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RESEARCH ARTICLE

FORMULATION AND EVALUATION OF NUTRACEUTICAL TABLET USING HERBAL DRUGS BY DIRECT COMPRESSION METHOD

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ABSTRACT

Aim: The objective of present study was to formulate and evaluate the nutraceutical tablets with different combination of herbal drugs. **Material and Method:** The nutraceutical tablet containing lactose and mannitol as diluent and containing natural drugs like clove and cinnamon which was prepared by direct compression method. The compressed formulations were subject to several evaluation parameters like appearance, thickness, weight variation, hardness and friability. **Results:** The results of all evaluation parameters of nutraceutical tablet were within the acceptable limit. Pre-compression studies of nutraceutical tablet show satisfactory results. The thickness, hardness, weight variation, and friability of nutraceutical tablet were found to in acceptable range. The *in-vitro* drug release of eugenol from optimised nutraceutical formulation was found to be 90.23%. Significant results were obtained from present study. **Discussion:** The finding of current investigation clearly found that the health promotion of the body could be done by nutraceuticals.

Keywords: Direct compression, Nutraceutical, Eugenol, *In-vitro* drug release.

INTRODUCTION

Oral route has been one of the most popular routes of drug delivery due to its ease of administration, patience compliance, least sterility constraints and flexible design of dosage forms.Tablets are defined as unit dose, temper evident solid preparations containing one or more active ingredients. Conventional drug delivery systems like tablets and capsules often dissolve rapidly in the gastrointestinal tract for absorption into the bloodstream give rise to inordinately high drug concentrations in plasma [1]. The concept of making utility of food as health promoting factor beyond its nutritional value is gaining acceptance with in public arena and among scientific community. Nutraceuticals contain health- supporting ingredients or natural components that have an ability health benefit for the body. [2] A 'nutraceutical' is a product isolated or purified from foods that is generally sold in medicinal forms not usually connected with food. A nutraceutical is bearing to have a physiological benefit or give protection against chronic disease. Term coined by Dr. Stephen L De Felice, Founder and Chairman of the Foundation for Innovation in Medicine, New Jersey, USA. Nutraceuticals sometimes referred as "functional foods", have caused heated debate because they change the traditional dividing line between food, and medicine. [3] A nutraceutical is "any non-toxic food component that has scientifically proven health benefits, including disease treatment or prevention." The functional component of the food must be standardized in the nutraceutical product and generate under good manufacturing practices (GMPs). [4] Increased public demand, trends in demography, socio-economic scenario. More researches and studies, nearly two thirds of the world's 6.1 billion people rely on the healing power of plant based materials for many reasons-availability, affordability, safety or their belief in traditional affordability, safety or their belief in traditional cures Medical benefits of food have been investigated for thousands of years. Modern nutraceutical industry began to develop in Japan during the 1980s. Various benefits of nutraceuticals are may help us live longer, may increase the health asses of our diet, help us to abstain particular medical condition, it have a psychological advantage from doing something for oneself, and may be sensed to be more "natural" than traditional medicine and less likely to produce unpleasant side-effects. [3, 5]

The nutraceuticals normally contains required amount of lipids, protein, carbohydrates, vitamins, minerals and other necessary nutrients depending upon their emphases. Nutraceuticals in the market contains both traditional foods and non-traditional. When a supplement tablet is ingested, the body must digest and absorb the nutrients. Nutraceutical may include a whole area of products like isolated nutrients, dietary supplements, herbal products and other processed foods. [5] The growing disapproval among the patients about the synthetic therapeutic agents and affect about their toxicological profile gave birth to the "Dietary Supplements Health and Education Act" (DSHEA) in USA in 1994. [5, 6] The concept behind the mode of action of nutraceutical dosage form is to provide functional benefits by enhancing the supply of natural building blocks. It works in to two ways that is to minimize diseases sign or to improve body performance. [2, 3]

Clove consists of dried flower buds of Eugenia caryophyllus, family Myrtraceae. The cloves on drying become perfectly crimson or brownish-black in colour. Clove is used as a dental analgesic, carminative, stimulant, flavouring agent an aromatic and antiseptic. Cinnamon consist of dried inner bark of shoots of coppiced trees of Cinnamon zeylancium Nees. Bark is

used as carminative, stomachic and mild astringent. [6] It has been used as an expectorant and demulcent. It is also used as an antispasmodic. The major diseases for prevention and or treatment of which, nutraceuticals have been associated are heart diseases, cancer, hypertension and diabetes.

MATERIALS AND METHOD

Materials

Clove, cinnamon were received from local market. All other ingredients such as mannitol, magnesium stearate and talc were purchased from Central Drug House (CDH) New Delhi, India. All ingredients used were of analytical grade.

Method

Nutraceutical tablets containing clove and cinnamon were prepared by direct compression method. Other ingredients like lactose was used as diluent, magnesium stearate as lubricant and talc as glidant. All the excipients along with API weighed as shown in Table 1 and passed through sieve no. 20. Then, all ingredients were mixed following geometric mixing excluding glidant and lubricant thoroughly for 15min.[4] The powder blend was thoroughly mixed with talc and magnesium stearate and compressed into a 400mg tablet using single rotatory punching machine (KI-150, Khera Instruments Ltd. New Delhi, India).

Table 1: Formulation table of nutraceutical tablet 400mg

Ingredients (mg)	F1	F2	F3	F4
Clove	100	-	100	-
Cinnamon	-	100	-	100
Lactose	290	290	-	-
Mannitol	-	-	290	290
Sodium Sachrine	2	2	2	2
Talc	4	4	4	4
Magnesium Stearate	4	4	4	4

Evaluation of Nutraceutical Tablets

Pre-compressional studies of powder blend

In development of new dosage form preformulation study is the prior step in the potential drug development. It is the principal investigation in the drug development to obtained information on the known properties of compound and the proposed development schedule. So, this preformulation investigation may merely confirm that there are no significant barriers to compound development. Following pre-compressional parameters were studied like angle of repose, bulk density, tapped density, compressibility indices etc.

Angle of repose

It is the maximum angle that can be obtained between the freestanding surface of powder heap and the horizontal plane. It was determined by using fixed funnel method. Specified amount of powder drug was transfer to the funnel keeping the orifice of the funnel blocked by thumb.When powder was cleared from funnel then measured its angle of repose and measured in θ [7].

Angle of repose (θ) = $\tan^{-1}$ h/r

Bulk density

It is the ratio of bulk mass of powder to the bulk volume. It is denoted by ρ_b. Bulk density is used to find out homogenecity.

Bulk density (ρ_b) = M/Vb

Where, M is the mass of the sample, Vb bulk volume

Tapped density

It is the ratio of the weight of powder to the minimum volume occupied in measuring cylinder. Tapped density is determined by placing a graduated cylinder containing a known mass of drug or formulation on a mechanical tapper apparatus which is operated at fixed no. of taps (1000) until the powder bed reached a minimum volume. [8]

Tapped density (ρt) = weight of powder blend/Minimum volume occupied by cylinder

Compressibility Indices

a. Carr's index

Based on the apparent bulk density and the tapped density, the percentage compressibility of the powder mixture was determined by the following formula.

Carr's index = Tapped density-Bulk density × 100/ Tapped Density

b. Hausner's ratio

It is an indirect index of ease of measuring of powder flow. Lower Hausner's ratio (<1.25) indicates better flow properties than higher ones (>1.25). [10]

Hausner's ratio = Tapped density/ Bulk density [7, 8]

Post-compressional studies of prepared nutraceutical tablets

The nutraceutical tablets were evaluated for various parameters after consideration of preformulation to overcome errors during formulation preparation. These are like appearance, thickness, weight variation, hardness and friability. All the evaluation parameters of all formulations are given in Table 2.

Physical appearance

The general appearance of tablet was studies visually in shape, color, texture and odour.

Thickness

The tablet thickness was calculated by Vernier calipers. Tablet was put in between two jaws vertically and measured thickness and 6 tablets were used for this test and expressed in mm. [8]

Weight variation

Weight variation test is run by weighing 20 tablets individually, calculating the average weight and comparing individual tablet weight to the average. The weight variation test would be a satisfactory method of determining the drug content uniformity of tablets.

Hardness

Hardness also termed as tablet crushing strength. The tablet hardness was determined by Monsanto hardness tester. The tablet was placed lengthwise between upper and lower plunger and force applied by turning a threaded bolt until the tablet fractures and measured hardness of tablet in Kg/cm^2 [7, 8].

Friability

It is determined by Roche friabilator, subjects a number of tablets to combined effects of abrasion and shock by utilising a plastic chamber that revolves at 25 rpm, dropping tablet from inches distance operated for 100 revolutions. Preweighed tablets were dusted and re-weighed and according to standard limit friability should be less than 1%. It is calculated by formula-

% Friability = Initial weight – Final weight / Initial weight. [9]

***In-vitro* drug release-** Dissolution profile of eugenol was determined at 37 ± 0.5°C at a stirring rate of 100 rpm using the USP dissolution apparatus II in 900 ml of simulated gastric fluid (0.1 N HCl) . Various aliquot samples were withdrawn with replacement simulated fluid of same amount at 5, 10, 15, 30, 45, and 60 min respectively. Samples were filtered using whatmann filter paper and taken absorbance at wavelength of 366 nm by UV spectrophotometer. [10]

RESULTS AND DISCUSSION

The nutraceutical tablet of clove and cinnamon was formulated by direct compression method. This technique was used for conventional from nutraceutical tablet which minimize processing steps and eliminated wetting and drying process. The physiochemical property show satisfactory results by nutraceutical tablet which are within the range of prescribed standards required for investigation of present study [7].

Pre- compression studies of powder blend

The powder blend was evaluated for various parameters and their results are shown in Table 2. The evaluation parameters such as angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio were found to be 21.12±0.11 to 27.46±0.12 (Θ),0.4071±0.21 to 0.4741±0.32 g/ml, 0.4132±0.17 to 0.4965±0.028 g/ml, 11.00±0.12 to 14.17±0.39, 1.11±0.012 to 1.17±0.13 respectively. After evaluation of preformulation parameters it showed that there is no presence of moisture in power and showed uniformity of powder blend [11]. After study of flow rate it conclude that powder blend exist optimum proportion that leads to maximum flow rate. So the result showed that the powder have good flowing property which does not cause affect the process of tablet punching. [7, 10]

Table 2: Pre compression studies of nutraceutical tablet containing clove and cinnamon

Pre-Compression Parameters	F1	F2	F3	F4
Angle of repose (θ)	21.12±0.11	24.32±0.12	27.46±0.12	22.14±0.17
Bulk Density (g/ml)	0.4649±0.12	0.4741±0.32	0.4541±0.21	0.4071±0.21
Tapped Density (g/ml)	0.4262±0.08	0.4132±0.17	0.4587±0.023	0.4965±0.028
Carr's Index	12.19±0.14	13.04±0.16	11.00±0.12	14.17±0.39
Hausner's Ratio	1.14±0.16	1.16±0.021	1.11±0.012	1.17±0.13

Table 3: Post- compression studies of nutraceutical tablet containing clove and cinnamon

Post- Compression Parameters	F1	F2	F3	F4
Thickness (mm)	1.2±0.1	1.2±0.21	1.2±0.21	1.2±0.21
Hardness (kg/cm^2)	5.5±0.2	4.8±0.11	4.31±0.21	5.21±0.033
% Weight Variation	0.399±0.021	0.399±0.034	0.397±0.012	0.398±0.019
% Friability	0.23±0.023	0.31±0.0.12	0.14±0.045	0.22±0.011
% *In- vitro* drug release	90.23	86.88	88.64	85.34

Table 4: Angle of repose as an indication of powder flow property [9]

Angle of repose	Type of flow
< 20	Excellent
20-30	Good
30-40	Passable
> 40	Very passable

Table 5: Carr's index as an indication of powder flow [15]

Carr's index (%)	Flow ability
5-15	Excellent
12-16	Good
18-21	Fair to passable
23-35	Poor
33-38	Very poor
> 40	Extremely poor

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Table 6: Hausner's ratio [15]

Hausner's ratio	Flow ability
< 1.25	Good
> 1.25	Poor

Post-compression study

The result from different physical parameters like thickness, hardness, weight variation, and friability of tablets was shown in table 3. The presence of active pharmaceutical ingredients, filler, glidant and lubricant is sufficient for provided bulk to the tablet which decrease risk during punching. The thickness, hardness, weight variation, and friability of nutraceutical tablet were founded to be in acceptable limit. It shows that the herbal drugs containing nutraceutical tablets have satisfactory disintegration profile due to their hardness within range of standard limit [12].

Physical appearance

The general appearance of tablet was found to be round in shape, brown in color, smooth texture, and odourless.

Thickness

The thickness of clove and cinnamon containing nutraceutical tablet was found to be 1.2± 0.1cm. It is depends upon the size of die and punches or a function of die fill and compression force. [3, 13]

Weight variation

The weight of 20 tablets was measured and it was found to be 0.397±0.012 to 0.399±0.034 for all formulations respectively. All the nutraceutical tablet containing clove and cinnamon passed weight variation test as the average percentage weight variation was within the USP limits of ±5%.

Hardness

The hardness of conventional nutraceutical tablet was found to be 4.31±0.21kg/cm^{2}to 5.21±0.033 for clove and cinnamon containing formulations. Mannitol containing formulation code showed more friable and less hardness than lactose as diluent. It is depend upon the compression force of punching machine and showed that it is sufficient for tolerating mechanical strength.Tablets showed sufficiently hard to resist breaking during packaging, shipment, and normal handling. [12, 13]

Friability-Friability of all formulations was found to be0.14±0.045 to 0.31±0.0.12 %.The friability of clove and cinnamon containing tablet was found to be in acceptable limit i.e. less than 1%. There no capping problem occurs in the tablets so it could be considered for commercial use. It produced no loss during shipping process [14].

***In-vitro* drug release-** The in-vitro drug release of eugenol from all nutraceutical tablets in 0.1 HCL was found to be 85.34 to 90.23%respectively in 1 h. The release of eugenol as a therapeutic agent from nutraceutical tablet is produce maximum release in F1 formulation due to presence of more amount of eugenol in clove than cinnamon as a main chemical constituent.Basically, eugenol is main chemical constituent of clove so, it provide more beneficial effect to the cinnamon containing tablets. The release profile of nutraceutical tablet was given in figure 1.[15]

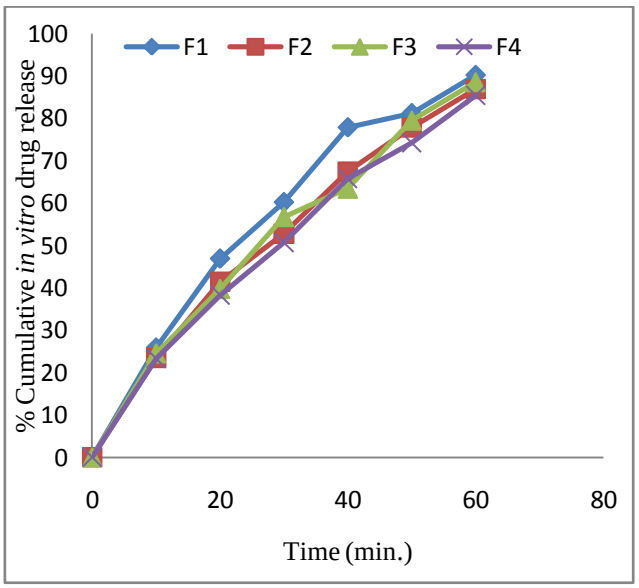

Figure 1: *In vitro* drug release profile of all formulations of nutraceutical tablets

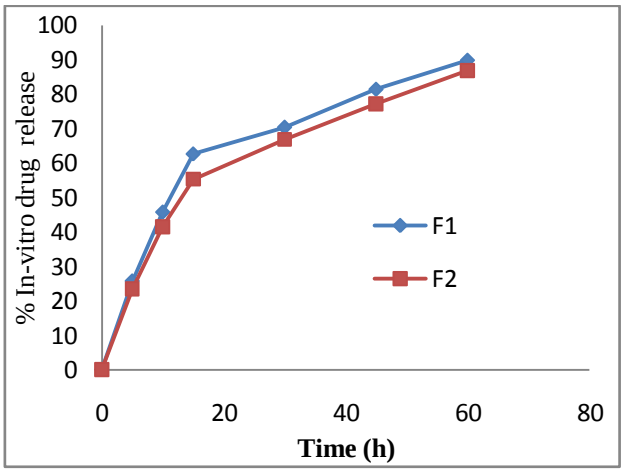

Figure 2: The in-vitro drug release profile of clove and cinnamon containing nutraceutical tablet

CONCLUSION

From the above study, we conclude that the nutraceutical tablets were prepared by direct compression method and gave satisfactory and acceptable result. Conventional tablet of nutraceutical shows immediate drug release due to direct compressed tablet. The formulation containing clove could be more beneficial as an analgesic due to the presence of eugenol than cinnamon containing tablet. From the above research work it was concluded that herbal nutraceutical tablet prepared in the form of cost effective tablet to minimize patients compliance in regarding supressing side effects and enhancing positive effects on the body.

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