective was to develop the method of preparation of *Trikatu* tablets so that the tablets meet the criteria of disintegration and hardness test. The present study involved preparation of *Trikatu* tablets by different methods namely wet granulation, direct compression and evaluation of the tablets.

MATERIALS AND METHODS

Black pepper fruits, long pepper fruits and dried ginger rhizomes were obtained from Balaji Trading Company, New Delhi. Starch, d-Mannitol, talc, magnesium stearate, sodium bicarbonate, ethanol, n-hexane, sodium starch glycolate, polyvinyl pyrrolidone, ethyl acetate, tartaric acid and menthol cryst were obtained from Loba chemie, Mumbai. Dicalcium phosphate dehydrate, glacial acetic acid and diethyl ether were procured from CDH, New Delhi.

Shodhna of *Trikatu*

The methanolic extracts of black pepper and long pepper fruits were prepared using soxhlet apparatus. The aqueous and alcoholic extracts of ginger rhizomes were prepared by maceration process[12,13]. The drug was macerated for 6 days with alternative stirring. The extracts were filtered and concentrated using rotary evaporator and then freeze dried using lyophilizer. Extracts were then standardized by standard plot method using HPTLC. Samples were spotted on pre-coated silica gel FL60254 aluminum plate by means of a Camag Linomate V sample applicator fitted with a 100 µL Hamilton syringe. Black pepper and long pepper extracts spotted plates were developed with solvent system consisting of hexane-ethyl acetate-glacial acetic acid (3:1:0.1 v/v/v)[14] [whereas ginger extract spotted plated were developed with solvent system consisting of diethylether-n-hexane (6:4 v/v)[15].

Formulation of *Trikatu* gutikas

Trikatu gutikas were prepared by different methods namely wet granulation & direct compression. *Trikatu* dispersible gutikas were prepared by direct compression method. The ratio of various excipients used in different batches for the formulation of tablets are represented in [Table 1, 2].

In wet granulation method slurry was made using binder with isopropyl alcohol. Drug extracts were mixed with slurry containing all other excipients. Then wet mass was sieved through sieve no 20 to obtain the granules. Compressed the granules using 10 mm flat punch, with hand operated single punch machine. The average weight of tablets was found to be 250 mg.

In direct compression method, drug extracts were mixed with excipients and compressed into tablets using 10 mm punch with single punch machine. The average weight of tablets was found to be 250 mg.

Evaluation of *Trikatu* gutikas

Trikatu gutikas prepared by various methods were evaluated for hardness, friability, weight variation test, disintegration test and *in vitro* dissolution studies. The hardness of tablets were determined using Monsanto Hardness tester and The friability of tablets were determined using Roche friabilator. The disintegration test was carried out using the disintegration test apparatus and their mean disintegration time was calculated[16,17].

***In-vitro* dissolution studies**: The *In-vitro* dissolution studies were carried out for calculating the percentage piperine release using USP Type II dissolution apparatus in 0.1 N HCL media at 100 rpm. Dissolution studies were carried out up to 40 min. Samples (5ml) were withdrawn at specified time intervals and percentage drug release was calculated by using UV spectrophotometer at 343 nm.

RESULT & DISCUSSION

Quantification of active principles through modern analytical tools is essential for establishing the authenticity, creditability, prescription and usage of Ayurvedic medicines/herbal formulations. "*Trikatu* churna´ is one of the oldest and popular Ayurvedic preparations, is official in Ayurvedic formulary of India used widely for disorder of respiratory tract and digestive system. It comprised of the fruits *Piper longum*, *Piper nigrum* and rhizomes of *Zingiber officianalis*.

HPTLC methods for determination of Piperine and 6-Shogaol from Trikatu Churna was developed. The black pepper, long pepper and ginger extracts were standardized by standard plot method [Figure 1, 2] for the estimation of piperine and 6- Shogaol content.

Table 1: Composition of excipients (in mg) for Tablets of *Trikatu*

Ingredients	DC1/WG1	DC2/WG2	DC3/WG3	DC4/WG4
Trikatu Extracts	60	60	60	60
Starch	12.5	-	17.5	-
Polyvinyl pyrrolidone	-	12.5	-	17.5
Microcrystalline cellulose	120	120	120	120
Dicalcium phosphate	42.5	42.5	47.5	47.5
Magnesium stearate	5	5	5	5
Talc	5	5	5	5

Average weight of the tablets was 250 mg

Table 2: Composition of excipients (in mg) for dispersible tablet of *Trikatu*

Ingredients	DS1	DS2	DS3	DS4	DS5	DS6	DS7	DS8	DS9	DS10
Trikatu extract	60	60	60	60	60	60	60	60	60	60
Sodium	5	5	5	5	5	5	5	5	5	5
Tartric acid	5	5	5	5	5	5	5	5	5	5
CRP	12.5			25	-	-	50			16.66
CCS		12.5		-	25	-		50		16.66
SSG			12.5	-	-	25			50	16.66
MCC	60	60	60	60	60	60	60	60	60	60
Mannitol	85	85	85	72.5	72.5	72.5	47.5	47.5	47.5	47.5
Aspartame	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Magnesium stearate	5	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5	5
Menthol	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Lemon flavour	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5

Average weight of the tablets was 250 mg

The concentration of piperine present in black pepper and long pepper extracts was found to be 36.0727 % and 23.026 % w/w respectively. The 6-shogaol content in ginger extract was found to be 3.5632 %.

The weight variation of all the tablets was found to be within the pharmacopoeial limits. Hardness of all the batches of tablets was near 2-2.5 kgf. Friability of the tablets was found less than 1% w/w for all the batches. The uniformity of the contents was under the prescribed pharmacopoeial limits. Disintegration time of *Trikatu* tablets were below 15 min except batch WG3 and WG4 [Table 3]. Among all batches, DC2 considered as better as it gives less disintegration time. The dispersion time of dispersible tablets was varying with the ratio of superdisintegrants added in the formulations as shown in [Tablet 4]. The batch DS8 has less dispersible time than other formulated batches.

Among eight batches of *Trikatu* tablets (wet granulation), one batch (DC3) showed less disintegration time and better release rate [Table 5]. Similarly in case of dispersible tablets among 10 batches, one batch (DS8) showed less dispersion time [Table 6].

Table 3: Physico-chemical evaluation parameters of *Trikatu* tablets

Formulated Batch	Weight Variation (%) (n=10)	Hardness Kgf (n=5)	Friability (%)	Disintegration Time (n=6)	Content uniformity (%) (n=6)
DC1	248±6.2783	1.7±0.63	0.5628	5min36sec±21sec	98.54±0.25
DC2	249±7.6953	2.04±0.77	0.4245	4min30sec±22sec	99.38±0.36
DC3	247±6.5871	2.12±0.75	0.6186	8min24sec±34sec	98.86±0.22
DC4	248±5.8925	2.35±0.82	0.4417	13min22sec±43sec	97.72±0.32
WG1	247±6.1783	2.18±1.07	0.3589	8min43sec±99sec	99.17±0.45
WG2	249±8.0471	2.42±0.86	0.2250	7min 22sec±105sec	98.94±0.38
WG3	248±6.7673	2.26±0.74	0.3974	21min16sec±146sec	98.63±0.30
WG4	248±7.1873	2.48±0.72	0.2716	25min41sec±262sec	99.21±0.43

Values are the mean ± SEM, n = Number of tablets

Table 4: Physico-chemical evaluation parameters of *Trikatu* dispersible tablets

Formulated Batch	Weight Variation (%) (n=10)	Hardness Kgf (n=6)	Friability (%)	Dispersion Time (n=6)	Content uniformity (%) (n=3)
DS1	248±8.1737	1.98±0.75	0.1298	10min 15sec±55sec	99.15±0.34
DS2	250±7.7613	2.05±0.58	0.2612	4min 32 sec±74sec	98.85±0.28
DS3	248±7.9850	2.14±0.36	0.2360	8min42sec±46sec	99.83±0.49
DS4	249±8.3271	1.85±0.58	0.1389	8min48sec±39sec	97.94±0.67
DS5	251±7.6645	1.94±0.55	0.1340	2min35sec±32sec	98.94±0.57
DS6	248±7.8357	2.10±0.47	0.1802	6min45sec±47sec	98.45±0.40
DS7	247±7.1835	1.82±0.41	0.3895	6min12sec±40sec	99.60±0.22
DS8	248±8.3328	1.90±0.53	0.3283	1min5sec±32sec	100.2±0.32
DS9	249±8.9320	2.12±0.62	0.3407	3min15sec±38sec	99.55±0.85
DS10	249±7.3892	1.95±0.52	0.4522	2min45 sec±40sec	99.36±0.59

Values are the mean ± SEM, n = Number of tablets

Table 5: Percentage release rate of formulated *Trikatu* tablets

Batch code / Time (min)	WG1	WG2	WG3	WG4	DC1	DC2	DC3	DC4
0	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5	20.694	2.263	23.119	1.455	23.847	11.640	35.002	5.173
10	37.508	3.072	38.478	1.940	40.337	35.164	49.553	18.107
15	41.469	4.123	42.681	2.748	47.774	47.963	54.807	42.682
20	46.885	4.446	47.935	3.233	54.88	53.756	60.546	51.978
25	50.523	5.254	54.645	3.556	59.172	58.526	65.720	58.364
30	51.330	7.922	55.535	4.284	62.647	63.295	69.276	63.537
35	52.867	10.350	56.020	5.496	66.286	66.852	70.651	69.600
40	54.969	17.946	57.151	12.287	90.934	67.903	88.920	87.707

Table 6: Percentage release rate of formulated *Trikatu* dispersible tablets

Batch code / Time (min)	DS1	DS2	DS3	DS4	DS5	DS6	DS7	DS8	DS9	DS10
0	0	0	0	0	0	0	0	0	0	0
5	15.359	23.847	28.858	18.754	31.203	29.293	23.442	37.589	34.840	48.906
10	35.083	46.067	44.700	38.073	34.597	38.074	42.358	52.866	46.238	57.151
15	49.876	48.421	55.858	48.987	45.510	50.959	50.118	54.483	54.160	63.133
20	56.100	53.190	61.436	56.747	49.795	57.878	57.636	57.717	58.364	63.860
25	56.640	58.040	64.669	59.657	54.800	61.597	61.355	60.385	60.385	64.911
30	57.470	59.415	65.154	59.899	59.495	61.921	61.920	62.163	61.112	68.225
35	58.040	60.385	68.710	60.869	60.546	62.486	62.240	63.295	61.921	69.864
40	59.415	62.325	96.760	61.920	63.537	64.022	63.376	69.600	62.891	81.480

CONCLUSION

The present study indicated that the developed dosage form will have advantages over the traditional form of *Trikatu* and offer lesser dose, ease of administration for paediatrics and geriatrics and improved patience compliance. Moreover, the developed dosage will have a fixed amount of content so minimizing the risk of administration of underdosage or overdosage of the formulation which will result in desired pattern of therapeutic action.

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