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Manufacturing and Evaluation of Formulated Nutraceutical Capsules Using Natural Extracts

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Abstract
Nutraceuticals are available in the form of isolated nutrients, herbal products, processed foods and dietary supplements in the form like capsules, tablets, etc. Manufacturing of nutraceuticals into capsules and tablets is a tedious process and it should be carried out under carefully controlled conditions. The objective of this study was to formulate and manufacture a nutraceutical product and evaluate the manufactured product to its quality. The formulated nutraceutical capsules containing Mangosteen extract powder and Grape seed extract were blended and filled into capsules. They were subjected to several evaluation parameters like pre-compression and post-compression studies such as physical appearance, weight variation, hardness and friability. The results of all evaluation parameters of the formulated nutraceutical capsule were within the acceptable limit. Pre-compression studies also had shown satisfactory results. The thickness, hardness, weight variation and friability were found to be in acceptable range. The finding of the present study assures that the formulated nutraceutical capsules meet the quality standards.

Keywords: Evaluation, Nutraceutical Capsules, Natural Extracts

1. Introduction
Nutraceutical, a portmanteau of the words 'nutrition' and 'pharmaceutical', is a food or food product that reportedly provides health and medical benefits, including the prevention and treatment of disease. Currently nutraceutical products have been emerging with high nutritious content. They are purported to provide extra health benefits, in addition to the basic nutritional value found in foods which are highly beneficial to human health (Clare M. H., 2005) [1].

Thousands of research has been conducted in the field of nutraceuticals and are offering various studies that revealed, these products are extremely active, have profound effect on cell metabolism, immune system, ageing, cancer, and often have little adverse effect (Gil, H; Ines, H; Patrick, A. B, 2003) [2]. This field is showing signs of more and more research and has yielded modern approaches in the prevention and management of chronic diseases using innovations of herbal remedies, food additives and non-traditional plants as functional foods.

With increasing health awareness, and the shift towards preventative health care and increased regulatory clarity, India's future in nutraceuticals industry looks promising, for both manufacturers and consumers nutraceuticals market has grown from $ one billion in 2008 to $1.8 billion in 2013, is likely to cross $ two billion in 2014 and is expected to top $ four billion by 2018. As they posses multiple therapeutic effect with lacking of unwanted effects hence attract more consumer interest. Nutraceutical market is seeing tidal growth mainly in United States, India and European countries. Global nutraceutical market is estimated as USD 117 billion (Shinde, N., 2014) [3].

Nutraceuticals are available in the form of isolated nutrients, and specific diets to genetically engineered foods, herbal products and processed foods, dietary supplements in the form like capsules, tablets, etc (Bhowmik, D *et al*., 2013) [4].

Some examples of nutraceutical extracts are lycopene from tomatoes, β-glucans from oat bran, isothiocyanates from cruciferous vegetables, lutein from kale Curcumin from turmeric, isoflavones from soybeans, catechins from tea, ellagic acid from grapes, Anthocyanates from redwine, capsaicinoids from pepper fruit, lignans from flax (Raj. K. Keservani *et al*., 2010) [5].

When these compounds from nutraceuticals are to be extracted and preserved for long term usage or commercial operations the sources have to be harvested, cleaned, preserved, packaged and stored so that the benefits are not compromised and are made bio-available when needed. Storing and packaging of these extracts is challenging due to the possibility of microbial contamination, pesticide residues, environmental conditions and extra care must be taken so that the product stability, quality, safety, variety, and convenience for consumers is ensured (Pathak. V. Y., 2011) [6].

Recently a convenient method of storage is in the form of granules (pills and tablets) out of which capsuling has been regarded as best and is the most versatile of all dosage forms in which one or more medicinal and inert ingredients are enclosed in a small shell or container usually made of gelatin or gluten (Reddy, V B., Deepthi A., Ujwala, P 2012) [7]. HPMC capsule is used in the formulations of extracts which are naturally occurring polymer cellulose and are used as coating polymer, bio-adhesive, in solid dispersion to enhance solubility and also as a binder in the process of granulation hence making it safe for normal consumption in humans (Moawia, M; Tabakha A.L., 2010) [8].

Manufacturing of nutraceuticals into capsules is a tedious process and it should be carried out under carefully controlled condition. It is important to monitor particle characteristics such as (composition, charge and size) to produce particular physicochemical and functional properties (such as optical, rheological, stability and release) (Garti, N; McClements J D., 2012) [9].

For effective quality of a product the manufacturing unit has to work under close monitoring conditions. The environmental conditions and the equipments in manufacturing must not interact with the formulated product and hence the proper manufacturing of nutraceuticals under required cGMPs (Current Good Manufacturing Practices) that will mandate appropriate quality control and process control testing from incoming materials to finished goods. It definitely increases the credibility of the products, and certainly provide additional leverage towards the safety and efficacy of the products being manufactured and catered to the customers (Nath, K. D., Yeevani, S. C., 2014) [10] according to the Food Safety and Standards Authority of India.

The packaging and sealing of these products must be tightly controlled and thereby providing a shelf stable, contaminate-free environment for the product, with enhanced quality and does not account for any nutrient loss (Khalsa S. *et al*., 2003) [11]. Thus the objective of the study is to formulate and manufacture a nutraceutical product and evaluate the manufactured product.

Materials and Methods

Materials

Ingredients such as mangosteen extract powder and grape seed powder were selected by comparing the COA. All other ingredients such as magnesium stearate and talc were purchased from Central Drug House (CDH) New Delhi, India. All ingredients used were of analytical grade.

Method of Manufacturing

Formulated Nutraceutical capsules containing Mangosteen extract powder and Grape seed extract were combined and filled by capsule filling machine. Then, all ingredients were mixed following geometric mixing excluding glidant and lubricant thoroughly for 15min. The powder blend was thoroughly mixed with magnesium stearate using octagonal blender machine (RC Engineering 50kg capacity) it is followed by granulation (Fluid bed dryer alliance 120kg). The flow ability and density of spray-dried particles were improved after granulation. Capsules produced by direct compression of granules showed lower crushing strength than the ones obtained from non-granulated material. Then it is filled into a 500mg capsule using semi-automatic capsule filling machine (Anchor Mark SA9, 8000/shift 12hrs). And it was polished by capsule polishing machine (Pharmachem industries). After it gets polished, it was counted by capsule counting machine (Anchor Mark SA9), and then it was sealed by induction sealing (Bhuvaneshwari - NA). At last packing was done manually.

Evaluation of Nutraceutical Capsules

Pre-compressional studies of powder blend

In development of new dosage form pre formulation 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 pre formulation 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.

$$\text{Angle of repose } (\theta) = \tan^{-1} h/r$$

Table 1: Angle of repose as an indication of powder flow property

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

Bulk density

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

$$\text{Bulk density } (\rho b) = M/Vb$$

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 caps (1000) until the powder bed reached a minimum volume.

$$\text{Tapped density } (\rho t) = \text{Weight of powder blend/Minimum volume occupied by cylinder}$$

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.

$$\text{Carr's index} = \text{Tapped density-Bulk density} \times 100/ \text{Tapped Density}$$

Table 2: Carr's index as an indication of powder flow

b. Hausner's ratio

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

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).

Hausner's ratio = Tapped density/ Bulk density

Table 3: Hausner's ratio

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

Post-compressional studies of Formulated nutraceutical capsules

The nutraceutical capsules were evaluated for various parameters after consideration of pre-formulation to overcome errors during formulation preparation. These are appearance, thickness, weight variation, hardness and friability.

Physical Appearance

The general appearances of capsules were studies visually in shape, colour, texture and odour.

Weight Variation

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

Hardness

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

Friability

It is determined by Roche friabilator, subjects a number of capsules to combined effects of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm, dropping capsule from inches distance operated for 100 revolutions. Pre weighed capsules 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.

Results and Discussion

Pre- compression studies of powder blend

The powder blend was evaluated for various parameters and their results are shown in Table 4. The evaluation parameters such as Angle of repose, Bulk density, Tapped density, Carr's index and Hausner's ratio were found to be 26.5 (Ɵ), 0.66 g/ml, 0.76 g/ml, 13.5, 1.15 respectively. All the evaluation parameters of formulated nutraceutical capsules are given in Table 4.

Table 4: Pre-Compression studies of Formulated nutraceutical capsule containing mangosteen and grape seed

Pre-Compression Parameters	Results
Bulk Density (g/ml)	0.66 ±0.00577
Tapped Density (g/ml)	0.76 ±0.00577
Carr's Index	13.5±0.08165
Hausner's Ratio	1.15±0.00816
Angle of Repose (θ)	26.5±0.05

Bulk Density

The Bulk density of Formulated Nutraceutical capsules is in the range of 0.66 g/ml and it was calculated depending on the mass of the sample and its bulk volume. According to the particle size distribution, particle shape and the tendency of particles to adhere together the bulk density varies. Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment.

Tapped Bulk Density

Tapped Bulk Density of the Formulated Nutraceutical capsules is 0.76 g/ml. The tapped density is an increased bulk density attained after mechanically tapping a container containing the powder sample.

Angle of Repose

Angle of Repose of Formulated Nutraceutical capsule determined by Fixed Funnel Method is 26.5. As the determined value is in between the range of 20-30 in the standard scale, it indicates the Formulated Nutraceutical Capsules has good powder flow property. Angle of repose is a characteristic related to inter particulate friction or resistance to the movement between the particles **(**Singh, I; Kumar, P., 2012) [12]. It is represented in the figure (1).

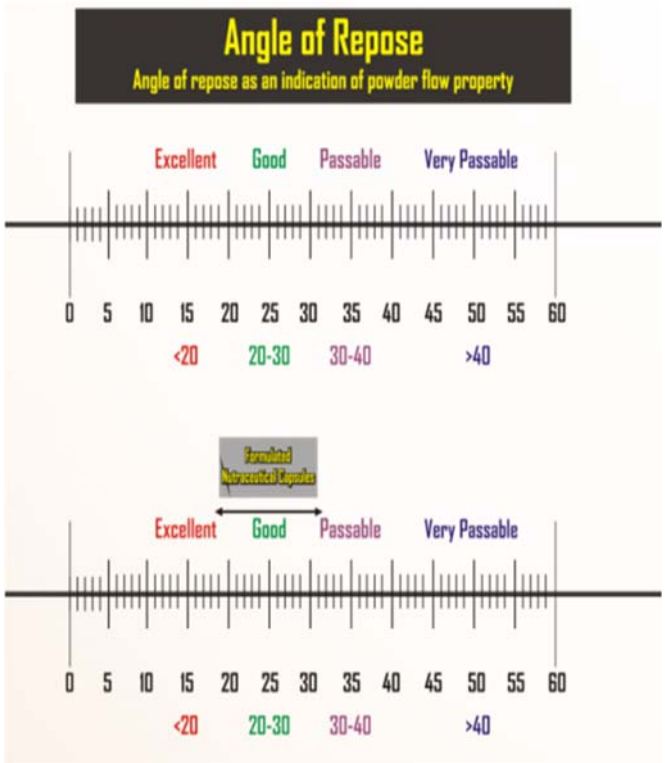

Fig 1: Angle of Repose

Carr's Index

Carr's Index of Formulated Nutraceutical Capsules is 13.5 and it measures the propensity of a powder to be compressed. As the determined value is in between the range of 11-15 in the Carr's Index standard scale, it indicates the Formulated Nutraceutical Capsules has good powder flow. Material is less compressible and has more flow ability. As the Formulated Nutraceutical capsule has free flowing powder, the interactions are less significant, and the bulk density (0.66 g/ml) and tapped density (0.76 g/ml) are closer in value. It is represented in the figure (2).

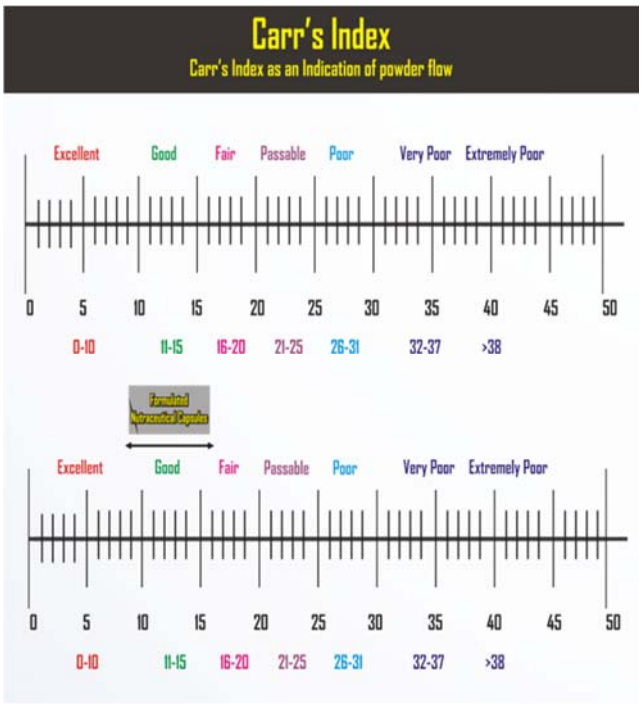

Fig 2: Carr's Index

Hausner's Ratio

Hausner's ratio of Formulated Nutraceutical capsule is 1.15. As the measured value is less than 1.25, it's indicates better flow properties. The Hausner's ratio which is calculated by tapped density and bulk density is an indirect index of ease of powder flow. It is represented in the figure (3).

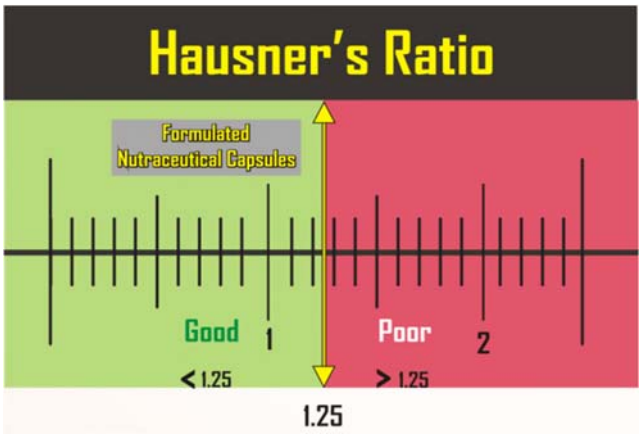

Fig 3: Hausner's Ratio

After evaluation of pre-formulation parameters it showed that there is no presence of moisture in powder and showed uniformity of powder blend. 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 capsule filling (Leon, 2009; Bhope, 2011)

Post-compression study

The result from physical parameters like hardness and friability of capsule was shown in table 5. The presence of active Nutraceutical ingredients, filler, glidant and lubricant is sufficient for provided bulk to the capsule which decrease risk during filling.

Physical appearance

The general physical appearance of the capsules were found to be unlocked cylindrical shape, dark green in colour, smooth texture and no trace of any foreign odours.

Hardness: The hardness of conventional nutraceutical capsule was found to be 6 kg/cm2 formulated nutraceutical product containing formulations. It is depend upon the compression force of punching machine and showed that it is sufficient for tolerating mechanical strength.

Friability: The Friability of the formulations was found to be 0.0010 %.The friability of formulated nutraceutical product containing capsule was found to be in acceptable limit i.e. less than 1%. Hence there will be no occurrence of capping problem in the capsules so it could be considered for commercial use.

Weight variation

The weight of 20 capsules was measured and it was found to be 0.499±0.00096. All formulated nutraceutical capsules passed weight variation test as the average percentage weight variation was within USP limits of ±5%.

Table 5: Post-compression studies of nutraceutical capsule containing mangosteen rind and grape seed

Post-Compression Parameters	Results
Hardness (Kg/cm^2)	6 ±0.05
% Friability	0.0010
% Weight variation	0.499±0.00096

The hardness, friability and weight variation of Formulated nutraceutical capsules were founded to be in acceptable limit. It shows that the Nutraceutical capsule containing natural extracts have satisfactory disintegration profile due to their hardness and friability within range of standard limit.

Conclusion

From the above study we conclude that our Formulated Nutraceutical capsules gave satisfactory and acceptable results. Capsules offer key advantages for formulators, manufacturers, physicians, patients, and health-supplement consumers. These advantages can significantly increase the likelihood of success and over-the-counter drug products and dietary supplements. The flow ability characteristic of a powder is directly related to both the physical properties of the material itself, as well as the specific processing conditions in the handling system**.** Poor flow leads to wastage, machinery maintenance problems and downtime, with associated costs. There are a number of test methods for evaluation of flow behaviour of powders (pre compression and post compression tests). A good manufacturing practice provides the system that assures proper design, monitoring, and control of manufacturing processes and facilities. Adherence to these regulations assures the identity, strength, quality, and purity of supplementary products by requiring that manufacturers adequately control manufacturing operations. This includes establishing strong quality management systems, obtaining appropriate quality raw materials, establishing robust operating procedures, detecting and investigating product quality deviations, and maintaining reliable testing laboratories. This formal system of controls at a nutraceutical company, if adequately put into practice, helps to prevent instances of contamination, mix-ups, deviations, loss of nutrients, failures, and errors. This assures that the

Formulated Nutraceutical Capsules meet their quality standards.

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