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HICEL™ SILICIFIED MICROCRYSTALLINE CELLULOSE, VERSATILE EXCIPIENT FOR NUTRACEUTICAL HERBAL TABLET FORMULATION

***Monika Tomar, Rohit Raj and Amit Raj Sinha**

Sigachi® Industries Private Limited, Dahej SEZ, Bharuch, Gujarat, India

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ABSTRACT

Nutraceutical herbal medicine and supplements demand increases day by day. Herbal medicine normally contains lipids, protein, carbohydrate, vitamins, minerals and other necessary nutrients depending upon their emphases. Generally, all herbal extracts powder nature is fine poor flowable, sticky powder and having poor compressibility. In this study, we have made 1600 curcumin tablet,1000 mg saw palmetto (Seranoarepens) tablet and 600 mg ginger tablet by direct compression method using two direct compressible binder Silicified Microcrystalline Cellulose (SMCC) and Microcrystalline Cellulose (MCC). Pre-compression of powder blend and post compression of Nutraceutical herbal extracts tablet were studied and compared. Result showed that thickness, weight variation, friability, hardness and content uniformity of all six formulations were within the acceptance limits. But the formulation having SMCC (F1, F2 and F3) gives better results regarding better flowability and compressibility, less weight variation in tablet weight, good tablet hardness, lower friability compared to the MCC based formulations (F4, F5 and F6). Hence, the study concluded that Nutraceutical herbal extracts tablet formulated using SMCC showed better characteristics, and tablet profile.

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INTRODUCTION

The use of herbal medicines and Nutraceuticals supplements continues to expand rapidly across the world, and in the last few years, herbal remedies have become more and more popular as alternatives to conventional pharmaceuticals because of its lesser side effects compared to chemical pharmaceutics. Herbal supplements come under nutraceuticals (Chakotiya, 2014). Nutraceuticals are products derived from food sources that provide extra health benefits, in addition to the basic nutritional value found in food. Depending on the jurisdiction, products may claim to prevent chronic diseases, improve health, delay the ageing process, increase life expectancy, or support the structure or function of the body. In the US, Nutraceuticals do not exist as a regulatory category, they are regulated as dietary supplements and food additives by the FDA under the authority of the Federal Food, Drug, and Cosmetic Act (Jon, 2019). Dietary supplement is a product that contains dietary ingredients (mineral, vitamin, amino acid etc).

****Corresponding author:*** **Monika Tomar,**
Sigachi® Industries Private Limited, Dahej SEZ, Bharuch, Gujarat, India

It is used by humans to supplement the diet by increasing the total daily intake, or a concentrate, metabolite, constituent, extract, or combinations of the ingredients (Ghana Medicine Association, 2013). Nutraceuticals are of these nutritional supplements which are used for health purposes other than nutrition. Dietary supplements can also be extracts or concentrates, and may be found in many forms such as tablets, capsules, soft-gels, liquids and powder (WHO, 2001). Mostly herbal extract powder is use as supplement because herbals have lots of mineral, vitamins and others properties (The growing use of herbal medicines, 2013). Herbal extracts are generally used in capsules and powders form but their formulation is a challenging task for formulators because of the high dose, bitter taste, very poor flow-ability and less compressibility. Inherent poor tableting properties of most herbal extracts creates problem in the manufacturing of tablets using direct compression method (SeemaAtram, 2014). To overcome the tableting issues of herbal extracts, selection of right excipient is essential. Silicified Microcrystalline Cellulose is a co-processed excipient of binder and glidant, specially designed for continuous manufacturing of tablets using direct compression method. Co-processing improves the product quality in terms of flowability and other physical

parameters. This results in better tablet profile compared to the physical blend of individual ingredients (Tomar, 2017). The present investigation is intended to formulate and evaluate the tablet profile of Curcumin, Saw Palmetto, and Ginger herbal extracts powder with Microcrystalline Cellulose (MCC) and Silicified Microcrystalline Cellulose (SMCC) using direct compression method. Curcumin isolated from Curcuma Longa, also known as Turmeric belongs to Zingiberaceae family. It is yellow, golden oranges colour granular powder and has been used in traditional medicines for centuries because it consists of natural bioactive hydrophobic polyphenols called curcuminoids having extensive pharmacological activities (antimicrobial, antioxidant, antimicrobial, radio protective, anti-inflammatory, cardio protective, neuro protective, anticancer properties) (Susan, 2017) Saw Palmetto is known as Serenoa Repens. It is extracted form dark purple berries of the Saw palmetto. It is used as natural diuretic and used to treat urinary tract infection (Fagelman, 2001). Ginger is a spice originated from the rhizomes of the plant Zingiber Officinal. Ginger extract is a yellowish-brown colour fine powder, used to treat nausea, vomiting after surgery, morning sickness, osteoarthritis, and dizziness. Being a strong antioxidant, antibacterial activities, it is also used to reduce inflammation (Seema Atram, 2014).

MATERIALS AND METHODS

Materials

Chemicals used along with supplier details are as follows: Microcrystalline Cellulose (HiCel^{TM}MCC 50M & 90M - Sigachi Industries Private Limited., Dahej, Gujarat), Silicified Microcrystalline Cellulose (HiCel^{TM}SMCC 50M & 90M - Sigachi Industries Private Limited., Dahej, Gujarat), Curcumin, Saw Palmetto and Ginger (Herbo Nutra, Delhi), Magnesium Stearate (Prachin Pharmaceuticals, Ahmedabad), Croscarmellose Sodium (Ascot Pharma Chem Pvt. Ltd., Gujarat), Purified Talc (Vital Pharma, Gujarat), Colloidal Silicon dioxide (Wacker, Germany).

Method

Nutraceutical tablets containing curcumin, saw palmetto and ginger were prepared by direct compression method. HiCel^{TM}SMCC 50 M and HiCel^{TM} SMCC 90 M were used as binder/ glidant, MCC 50M and 90M were used as binder, colloidal silicon dioxide used as glidant, croscarmellose sodium was used as disintegrate and magnesium stearate and purified talc were used as lubricant. All the excipients along with API weighed as shown in Table 1. Binder/glidant and disintegrate were mixed for 10 minutes in powder blender (model no. TRMIX-20) then add API and mixed again for 15 minutes. The powder blend was lubricated with magnesium stearate and purified talc for 3 minutes. Compressed tablets using ten stations rotatory mini press tablet punching machine (Model no. "D" SAT 10).

Physical Characteristics of Nutraceutical Herbal Extracts

Pre-compressional studies of blend products: Pre-formulation study is the primary step for new dosage form development to identify the barriers in tablet manufacturing process. It is the principal investigation in the drug development to obtain information on the known properties of compound and proposed development schedule. Following pre-compressional parameters were studied like angle of repose, bulk density, tapped density, hausner's ratio and compressibility index.

Angle of Repose: Angle of repose obtained between free standing surface of powder heap and the horizontal plane. It was determined by using the fixed funnel method. 20 gm of final blend powder was poured into funnel keeping the orifice of the funnel blocked by thumb. When powder was cleared from funnel then measured the peak height (Saha, 2017).

Bulk density: Bulk density is the ratio of bulk mass to the bulk volume. Bulk density measured by Scott Volumeter. Weight empty cup, place it under the chute and powder is pour into funnel through volumeter, at a rate suitable to prevent clogging, until the cup overflows. Level the excess powder and weight the filled cup (United State Pharmacopeia, 2018).

Tapped density: Tapped density is a ratio of the weight of powder to the minimum volume occupied in the measuring cylinder. Tapped density is determined by placing a graduated cylinder containing a known mass of final blend powder on a mechanical tapper apparatus (Model No. ETD 1020) which is operated at fixed number of tapped (500) until powder bed reached a minimum volume.

Hausner's ratio: It is indirect index of ease of measuring of powder flow. Lower Hausner's ratio (<1.25) indicates well flow property.

Hausner's Ratio = Tapped density/ Bulk density

Compressibility Index: Compressibility index known as carr's index. Based on the apparent bulk density and the tapped density. Percentage compressibility is calculated by below formula

Compressibility index = Tapped density - bulk density ×100/ Tapped density

Post-compressional studies of Nutraceutical tablets: The Nutraceutical tablets were evaluated for various parameters like appearance, weight variation, thickness, hardness, friability, tablet disintegration.

Physical appearance: The general appearance of nutraceutical tablet was studied visually in shape, colour, texture.

Weight variation: Weight variation test is performed by weighing 10 tablets individually, calculating the average weight and comparing the individual tablet weight to the average. The weight variation test would be a satisfactory method of determining the drug content uniformity of the tablets (Nagaich, 2014).

Thickness: The tablet thickness was calculated by Vernier callipers using 10 tablets. Tablets were putted in between two jaws vertically and measured thickness.

Hardness: Randomly 10 tablets were taken from each batch. Electronic digital hardness test machine (Model No.-TH1050 M) was used to analyze tensile strength of tablets. Single tablet was placed between two anvils, force was applied to the anvils, and the tensile strength that just required to break the tablet was recorded. Finally, the reading was noted in Newton (Sinha, 2018).

Table 1. Composition of Nutraceutical tablets

Ingredients (mg)	F1	F2	F3	F4	F5	F6
Curcumin	1250	--	--	1250	--	--
Saw palmetto	--	265	--	--	265	--
Ginger	--	--	250	--	--	250
HiCel^{TM}SMCC 50M	270	--	--	--	--	--
HiCel^{TM}SMCC 90M	--	704.25	317.06	--	--	--
MCC 50M	--	--	--	254	--	--
MCC 90M	--	--	--	--	699.25	314.06
Colloidal Silicon Dioxide	--	--	--	8	5	3
Croscarmellose sodium	60	26.25	27	60	26.25	27
Magnesium Stearate	20	--	--	20	--	--
Purified talc	--	4.50	5.99	--	4.50	5.99
Total (mg)	1600	1000	600	1600	1000	600

Table 2. Powder characteristics indicative of the powder quality

Types of flow	Angle of repose (°)	Compressibility index (%)	Hausner's ratio
Excellent	25-30	<10	1.00-1.11
Good	31-35	11-15	1.12-1.18
Fair	36-40	16-20	1.19-1.25
Passable	41-45	21-25	1.26-1.34
Poor	46-55	26-31	1.35-1.45
Very poor	56-56	32-37	1.46-1.59
Very-very poor	>66	>38	>1.60

Table 3. Pre compression studies of powder blend containing herbal extracts

Pre-compression Parameters	F1	F2	F3	F4	F5	F6
Angle of repose (°)	26	30	31	28	33	34
Bulk density (g/CC)	0.65	0.42	0.54	0.62	0.50	0.50
Tapped density (g/CC)	0.69	0.52	0.69	0.68	0.69	0.69
Hausner's Ratio	1.06	1.24	1.28	1.10	1.38	1.38
Compressibility Index (%)	5.81	19.23	21.74	8.82	27.53	27.54

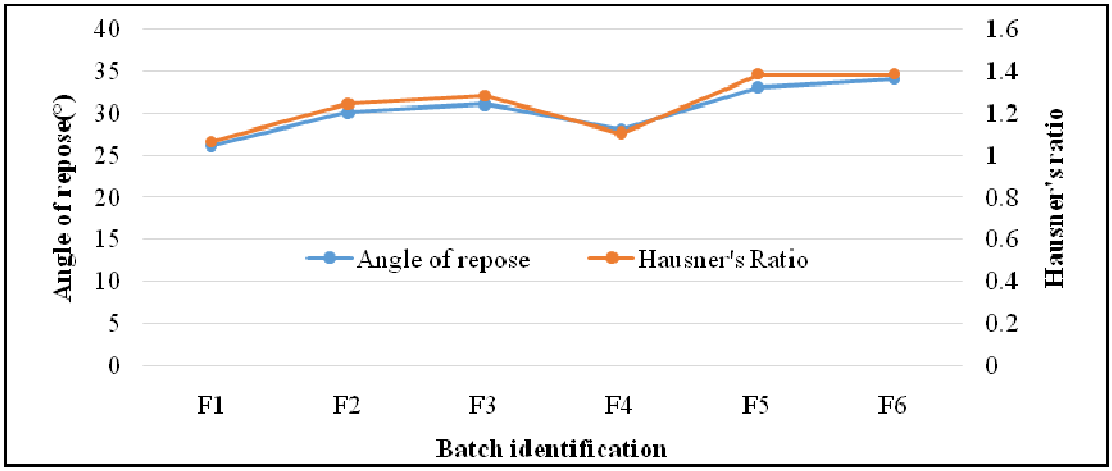

Fig 1. Flow properties of the final blend of Nutraceutical herbal extracts

Fig. 2. Curcumin, Saw palmetto and Ginger Nutraceutical herbal tablet images

Friability: 10 tablets were taken and weighed by using electronic digital balance which was considered as the initial weight. All the tablets were placed in the drum of friability tester (Model No. FT1020) and allowed rotate 100 times at 25 rpm. After 100 revolutions, tablets were removed and re-weighed which was considered as the final weight. The percentage friability was calculated by below mention formula. As per USP, the tablets should not lose more than 1% of their total weight (Lachman Leon, 2009).

Friability = Initial weight - final weight x 100 / Initial weigh

***In vitro* Disintegration Time:** This test was carried out at 37±2°C in 800 ml Demineralized water. Six tablets were taken and one tablet was introduced in each tube, disk was placed and basket was positioned in one litre beaker containing 37±2°C temperature of water. Note down tablet breaking time. Noted the time when the tablet broke down into smaller particles.

RESULTS AND DISCUSSION

The Nutraceutical tablet of curcumin, saw palmetto and ginger were formulated by direct compression method. This method was used to for conventional form Nutraceutical tablet which minimize processing steps and eliminated wetting and drying process. The physico-tableting property shows satisfactory results in Nutraceutical tablets which are within the range of prescribed standard (Table 2).

Pre-compressional studies of blend products: Prepared blend was analysed for various flow properties such as Carr's index, Hausner's ratio. Angle of repose and result are tabulated in Table 3. The compressibility index for all the formulations was found to be within the standard range, which indicates good to fair flow properties. There were further analysed by determining the angle of repose, which were within the range.

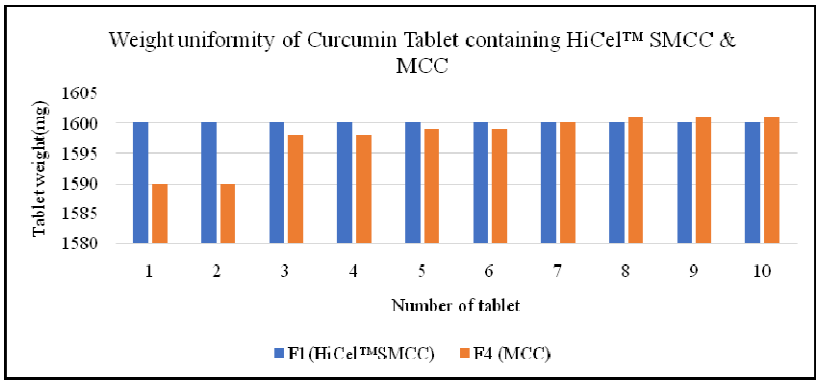

Fig 3. Weight uniformity of Nutraceutical Curcumin herbal extract tablets

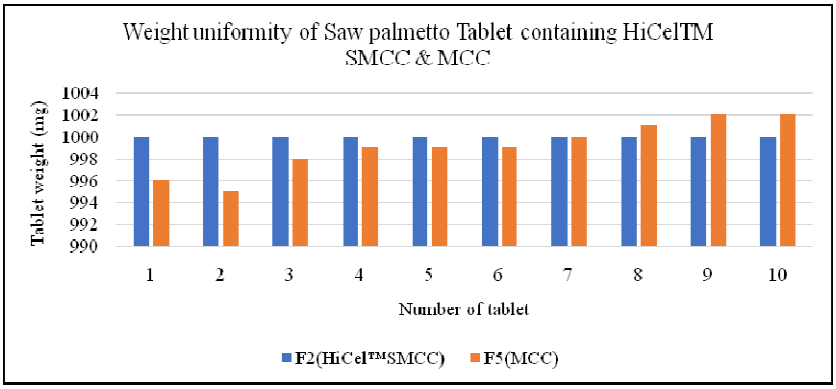

Fig 4. Weight uniformity of Nutraceutical Saw palmetto herbal extract tablets

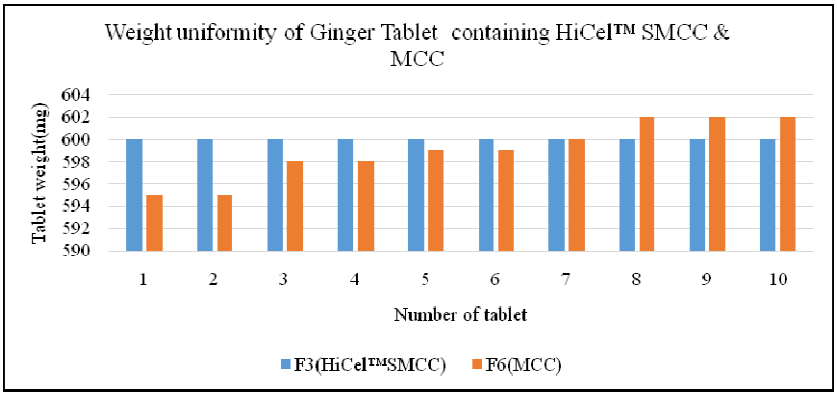

Fig 5. Weight uniformity of Nutraceutical Ginger herbal extract tablets

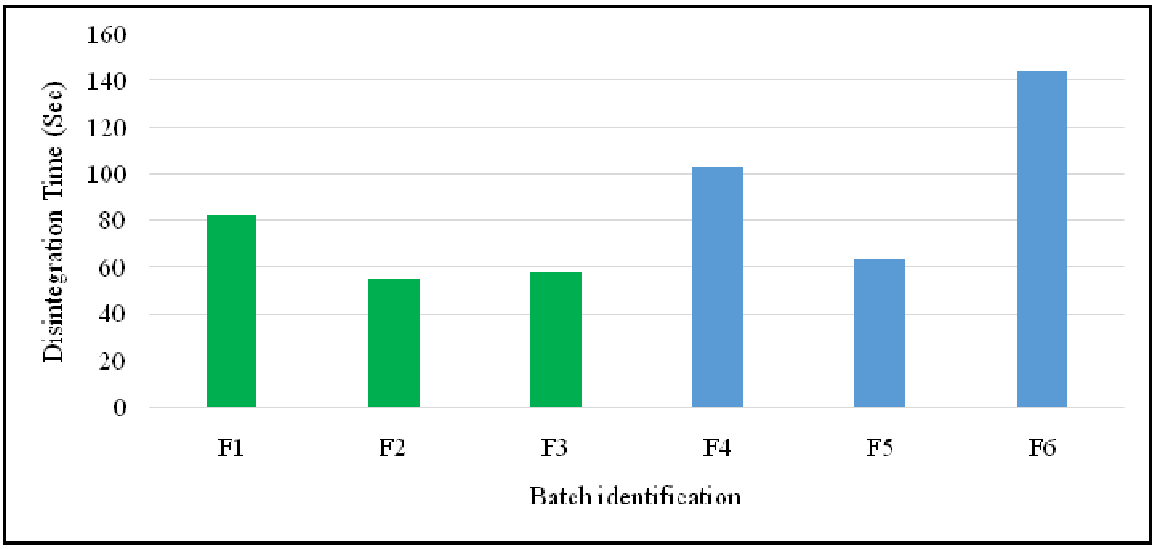

Fig 7. In-Vitro disintegration time of all Nutraceutical herbal formulation tablets

Table 4. Post compression studies of Nutraceutical herbal extract tablet

Post-compression Parameters	F1	F2	F3	F4	F5	F6
Tablet colour	Yellow	Ochre yellow	Brown	Yellow	Ochre yellow	Brown
Avg. Weight (mg)	1600	1000	600	1600	1000	600
Avg. Thickness (mm)	6.0	5.0	5.0	6.0	5.0	5.0
Avg. hardness (N)	200	45.10	74.2	100	21	35
Friability (%)	0.00	0.03	0.02	0.052	0.44	0.08
Disintegration Time (HH:MM: SS)	00:01:23	00:00:55	00:00:58	00:1:43	00:1:03	00:2:25

Formulation based on HiCel™ SMCC (F1, F2 and F3) Showed lower angle of repose for all the three herbal extracts. The Hausner's ratio for formulation F1, F2 and F3 are less indicating free flow properties.

Post-compressional studies of Nutraceutical tablets: The result from different physical parameters like appearance, weight variation, thickness, hardness, friability and *in vitro* disintegration of tablets were shown in Table 4. The presence of binder, glidant, disintegrant and lubricant is providing sufficient bulk to the tablet which decreases risk during punching. All tableting parameters like thickness, weight variation, hardness, friability and disintegration time are found to be in the acceptable limit. It shows that the herbal drugs containing Nutraceutical tablets have satisfactory disintegration profile due to their hardness within the range of standard limit.

Physical Appearance: Curcumin and Saw palmetto Nutraceuticals tablets were found to be round shape and Ginger Nutraceutical tablet was found elongated shaped, smooth texture and free form all the defects i.e. lamination, capping, sticking etc.

Weight variation: The weight variation of 10 tablets was measured and found within the acceptable limit. All Nutraceuticals formulation tablet average weight variation test passed within the USP limits of ±5% and shown in table 4. However, tablets formulated with HiCel^{TM}SMCC have less weight variation compared to MCC.

Thickness: Thickness of all Nutraceuticals were found within the acceptable limit ±0.1 mm. it depends upon the size of die and punches or a function of die filling and compression force. Curcumin tablet has 6 mm saw palmetto and ginger tablets have 5.0 mm thickness. Results shown the uniformity in the thickness of all the tablets.

Hardness: Hardness of Nutraceutical herbal extract tablets batch no. F1, F2 and F3 was found good. Formulation using MCC shows less tablet hardness compared to HiCel^{TM}SMCC based formulation.

Friability: The Maximum and minimum friability among the 6 formulations were found to be 0.44% and 00% respectively. However, formulation F1, F2 and F3 which is based on HiCel^{TM}SMCC had the least friability. The percentage friability of all the formulation is less than 1% ensuring that the tablet was mechanically stable.

***In vitro* Disintegration Time:** All batches tablet of Nutraceutical herbal extract are having less than 5-minute disintegration time. However, F1, F2 and F3 formulation which is based on HiCel^{TM}SMCC gives lower disintegration time compared to the formulation F4, F5 and F6 which is based on MCC.

Conclusion

From the above study, we conclude that HiCel™ SMCC is the best excipient for Nutraceutical herbal extract tablet, it solved all problems i.e. improved final blend flowability, remove sticky nature of API and increased compressibility. We have prepared herbal extract curcumin, saw palmetto and ginger tablets with HiCel™ SMCC by direct compression method and HiCel^{TM} SMCC delivered very good tablet profile. All formulation tablets are having higher tablet hardness 200, 45.10 N, 74.20 N respectively comparative to Microcrystalline cellulose containing tablet.

Microcrystalline cellulose tablet has less tablet hardness and higher disintegration time.

Conflicts of interests: The authors state and confirm no conflict of interests. No direct funding was received for this study.

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