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DISINTEGRATION, FRIABILITY, AND WEIGHT UNIFORMITY TESTS OF HERBAL TABLETS OF INDIAN MARKET

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ABSTRACT

In recent years, trend of herbal medicines has been increased. Consequently, numerous herbal formulations have been introduced in market by Asian and European countries. There is few or no quality control exercise of herbal drugs. Tablet disintegration, friability, and uniformity of weight characterisations are used in modern pharmaceutical research, development, and quality control. Here, we have performed disintegration, friability, and uniformity of weight tests of various herbal tablets. All tablets samples under study were almost disintegrated within 30 min., but two tablet samples were disintegrated after 40 min. Good result acceptance was noticed for friability and tablet uniformity test of these herbal tablet samples. At significant level $p \leq 0.05$ no difference was noticed for disintegration and friability tests. But, variation within twenty tablets weight has been noticed for uniformity of tablet test, which was significantly different at $p \leq 0.05$, even though overall test was complied. To ensure the quality and efficacy of herbal products, quality control, including the disintegration, friability, and weight uniformity, are therefore recommended, even though these products are not regulated under the Pharmaceutical Affairs Law.

Keywords: Tablet disintegration, Tablet friability, Tablet uniformity of weight; Quality control

1. INTRODUCTION

In the recent years trend of herbal medicines has been increased. Herbal medicines trends are growing quickly and became a major part of the economy (60 million USD) [1,2]. The literature reveals that even today in Western medicine, and despite progress in synthetic chemistry, plants are the backbone of primary health care and approximately 80% population still relies upon plants [1]. It is a well known fact that India and China are hubs of herbal drugs. Same time, various herbal products, pharmaceutical formulations have been introduced in the market by Asian and European countries [1-7]. Consequently, adulteration, misbranding, and poor quality control management of herbal drugs at its apex point [8-12]. There is few or no quality control exercise of herbal drugs [1,7,9]. To ensure the quality and efficacy of herbal products, it is important that the correct original plant species and basic quality control tests should be used, so that products are manufactured appropriately, and that consistent quality and composition are assured [9-15]. However, these measures alone are not sufficient for quality control. Disintegration, friability, and uniformity of weight tests have been considered as major quality control tests performed by each good manufacturing practice (GMP) certified company after the production of drugs [11-18].

Disintegration is defined as complete when the tablet appears to have no palpable firm core [19]. Disintegration is itself a major part of quality control, same time it is a precursor to dissolution [11,13]. In vitro disintegration behavior ensures the safe and reliable dose form release. Tablet disintegration is different for different tablets depend upon the target of drug [17]. Disintegration test decides the drug absorption rate through the targeted drug delivery (e.g. mouth, stomach, and intestine). Only, disintegration and dissolution factors decide the effective time of the drug. Disintegration of herbal drugs is very crucial due to the presence of multiple ingredients and unpredictable disintegration time [9-14]. Poor disintegration can lead to poor drug delivery and these things may defame even a very good drug. In commercial produced tablets, the active ingredient is very low (1-10 mg), which has critical impact on any small variation with tablet weight uniformity [13,17]. Though, herbal drugs tablets having multiple matrixes having significant variation with a variation of tablet weight [1,2].

Tablet friability is the propensity of a tablet to loosen constituent particles due to mechanical shock, friction, and abrasion [5,7,9,11,20]. It is the most important parameter because high friability leads to

unacceptable loss of drug content during downstream processing, storage, and handling [9,11,13-17]. Low friability can cause the potential loss in therapeutic effects due to damage of tablet quality. In reality, these three tests are the routine tests carried out to supplement the other test, including the tablet tensile strength, crushing strength, and indentation hardness [9,11]. In herbal drugs, tablets, the composition of whole mass of plant (e.g. leaf, stem, bark, root) may adversely affect the friability of tablet [5,9].

Ideally, these three tests (disintegration, friability, and uniformity of weight) could have been used extensively to facilitate tablet product development [5,7,9]. These tests have been considered as the deciding factor whether as batch of tablet will fail or passes the acceptance criterion [19-21]. Non compliance of these three tests triggers a chance of change in formulation or compaction parameters (speed, pressure and tool design). Essentially, these three tests have been mostly used as a tool for quality control [17-21].

To maintain the quality of herbal drugs, successful integration of disintegration, friability, and uniformity of weight tests is critical. Therefore, the goals of this research were to check the disintegration, friability, and uniformity of weight of thirteen herbal drugs and to establishment of correlations between disintegration and friability studies at a significant level ($p \leq 0.05$). To our knowledge, this is the first study to perform disintegration, friability, and uniformity of weight tests of herbal or health food products containing herbal content.

2. MATERIAL AND METHODS

2.1. Herbal drugs collection

Eleven herbal drugs were collected from two different sources as mentioned in Table -1. As per the Ayurvedic Pharmacopoeia of India (API) all these herbal have multiple applications in Indian medicine system (Table -1). All these herbal products have multiple ingredients and multiple applications (Table -1).

2.2. Disintegration test

In the disintegration studies six tablets were tested according to the USP <710> standard method using a MAC model 702/3151 apparatus (Macro Scientific New Delhi, India) [19]. The time necessary for each tablet to disintegrate at 37 ± 0.5 ºC in DI water to the point where it was small enough to pass through the mesh at the bottom of the basket was recorded. According to the FDA guideline, a time of less than 30 s is required, for a product to be considered [19].

2.3. Friability test

Tablet friability was determined according to USP <1216> protocol [20]. In brief, twenty tablets were weighed (W_1) and

placed into the friabilator (MAC model 702/3152 apparatus, Macro Scientific New Delhi, India) that was rotated at 25 rpm for 4 min. The tablets, then were reviewed after removal of fines (W_2), and the friability was calculated as: % Friability = 100 x $(W_1-W_2)/W_1$ [20].

2.4. Uniformity of weight

Tablet uniformity of weight was determined according to USP <2091> protocol [21]. All the activities were performed on Electronic Weighing Balance (Shimadzu, Japan, Mode AX200). In brief, twenty tablets were weighted once and average weight (W_1) was noticed. These twenty tablets were weighted individually and weight (W_2) was noticed. The % of uniformity of weight was calculated as: % uniformity of weight = 100 x $(W_1-W_2)/W_1$ [21].

2.5. Statistical Analysis

All the quantitative tests were performed in triplicates. The results are presented as ±mean of triplicate observations. All the data were analyzed using the Excel Window 8 version software. Statistical analysis was done by analysis of variance (ANOVA) followed by Tukey's test. $p \leq 0.05$ was considered to be statistically significant.

3. RESULTS AND DISCUSSIONS

WHO data indicating that the world is moving towards traditional medicines and same time main focus of medicines manufactures is to increase efficacy, safety and cost effectiveness of herbal medicines [19-21]. In the current study, the observed results of the studies have been tabulated under Table -2. It was noticed that at $p \leq 0.05$ results statistically significant. Noncompliance of two results was noticed of supplier S2. The results of Trifala Guggul and Keshar Guggul were not complied with the API, USP, BP and IP. Uniformity of weight test was within limit 5 %, though significant difference was noticed in individual tablet weight. Friability test was within the limit (not more than 1.5 %), and no significant difference was noticed (Table - 2).

These preliminary studies were performed with an intention to check the response of herbal tablets considering three main parameters (disintegration, friability, and uniformity of weight) of quality control described in the pharmacopeia [19-22]. There is a direct relationship between therapeutic activities and these tests. These tests are not yet obligatory to be performed in the case of herbal drugs, but these tests are the demand of time to uplift the quality standard of herbal drugs in world market [22]. Scientific background, including basic quality control studies may manage the rumors or misinformation or defaming of herbal drugs. Good quality control exercises, including these tests in an herbal pharmaceuticals sector may be a good

answer for those who are always calming public safety as its reason, though the truth is the protection of their monopoly of healthcare market [23]. It is true that based on the WHO guidelines; the active pharmaceutical constituents of herbal drugs should be analyzed by standard methods before the accomplishment of clinical trials [24,25]. Same time it is not an easy task because herbal drugs possess a variety of complex constituents [24-28]. So, basic or preliminary studies, including harness, dissolution, disintegration, friability, and uniformity of weight are beneficial for quality control of herbal drugs. These quality control parameters are the determining factors in obtaining tablets that are suitable for an administration.

Friability is the lack of resistance to abrasion, when subjected to mechanical action. The friability determined for the herbal tablets under study was less than 1.5%, within the acceptable limit of USP/IP/BP. This ensured that the tablets were produced with appropriate characteristics of cohesion between the particles, to withstand the impact of manipulation and transport. At significant level, no difference was noticed, which confirms the good formulation of tablets under study.

As per USP/BP/IP tablets must be sufficiently hard to resist breakage during packaging, handling and transport. However, tablets should be able disintegrate after they are administrated, or breakable while the partial dose is required. Disintegration test was within the limit (not more than 30 min) for nine tablets and a significant difference was noticed among different tablets. Trifala Guggul and Keshar Guggul were not within the limit (not more than 30 min) for disintegration test (Table - 2). In recent studies, based on formulations of herbal tablets, disintegration time up to 60 min has been accepted. In the present study two Guggulu formulations have higher time between 42 to 45 min which may be due to the higher content of the gum material present in tablets. Immediate-release tablets must be disintegrated within 10 min and average and slow-release tablets must be disintegrate within 30 and 60 min respectively. Disintegration is a deciding factor for the release of active ingredients present in the tablets/ capsules etc.

Table 1: Medicinal applications of different herbal drug samples under study [2].

S.No.	Tablet Name	Ingredients	Medicinal applications
1.	Mahashankh Vati	Piper longum), Plumbago zeylanica, Baliospermum montanum, Purified Mercury, Purified Sodium Biborate, Sodium Carbonate, and Potassium Carbonate.	Bloating of gas, Acidity, Indigestion, Diarrhea, Peptic Ulcers, Bowel Syndrome and Ulcerative Colitis.
2.	Kutazghan Vati	Connessi, Holarrhena antidysenterica and Aconitum heterophyllum.	Antidiarrheal, Antidysenteric, Antimicrobial, Anthelmintic, Astringent, Aam Pachak, Antiamoebic and Haemostatic
3.	Chandraprava Vati	Camphor, Acorus calamus, Cyperus rotundus, Andrographis paniculata, Tinospora cordifolia, Cedrus deodara, Curcuma longa, Aconitum heterophyllum, Berberis aristata, Piper longum, Plumbago zeylanica, Coriandrum sativum, Terminalia chebula, Belliric, Terminalia bellirica, Emblica officinalis Gaertn, Piper chaba, Embelia ribes, Piper chaba, Zingiber officinalis, Piper nigrum, Purified Copper Iron Sulphate, Hordeum vulgare, Rock salt, Operculina turpethum, Baliospermum montanum, Cinnamomum tamala, Cinnamomum zeylanicum, Elettaria cardamomum, Shilajatu and Guggulu.	Urinary tract infection, constipation, bloating, abdominal colic pain, low back pain, cold, cough, rhinitis, bronchitis, asthma, eczema, dermatitis, pruritus, piles, liver, spleen diseases, anaemia, semen defects and gynaecological problems.
4.	Sarpagandha Ghan Vati	Rauvolfia serpentine, Trachyspermum ammi, Nardostachys jatamansi, Cannabis sativa and Piper longum	Lack of adequate sleep, hypertension and dizziness.
5.	Sanjivani Vati	Embelia ribes, Zingiber officinalis, Piper longum, Chebulic Myrobalan fruit rind, Belliric, Terminalia bellirica, Emblica officinalis Gaertn, Acorus calamus, Tinospora cordifolia, Semecarpus anacardium, Aconitum ferox and cow urine.	Dyspepsia, Lack of digestion, Snake bite and Chronic fever
6.	Agnitundi Vati	Purified Mercury, Aconitum ferox, Sulphur, Trachyspermum roxburghianum, Terminalia chebula, Terminalia bellirica, Emblica officinalis Gaertn, Hordeum vulgare, Plumbago zeylanica, Rock salt, Cuminum cyminum, Sochal salt, Embelia ribes, Common salt, Borax, Purified Strychnos nux vomica and Lemon juice.	Digestion, fever and indigestion.
7.	Punarnavadi Guggulu	Boerhaavia diffusa, Ricinus communis, Zingiber officinalis, Commiphora mukul, Ricinus communis, Operculina turpethum, Baliospermum montanum, Tinospora cordifolia, Terminalia chebula, Terminalia bellirica, Emblica officinalis Gaertn, Zingiber officinalis, Piper nigrum, Piper longum, Rock salt, Purified Semecarpus anacardium, Embelia ribes, and Bhasma of Copper-Iron Pyrite.	Gout, sciatica, low back ache, spondylosis, rheumatoid arthritis, and such other skeleto-muscular and joint disorders.
8.	Kaishore Guggul	Haritaki, Vibhitaki, Amalaki fruit rind, Tinospora cordifolia, Commiphora mukul, Pepper, long pepper, ginger, Embelia ribes, Baliospermum montanum, Operculina turpethum and Ghrita.	Anti aging, skin health promoter, joint health, natural blood cleanser, and useful as supportive dietary herbal supplement.
9.	Triphala Guggul	Terminalia chebula, Terminalia bellerica, Emblica officinalis and Commiphora mukul.	Weight loss, piles, fistula and inflammatory conditions.
10.	Kanchanar Guggul	Bauhinia variegate, Terminalia chebula, Terminalia bellerica, Emblica officinalis, Zingiber officinale, Piper nigrum, Piper longum, Crataeva nurvala, Elettaria cardamomum, Cinnamomum Zeylanicum and Commiphora mukul.	Cervical lymphadentis, fibroid, cysts, tumor, tumor, ulcers, wounds distension, skin diseases And fistula.

Table 2: Disintegration test, friability test, and uniformity of weight test of eleven different samples. Here; S1 (IMPCL, a govt agency) and S2 (Himalaya) are two different suppliers.

Tablet Name	Supplier Name	Average Weight (mg)	Disintegration Test (min)	Friability Test (%)	Weight Uniformity Test (%)
Mahashankh Vati	S1	311.47	19.15±1.25	0.058±0.011	-2.97 to 3.28
Kutazghan Vati	S1	282.15	29.35±2.41	0.094±0.018	-3.46 to 3.38
Chandraprava Vati	S1	344.31	22.40±2.16	0.074±0.021	-0.91 to 0.51
Sarpagandhaghan Vati	S1	284.23	05.27±0.55	0.483±0.082	-0.74 to 1.74
Sanjivani Vati	S1	132.01	19.52±1.51	0.055±0.014	-6.21 to 0.23
Agnitundi Vati	S1	155.46	22.31±2.22	0.087±0.023	-1.71 to 1.37
Punarnavadi Guggul	S1	346.52	22.36±2.15	0.063±0.019	-1.45 to 0.28
Kaishore Guggul	S1	343.45	25.21±2.44	0.068±0.012	-1.25 to 0.62
Triphala Guggul	S2	762.17	44.35±3.22	0.021±0.008	-2.68 to 2.51
Kaishore Guggul	S2	753.22	42.32±2.54	0.038±0.018	-2.82 to 2.34
Kanchanar Guggul	S1	334.41	22.46±1.56	0.086±0.023	-1.64 to 1.97

4. CONCLUSION

In conclusion, these preliminary studies could be considered as one of the toll for incorporating quality standards to herbal tablets. There is a direct relationship between therapeutic activities and these tests. These basic studies are necessary to establish the herbal pharmaceutical preparations based on sound scientific background. Here, our basic motto to enrich the Ayurvedic manufacturing, and there is no intention to apply any hard and fast rules directly without any scientific background. Here, at significant level $p \leq 0.05$ no difference was noticed for disintegration and friability tests. But, variation within twenty tablets weight has been noticed for uniformity of tablet test, which was significantly different at $p \leq 0.05$, even though overall test was complied.

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6. Conflict of interest

The authors declare that there are no conflicts of interest.

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