

Available online at [GSC Online Press Directory](https://www.gsconlinepress.com/)

GSC Biological and Pharmaceutical Sciences

e-ISSN: 2581-3250, CODEN (USA): GBPSC2

Journal homepage: <https://www.gsconlinepress.com/journals/gscbps>

(RESEARCH ARTICLE)



A technical note: Characterization and evaluation of novel, ready to use co-processed excipient in nutraceutical herbal vitamin and amino acid formulations

Tomar Monika ¹ and Sinha Amit Raj ^{2,*}¹ *Sigachi Industries Limited, Dahej SEZ, Bharuch, Gujarat, India.*² *Sigachi Industries Limited, 4th Floor, Kalayan's Tulshiram Chambers, Madinaguda, Hyderabad, Telangana (India).*

Publication history: Received on 16 May 2020; revised on 21 May 2020; accepted on 24 May 2020

Article DOI: <https://doi.org/10.30574/gscbps.2020.11.2.0142>

Abstract

A tablet is composed of different excipients and drug. All excipients have different properties with applications. Excipients are used to provide bulk and help to bind API into a dosage form, excipient should be inert in nature with respectable physical properties. Because the physical properties play a very important role during tablet compaction. However, maximum individual excipients do not have enough physical properties especially flowability. To fulfil these requirements co-processed excipient have been starting to use in formulation industries to make tablet and capsules. All co-processes excipients have superior flowability and other physical properties and now co-processed excipients have made their own place in pharma industries. BARETab[®] Nutra is also a co-processed excipient, but it is a ready to use premix for direct compressible tablet and contains four different excipients like binder, glidant, disintegrant and lubricant. This study is aimed at making herbal extracts, vitamins and non-essential amino acids tablet, using BARETab[®] Nutra by direct compression method and evaluate in-vitro parameters like hardness, friability, disintegration time and drug released profile. Ready to use premix BARETab[®] Nutra delivers good tableting parameters in herbal tablet Glucosamine, vitamin tablet Pyridoxine hydrochloride and non-essential amino acid Cysteine tablet like as higher tablet hardness, less friability, less disintegration time and uniform tablet weight. All tablets carried equal amount of drug which is proved by dissolution test.

Keywords: Ready to use premix; Surface area; Scanning Electron Microscope; Fourier-transform infrared spectroscopy; Drug released profile

1. Introduction

Now, co-processed excipients are not new for formulation industries. It is used widely to make direct compressible tablet formulations [1]. Co-processed excipient is an innovative combination of two or more than two excipients by co-processing [2]. Co-processing excipients has a fabulous physical property such as higher bulk density, larger surface area, outstanding flowability and homogeneous particle size distribution, all physical parameters very helpful to deliver good quality of tablet with higher tablet hardness with lower friability, less disintegration time and homogeneous drug distribution in all tablets [3]. However, when we mix API with disintegrate, glidant and lubricant for make a blend for tableting it might be creating batch to batch variation in tablet quality [4]. It may happen due to different bulk density and particle size of the material and sometime due to different blending time. To solve above mentioned problems, excipient manufacturers did lots of R&D and made a ready to use premix for direct compressible tablets formulations [5].

BARETab[®] Nutra is a ready to use premix, and combination of multifunctional ingredients which are required to make a tablet formulation. It contains binder, glidant, disintegrant and lubricant. BARETab[®] Nutra is specially designed for

* Corresponding author: Sinha Amit Raj

nutraceutical formulations. It is very helpful to deliver good quality tablets and it controls rejections during tableting in production [6]. 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 [7]. Mostly herbal extract powder is use as supplement because herbals have lots of mineral, vitamins and others properties [8].

Nutraceuticals supplements and herbal medicines are continuing 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 pharmaceuticals. Nutraceuticals are products derived from food sources that provide extra health benefits, in addition to the basic nutritional value found in food [9]. 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 [10]. 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 [11].

In the present study, BARETab® Nutra ready to use premix is using to make Herbal extract Glucosamine, Pyridoxine HCl Vitamin and Cysteine non-essential amino acid tablet and evaluate *in-vitro* of the all formulations [12]. *In vitro* test includes, tablet physical evaluation, hardness, weight uniformity, disintegration and drug released profile by *in-vitro* dissolution test [13]. The present study is aimed at preparation and evaluation of ready to use premix BARETab® Nutra. Evaluation test comprises of FTIR test, Particle size distribution, bulk density, specific surface area and scanning electron microscopic characteristics.

2. Material and methods

2.1. Material

BARETab® Nutra, filler, binder and disintegrant manufactured at Sigachi Industries Ltd. in Dahej, Gujarat. Glidant purchased from Nikon Corporation, Wacker Germany, lubricant purchased from Sun Shine private Limited, India, Glucosamine purchased from Herbo Nutra Delhi, India and Vitamin, and amino acids API's are purchased and Chemzone pharma, Ahmedabad, Gujarat (India), others chemicals AR grade are used in this study.

2.2. Method

2.2.1. Characterization of BARETab® Nutra

2.2.2. Fourier-transform infrared spectroscopy

Make a mixer of BARETab® Nutra and KBr in 3:1 ratio and make a homogenous mixer in mortar and pastel. Take sample in IR sample cup and placed the sample cup into sample compartment in IR, run the sample in IR Spirit (Shimadzu DRS Model) [14].

2.2.3. Scanning electron microscope

Take approximate 1 to 2 milligram sample and mounted on double sided taped on aluminum stabs. Placed stabs into sample compartment into microscope. Micrographs were taken at appropriate magnification and particles surface visualization detailed analyzed by scanning electron microscope at SICART university, Anand, Gujarat (India)[15].

2.2.4. BET surface area analysis

Take 0.1380 g sample in sample cell and charge nitrogen gas at low pressure dose 10.00 cm³/g STP and -195.73 0C temperature. Surface area of both samples were analysed by using Micromeritics surface analyser at CMCRI Bhavnagar, Gujarat (India) [16].

2.3. Physical evaluation of BARETab® Nutra

2.3.1. Untapped density

Untapped bulk density analysed by Scott volumeter. Weight empty cup, place it under the chute and 10g of each sample is poured into funnel through volumeter, at a rate suitable to prevent clogging, until the cup overflows. Level the excess powder and weight the filled cup [17].

$$\text{Untapped density (g/ml)} = (\text{Sample Mass (g)}) / (\text{Sample Volume (ml)}) \quad (\text{i})$$

2.3.2. Tapped density

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.

$$\text{Tapped density (g/ml)} = (\text{Sample Mass (g)}) / (\text{Sample Volume (ml)}) \quad (\text{ii})$$

2.3.3. Hausner's ratio

It is indirect index for ease of measuring powder flow. Lower Hausner's ratio (<1.25) indicates good flow property [18].

$$\text{Hausner's Ratio} = (\text{Tapped density}) / (\text{Untapped density}) \quad (\text{iii})$$

2.3.4. Compressibility

Compressibility known as carr's index. Based on the apparent bulk density and the tapped density. Percentage compressibility is calculated by below formula [18]

$$\text{Compressibility (\%)} = (\text{Tapped density} - \text{bulk density}) / (\text{Tapped density}) \times 100 \quad (\text{iv})$$

2.3.5. Angle of repose

Angle of repose obtained between freestanding 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 the peak height was measured [19].

2.3.6. Particle size distribution analysis

Particle size was analysed at Cubic Analytical Solution, Ankleshwar, Gujarat using laser diffraction (Malvern instrument, Mastersizer v3.63).

2.4. Herbal extract, vitamin and amino acid description blend preparation [20]

2.4.1. Herbal extract glucosamine hydrochloride

Glucosamine HCl extracted powder was yellowish colour, sticky and hygroscopic in nature, it is an amino sugar and used as health supplements. It has very poor flowability [21].

Weight accurately Glucosamine HCl and BARETab® Nutra amount and transferred into powder blender (Reva Pharma machinery, TRMIX-20), blend the material for 10 minutes at 25 RPM. Tablet ingredient quantity is mentioned in Tablet:1. Glucosamine HCl blend has ready for tablet punching.

2.4.2. Pyridoxine hydrochloride (vitamin B6)

It is white color crystalline powder with very poor flowability, it is used as a health supplement.[22]

Weight accurately Vitamin B6 and BARETab® Nutra quantity and transfer into powder blender (Reva Pharma machinery, TRMIX-20), blend the material for 8 minutes at 25 RPM. Tablet ingredient quantity is mentioned in Tablet:1. Vitamin B6 blend is now ready for tablet punching.

2.4.3. Non-essential Amino Acid Cystine

Cysteine is a non-essential Sulphur amino acid, it has off white color, poor flowability and compressibility, which plays a critical role in methionine, taurine and glutathione metabolism, also an important component of hair, nails and the keratin of the skin. It is used as food supplement [23].

Weight accurately Cystine and BARETab® Nutra quantity and transfer into powder blender (Reva Pharma machinery, TRMIX-20), blend the material for 10 minutes at 25 RPM. Tablet ingredient quantity is mentioned in Tablet:1. Cystine blend is now ready for tablet punching.

Table 1 Nutraceutical tablets manufacturing details

Ingredient Name	Quantity (W/W %)		
	Glucosamine HCl	Pyridoxine HCl (Vit.B6)	Cysteine
BARETab® Nutra	43.33	39.39	37.5
Glucosamine HCl	56.67	--	--
Pyridoxine Hydrochloride (Vitamin B6)	--	60.61	--
Cysteine	--	--	62.5

2.5. Tablet compression

All sample tablets were manufactured by using 10 station Proton Mini Press (MINI PRESS 10 “D”) using D tooling dies and punches and all formulations manufactured at the same compression force. Glucosamine HCl and vitamin B6 tablet manufactured with 8mm round, flat die-punches and Cystine tablet punched with 18 mm round, flat die-punches [24].

2.6. Evaluation of formulation Tablet

2.6.1. Physical appearance

The general appearance of all formulated tablets was studied visually in shape, colour, texture.

2.6.2. Weight variation

Weight variation test was performed by weighing 10 tablets individually using four-digit digital weighing balance (Mettler Toledo, MS304S/A01), calculating the average weight of every formulations [25].

2.6.3. Thickness

All formulated tablet thickness was calculated by Vernier callipers using sample size of 10 tablets. Tablet was putted in between two jaws vertically and the thickness measured.

2.6.4. Hardness

Randomly 10 tablets were taken from each sample. Electronic digital hardness test machine (TH1050 M) was used to analyse hardness of tablets. Single tablet was placed between two anvils, force was applied to the anvils, and the tensile strength that was just required to break the tablet was recorded. Finally, the reading was noted in Newton [26].

2.6.5. 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 (FT1020) and allowed rotate 100 times at 25 rpm. After 100 revolutions, 10 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.

$$\text{Friability (\%)} = (\text{Initial weight(mg)} - \text{Final weight(mg)}) / (\text{Initial weight (mg)}) \times 100 \quad (\text{v})$$

2.6.6. In vitro disintegration time

Disintegration time of paracetamol tablets were analysed by using tablet disintegration tester (Labindia, DT 1000) 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 liter beaker containing 37±2°C temperature of water. Note down tablet breaking time. Noted the time when the tablet broke down into smaller particles [27].

2.6.7. In vitro dissolution profile

All Nutraceutical tablet formulations drug released profile was analysed by using dissolution test apparatus (Labindia, DS 8000) and followed by USP method, apparatus type 2 (paddle). speed 50 rpm in 900 ml distilled water at 37±2 °C medium temperature for Cystine and vitamin B6 tablet and for glucosamine HCl tablet speed 75 RPM and medium 900

ml distilled water was used. Randomly select 6 tablet and one tablet introduced in each beaker of dissolution. 5 ml Sample were withdrawal from each beaker at different time intervals 5, 10,15, 20, 25, 30, 40, 45 and 60 minutes. Samples filter with Whatman filter paper (42). Take 1 ml sample from the beaker and transfer into 10 ml of volumetric flask and makeup the volume up to the mark. Repeat the same procedure for all remaining 5 tablets containing samples. Checked all sample and standard absorbance using UV Spectrophotometer (Shimadzu model no-1900) at different-different wavelength, Cystine at 202.6 nm, Glucosamine at 191.4 nm and Vitamin B6 at 285.1 nm. Calculate average drug released profile with the help of below mention formula's [27].

Amount of API released (mg) = (Conc.of released drug × dilution factor × Volume of dissolution medium)/1000 (vi)

Drug released (%) = (Amount of drug released)/ (Dose of drug) × 100 (vii)

3. Results and discussion

3.1. Characterization of BARETab® Nutra

3.1.1. Fourier-transform infrared spectroscopy

Lubricant, glidant and super disintegrant have coated on binder/filler, because individual material FTIR peeks have shifted. FTIR image shown in Fig 1.

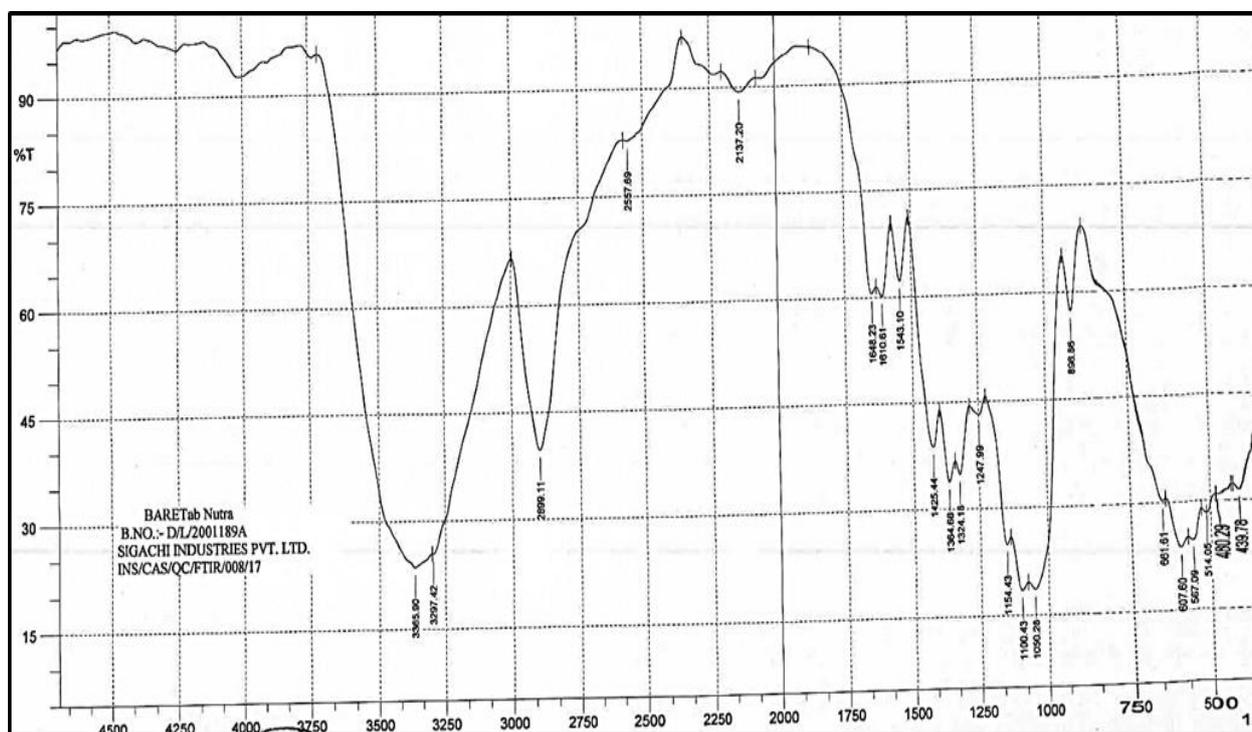


Figure 1 FTIR image of BARETab® Nutra

3.2. Scanning electron microscope images

BARETab® Nutra single particle contains binder, filler, glidant, disintegration and lubricant. All BARETab Nutra SEM images shown that all materials have coated to each other and shown in fig:2. BARETab Nutra improved particles size and surface area which helped to made homogenous mixing with API. Flowability enhanced tablet weight uniformity and specific surface area increased compressibility.

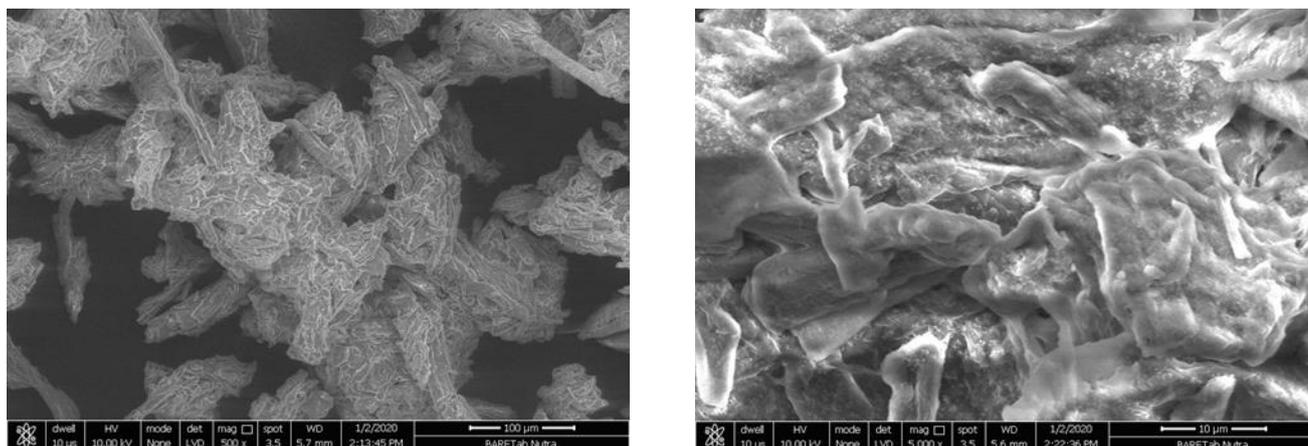


Figure 2 Scanning electron microscopic images of BARETab® Nutra at different magnifications

3.3. BET surface area

The BET specific surface areas of BARETab® Nutra was 2.3 m²/g and higher surface area positive impact on tableability. Potentially due to the numerous hydrogen bonds between the larger bonding surface area of adjacent particles to the mechanical interlocking. BARETab® Nutra have gave more tablet hardness due to the presence of interparticle bonds and the force of these bonds helps to achieve higher tablet hardness.

3.4. Physical evaluation

Physical attributes have potential impact on tableability. Powder flow is influenced by bulk density, shape and particle size. Lower bulk density facilitates compressibility however low bulk density hindered flowability. BARETab® Nutra has 0.38 g/ml untapped bulk density and 0.49 g/ml tapped density. Hausner ratio and compressibility index are considered as indirect measurements of powder flowability, the hausner ratio is indicative of interparticle friction, while the Compressibility index shows the aptitude of a material to diminish in volume. As the values of these indices increase, the flow of the powder decreases. It has 1.24 hausner ratio and 23. Compressibility index. Increasing value is an indication of decreasing flowability. BARETab® Nutra has excellent flowability which is represented by angle of repose, it 30°. Less angle of report of excipients help to improved API flowability, which impact the final tablet quality. It has average particle size distribution D50 117 µm. All physical parameters are mentioned in tablet no.2.

Table 2 Physical Evaluation of BARETab® Nutra

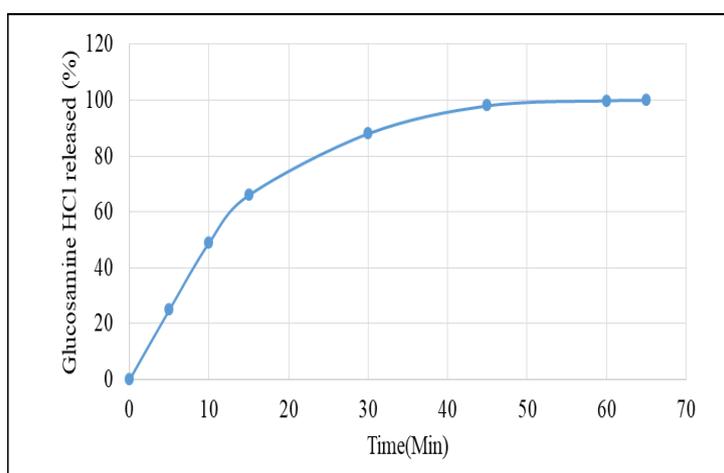
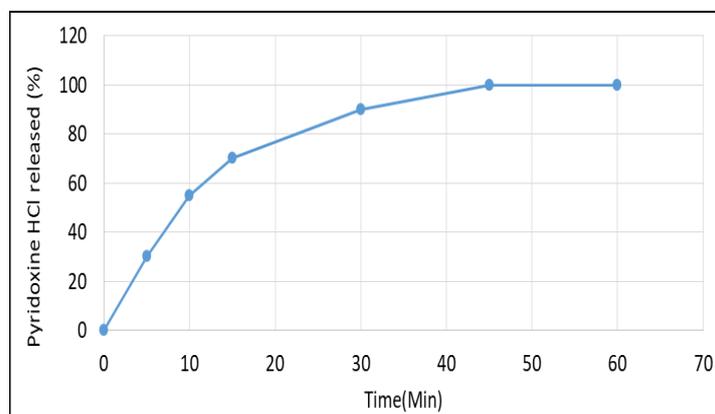
Characteristics	Result
Untapped Bulk density	0.38
Tapped bulk density	0.49
Hausner Ratio	1.29
Compressibility Index	22.45
Angle of Repose	30
Average particle size, D50	117

3.5. Evaluation of Glucosamine HCl, Pyridoxine HCl and Cysteine Tablet

Tablets are round shape, flat and white color, odorless with smooth surface and free from all defects like capping, sticking, lamination and weight variation. All formulated tablets have weight uniformity and tablet hardness good. There is no loss have observed during friability test and found very less disintegration time and shown in Table :3. All formulation have excellent drug released profile shown in Fig: 4, 5 and 6.

Table 3 Glucosamine HCl 85 mg, Pyridoxine HCl 100mg and Cystine 500 mg Tablet Evaluation

Characteristics	Glucosamine HCl	Pyridoxine HCl	Cystine
Description	Round flat off white color tablet	Round flat off white color tablet	Round flat off white color tablet
Average Tablet weight (mg)	150.0	165.0	800.0
Diameter (mm)	8.0	8.0	18.0
Thickness (mm)	2.2	2.2	5.8
Hardness (N)	95.9	62.8	88.7
Friability (%)	00.0	00	00
Disintegration Time (Sec)	26.0	10.7	9.5
Dissolution Time (min)	60	45	60

**Figure 4** Glucosamine hydrochloride Released Profile**Figure 5** Pyridoxine Hydrochloride Released profile

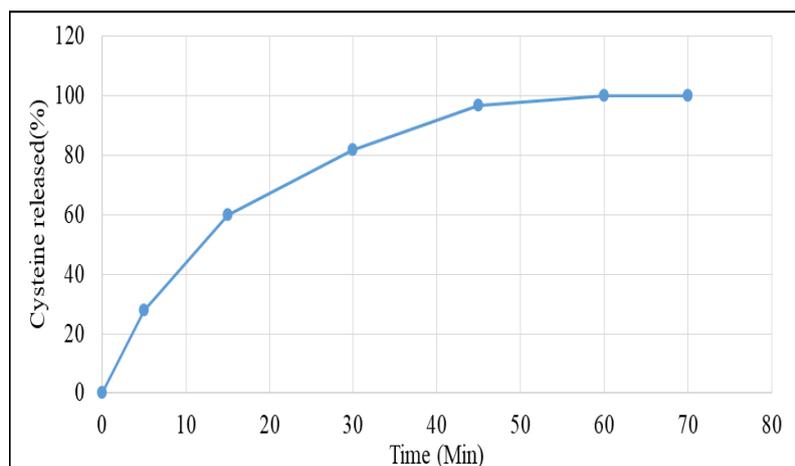


Figure 6 Cystine Released profile

4. Conclusion

In this study, we have elucidated that BARETab® Nutra has multi-functional properties and ready to use premix for nutraceutical health supplement's, its particles are more homogeneous, larger surface area and more bulk density and compressibility. FTIR and SEM study proved all four-material coated to each other's. Glucosamine HCl, Pyridoxine HCl and cystine tablet have higher tablet hardness and less disintegration time and no loss observed during friability which is shown in table: 3. All tablets were free from all defects. All three formulated tablets have weight uniformity and drug released profile. Glucosamine HCl content released more than 80%, Pyridoxine HCl content released more than 85% and cystine content released more than 80% in 30 minutes.

Compliance with ethical standards

Acknowledgments

The authors are very thankful to Faculty of CMCRI-CSIR Bhavnagar, Gujarat (India) for analysis of BET surface area.

Disclosure of conflict of interest

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

References

- [1] Liew KB, Anand G and Uttam KM. (2019). A review on co-processed excipients: Current and future trend of excipient technology. *International Journal of Pharmacy and Pharmaceutical Sciences*, 11(1), 1-9.
- [2] Ayyappan J, Umapathi P and Darlin Q. (2010). Development and evaluation of a directly compressible co-processed multifunction sustained released agent for tablets. *International Journal of Pharmacy and Pharmaceutical Sciences*, 2 (4), 1-10.
- [3] Ujjwal D, Rohini C, Priti M and Ruchira C. (2012). A review: co-processed excipients. *International Journal of Pharmaceutical Sciences Review and Research*, 12(1), 93-105.
- [4] Aljaberi A, Ardakani A, Khadair A, Abdel-Rahim AS, Meqdadi, Ayyash M, Alobaidi GM and Al-Zoubi N. (2013). Tableting functionality evaluation of Prosolv Easytab in comparison to physical mixtures of its individual components. *Journal of drug delivery of science technology*, 23 (2), 499-504.
- [5] Amit R and Monika T. (2020). Study of Powder and Tableting functionality towards evaluation and Characterisation of BARETab PH (All in One Excipient) as a substitute of conventional physically mixed Microcrystalline Cellulose, Croscarmellose Sodium, Silicon dioxide and Purified Talc in a PCM formulation. *Journal of Harmonized Research Publications*, 9(2), 27-36.
- [6] BARETab™. (2019). The beginning of end of single excipient usage. *Express pharma journal*, 16(1), 129.

- [7] Upendra N, Ashok KP, Charu B and Neha G. (2014). Formulation and evaluation of nutraceutical tablets using herbal drugs by direct compression method. *Journal of drug delivery & therapeutics*, 4(2), 47-51.
- [8] Ankita SC, Raman C, Monika T, Pallvai T, Alka N, Rakesh and Arora A. (2014). In Silico Herbal bioprospection targeting multi-drug resistant *Pseudomonas aeruginosa*. *International Journal of interdisciplinary & Multidisciplinary Studies*, 2(2), 163-176.
- [9] Jon C Tilburt and Ted J Kaptchuk. (2019). Herbal medicine research and global health: an ethical analysis. *Bulletin of the world health organization*.
- [10] Ghana Medicine Association. (2013). Herbal Medicine Research. *Ghana Medical Journal*, 47(3), 100.
- [11] WHO/EDM/TRM/2000.1, General guidelines for methodologies on Research and evaluation of traditional medicine. Geneva: World Health organization 2000.
- [12] Nagaich U, Pal AK, Bharti C and Gulati N. (2014). Formulation and evaluation of Nutraceutical Tablet using herbal drugs by direct compression method. *Journal of drug delivery & Therapeutics*, 4(2), 47-51.
- [13] Seema Atram. (2014). Recent development of herbal formulation: A novel drug delivery system. *International Ayurvedic Medical Journal*, 2(6), 953-958.
- [14] Ashok K and Ramaswamy. (2014). Phytochemical screening by FT-IR Spectroscopic analysis of leaf extracts of selected India medical plants. *Internal Journal current microbiology applied sciences*, 3(1), 395-406.
- [15] Donovan N, Leonard Gary W and Chandler SS. (2012). *Characterization of Materials*, second edition. Wiley online library.
- [16] Aridizzone S, Francesco SD, Patrizia Raman M and Mussini T. (1999). Microcrystalline cellulose powder structure, surface features and water sorption capabilities. *International Journal of Biological Macromolecules*, 26, 269-277.
- [17] Monika T, Amit RS and Ajay KS. (2017). Process and development of co-processed excipient Silicified Microcrystalline Cellulose and manufacture paracetamol tablet by direct compression. *International Journal of [19] Pharmaceutical Sciences review and research*, 32 (2), 191-196.
- [18] United states pharmacopeia. (2018). General chapter: Bulk density, 40-NF 35.
- [19] United states pharmacopeia. (2018). General chapter: Powder flowability, 40 (1), NF 35.
- [20] Monika T, Amit RS and Ajay KS. (2018). Silicified microcrystalline cellulose, modern co-processed excipient for low dose solid dosage forms" *European Journal of Biomedical and Pharmaceutical sciences*, 5 (2), 722-731.
- [21] M Pasierb and W Wu. (2012). Physiological concentrations of glucosamine sulfate and glucosamine HCL can downregulate interleukin-1, KININS and MMPS in human osteoarthritic chondrocytes. *Elsevier*, (20) S47.
- [22] Patrick JS and Martha SF. (2015). Vitamin B-6. *Advance in nutrition an international review journal*, 6(1), 132-133.
- [23] Noelia Clemente Plaza, Manuel Reig García-Galbis and Rosa María Martínez-Espinosa. (2018). Effects of the Usage of l-Cysteine (l-Cys) on Human Health. *NCBI*, 23(3).
- [24] Lachman L, Lieberman HA and Kanig JL. (2009). *The theory and practise of industrial pharmacy*. 3rd edition Varghese publishing house. Second edition, 182-184, 296-303.
- [25] Aulton ME. (2002). *Pharmaceutics the science of dosage design* Churchill Livingstone. Second edition, 134.
- [26] Rojas J, Lopez A, Guisao S and Carlos O. (2011). Evaluation of several microcrystalline celluloses obtained from agricultural by-products. *Journal of advanced pharmaceutical technology & research*, 2(4), 144-150.
- [27] United states pharmacopeia. (2018). General chapter: Dissolution and disintegration, 40-NF 35, 2270-2274.

How to cite this article

Tomar M and Sinha AR. (2020). A technical note: Characterization and evaluation of novel, ready to use co-processed excipient in nutraceutical herbal vitamin and amino acid formulations. *GSC Biological and Pharmaceutical Sciences*, 11(2), 233-241.
