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Influence of granulation process parameters on food tablet properties formulated using natural powders (*Opuntia ficus* and *Chlorella* spp.)

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Running title: Tablets based on natural powders.

Abstract

In this research two natural health supplements, cactus flour (*Opuntia ficus*) and microalgae biomass (*Chlorella* spp.) have been examined as novel ingredients to formulate health supplement tablets. The physical and mechanical properties of the pure powders were quantified, and their ability to be tableted directly without additional processing was investigated. High-shear wet granulation (HSWG) was explored to improve the flowability and compression characteristics of the powders. Using an L9 Taguchi experimental design, the effect of critical process parameters of HSWG was examined on quality attributes of tablets. Tablets were successfully formulated without the addition of excipients following wet granulation. Consistent and acceptable quality tablets were produced based on the optimal processing conditions determined by L9 Taguchi design. The tablet tensile strength achieved was 0.91 ± 0.05 MPa with a disintegration time less than 30 min and a friability value of 0.05 ± 0.02 %. The tablets obtained in the present study are comparable with commercial available natural supplement tablets in terms of disintegration time, friability and tensile strength. The research provided a basis for the potential use of Cactus (*Opuntia* spp.) and microalgae (*Chlorella* sp.) powders as novel ingredients for the development of dietary supplements tablets, and to be used as excipients for the production of pharmaceutical tablets.

Key words: cactus, microalgae, tableting, high shear wet granulation.

1. Introduction

The demand for food enriched with natural supplements has increased greatly during the past twenty years [1]. The natural health market is focused on the development of new products incorporating novel ingredients with the absence of chemical substances or artificial colours. These products are intended to satisfy the nutritional needs of the consumer, improving life style and preventing chronic diseases [2]. *Opuntia ficus* commonly named Cactus is a xerophytic plant that makes a considerable contribution to the human diet, especially in México. It is an important source of nutritional compounds and traditionally, it is used for the treatment of gastritis, fatigue, dyspnoe and liver injury following alcohol abuse [3].

However, with exception of México, products derived from *Opuntia* are still rare in the European, Asian and US market.

Microalgae are photosynthetic microorganisms that under certain condition are able to produce biomass which is rich in bioactive compound such as proteins, fatty acids, antioxidants, vitamins and polysaccharides [4]. In recent years the commercial applications of microalgae biomass have drastically increased. For example, microalgal biomass can be used to enhance the nutritional value and organoleptic properties of foods (colour, flavour and texture) such as pasta, bread, mayonnaises and gelled desserts [5]. Microalgae are considered a potential source of biologically active chemicals with positive health benefits, such as lowering cholesterol, preventive action against atherosclerosis or anti-tumoral action assisting disorders such as gastric ulcers, wounds, constipation, anaemia, hypertension, diabetes, infant malnutrition and neurosis [6, 7]. Some of the most

studied microalgae and commercially produced at large scale are *Chlorella* spp. and *Spirulina* sp. [8,9].

Tablets are one of the popular dosage forms for personal administration of drugs and nutritional supplements [10]. Recent research has focused on the development of novel formulations of food tablets, consisting of powdered fruits or plants as natural products, and is recommended for all categories of consumers [11]. Some natural tablets have been produced by several authors e.g. *Spirulina* and date [11], pitaya and guava mixed powder blend [12], green and ripe mango [13], pitaya/maltodextrin [14], *Ficus deltoidea* [15,16], *Terminalia chebula* fruit [17]. One of the keys to manufacturing natural supplement tablets is the transformation of the supplement powders into compact tablets, without the requirement to add excipients. To achieve this, the powder should display good flow and compression properties. These characteristics help overcome problems associated with critical quality attributes and the post-processing handling, packaging and storage [18]. However, some natural powders are not suitable for tableting because of the physicochemical composition or mechanical properties, and cannot be compressed directly into tablets [19]. The granulation process is a common technique used to improve the tableting characteristics of such powder blends. The process allows the improvement of flow properties of the mix preventing ingredients segregation conducting to better compression characteristics of the tablet mixture and reduce dust during handling [20]. In particular, high shear wet granulation is a popular technique that allows converting fine cohesive powders into relatively dense granules. Wetted powder particles are mixed, densified and agglomerated under the action of shearing and compaction forces imposed by the impeller and smaller chopper blade turning at high speeds cutting down large agglomerates [21].

For satisfactory performance, tablets must have certain required properties. Three of the most important quality parameters are adequate strength, low friability and acceptable disintegration times [22]. The hardness of the tablets (breakage strength) is a critical quality attribute used to control the tablet manufacturing process. For certain pharmacological tablets, a minimum hardness of 45 N is required [11].

Food travels down to the oesophagus at a rate of approximately 3 to 4 cm/sec and all food should have left the stomach within 2 to 4 hours; this time frame provides a context for the disintegration/dissolution parameters.

To produce tablets with the best possible values for the above three quality parameters, the effect of granulation process factors on these parameters must be known. The Taguchi method is a robust experimental design used to identify the factors affecting the response by minimising variability in a product or process by minimising the effects of uncontrollable factors (noise factors). In the Taguchi design, these noise factors can be controlled during experimentation. Higher values of the signal-to-noise ratio (S/N) identify control factor settings that minimise the effects of the noise factors hence it can determine optimal processing parameters to improve the product quality [22, 23].

In summary, the aim of this research is to formulate Cactus and microalgae powder-based natural supplement tablets and to explore the effects of relevant wet granulation process parameters on the final critical quality attributes of the tablets.

2. Materials and methods

2.1 Cactus and microalgae powders

Cactus (*Opuntia ficus*) powder was obtained from a commercial supplier in Coahuila, México (Kaktus, México). *Chlorella* (*Chlorella* spp.) powder was purchased from a local supplier (Isawari Ireland Ltd., Hillberry, Ireland). For comparison, commercial tablets were also obtained from a local supplier in Cork, Ireland.

The initial moisture of the commercial tablets samples was in the range of 12-45% wb and it was obtained experimentally.

The material properties including moisture content, water activity, bulk density, tapped density and particle size of the powders were determined following standard procedures. All determinations were carried out in triplicate. Moisture was determined using a tray vacuum oven at 60 °C for 48 h (Gallenkamp, UK). Water activity was determined using a Labmaster AW (Novasina AG, Switzerland). The bulk and tapped density of the powders were measured using a Stampf volumeter STAV 2003 (J. Engelsmann AG, Ludwigshafen, Germany). A constant mass of powder was poured into the graduated cylinder and tapped 1250 times to the extreme powder bulk density. The flow properties calculated were the Hausner Ratio [24] and Carr's Index [25]. The particle size was determined using a laser light scattering method based on Malvern Mastersizer (Malvern Instruments Ltd., UK).

2.2 Tablet formulation

Tablets were prepared using a tableting pressing machine (FETTE E1 Schwarzenbek, Model D-2053, Germany) operating at ~60 tablets per minute. The machine was fitted with a circular punch and dies set with settings adjusted to a consistent pressure load. An initial series of tests were conducted to ascertain the tableting performance of each powder individually, Cactus or *Chlorella* spp. It was found that it was not possible to form stable tablets using Cactus alone. Hence it was decided to employ wet granulation process in the powder mix before tableting. Preliminary studies (data not shown) were carried out to define the range of mixing of Cactus and *Chlorella* spp. powders, selecting a ratio of 70/30 for Cactus and *Chlorella* spp. respectively.

Wet granulation process was performed using a high shear mixer granulator equipped with a vessel capacity of 4 L, a chopper, an impeller and a flow controller as shown in Figure 1. (ProCept 4M8, Belgium).

Each batch contained 350 g of the total mixed powder comprised of 70% of Cactus and 30% of *Chlorella* spp. (w/w).

The binder liquid used was distilled water and it was observed that the water used for the experimental set was below 20 % w/w. After the wet granulation process, the mixtures were dried in a tray vacuum oven (Gallenkamp, UK) at 60 °C for 12 h. The moisture content of the dried granules was less than 6% for all the batches in this study. The granules were milled using a burr grinder (KruppsGVX1/2, UK) in order to obtain a powder with a mean particle size <450 µm. Subsequently, each batch was sieved to remove any granules less than 150 µm in diameter in order to achieve a uniform size distribution. The mass yield was in the range ~90%.

2.3 Experimental design

Taguchi experimental designs are fractional factorial designs defined by orthogonal arrays. The orthogonal array has two main properties, each column contains each setting of that variable the same number of times and every pair of two columns contains all possible combinations of the settings of those two variables. This method has become a very important tool in modern industrial processing due it to applies statistical designs that have maximum efficiency with minimum experimental requirements and it does not require fitting mathematical models to experimental data [26]. An L-9 array was chosen (which permits analysing up to four factors at three different levels) to analyse the effect on granulation parameters on the characteristics and compatibility of tablet raw materials.

These variables were: (1) impeller speed of the granulator (50, 100 and 150 rpm); (2) chopper speed of the granulator (500, 700 and 900 rpm); (3) wetting rate (10, 12 and 14 mL/min); (4) mixing time (2, 4 and 6 min). During the experimental setup, it was observed that was necessary to change the minimum level of the chopper speed to accommodate the technical limitations of the equipment (500 rpm).

The experimental matrix for all the conditions tested is presented in Table 1. The outcome of a set of data like this is the best of 81 possible combinations of three settings of four variables. Although an absolute optimum might not be reached, it satisfies to provide an integrated process improvement and consistency of performance.

An ANOVA was done to determinate the contribution and the statistical significance of each factor. Optimum levels were determined based on the

response of tensile strength (Bigger is better) and this response as well as other tablets properties were estimated at these optimum levels.

All data analysis was carried out using STATISTICA 7.1 Software (StatSoft, Inc., Tulsa, OK, USA) and Excel (Microsoft, 2011).

A verification experimental run was performed at the optimum settings in order to validate the optimisation process.

2.4 Physico-mechanical properties of tablets

The physico-mechanical properties of the tablets obtained were performed according to the European Pharmacopoeia (EP) [27]. The friability was determined by taking 20 tablets of each formulation using a friability tester (Erweka TA 40, Germany). The hardness consisted in the determination of crushing strength of 20 tablets for each formulation using a hardness tester (Erweka TBH 30 MD, Germany). The disintegration time was evaluated using six tablets for each formulation utilising a disintegrator tester (Erweka ZT 31, Germany). The disintegration time was reached when the six tablets were completely disintegrated. The tensile strength of cylindrical convex-faced compacts was calculated following the equation reported by [28].

$$\sigma_t = \frac{10 P}{\pi D^2 (2.84 \frac{t}{D} - 0.126 \frac{t}{W} + 3.15 \frac{W}{D} + 0.01)} \quad (1)$$

Where σ_t is the tensile strength, P is the fracture load (N), D is the diameter, t is the thickness and W is the wall height of the tablet. Figure 1 illustrates the tablet geometry for the tablets analysed (Produced and commercial).

3. Results and discussion

3.1 Ingredient powder properties

Powder properties were analysed in order to determine qualities of raw materials used in the present study. These properties are of particular relevance to direct compression of powders for tableting process.

Moisture content is a well-known property related to powder flowability and thus its determination has a great interest. Moisture content values are shown in Table 2. *Chlorella* spp. and Cactus powders presented a moisture content of 5.55 and 5.00 respectively, these values being in a typical range in comparison with other fruits powders used in tablet formulations such as pitaya (5.09), guava (5.31), green mango (4.26) and ripe mango (4.31) [12,13].

Moisture content in Cactus powders was higher, indicating more hygroscopic characteristics than *Chlorella* spp. powder, this difference being due to the different sugar content between the powders.

Powder's moisture content can influence the tablet strength by reducing bulk density and affecting the volume reduction of the mass after compression [29].

However, it is unlikely that the moisture content of the evaluated powders influences tableting characteristics due to the tablets will not be obtained by direct compression of the powders.

In this study, though, moisture content quantification and control will assist in the process design in terms of maintaining an adequate flowability of the powder. It is known that moisture content affects the cohesion of powders due to formed liquid bridges between particles [29]. Increasing moisture content may result in powder

aggregation, low flowability and caking. Moreyra and Peleg et al. [30] showed that at ambient temperature, caking does not occur at water activities of less than about 0.45. The obtained water activity for *Chlorella* spp. (0.22 ± 0.05) is below this value. However, the obtained value for Cactus powder (0.44 ± 0.01) is highly close to this limit. Therefore, relative humidity and temperature will be needed to control in order to facilitate storage and handling of Cactus powder.

Regarding microbial stability of food powders, it can be observed that the moisture content values are below 10%, this being the maximum value in order to prevent spoilage [31]. In relation to water activity, it has been reported that a product with a water activity lower than 0.6 is microbiologically stable [32]. The obtained values for both studied powders are below this limit, indicating no optimal growth for spoilage microorganism and pathogens.

The Carr index (CI) and Hausner ratio (HR) are both measures of powder flowability directly related to the tableting process. Based on Carr index (CI) and Hausner ratio (HR) high values indicate that both powders present poor flowability this could be linked to their physical properties [24].

Hausner ratio was higher for *Chlorella* spp. in comparison with Cactus powder, being these materials considered as medium-flowing powders, and thus can be easily compressible and may form strong coherent junctions [30]. Other reports had mentioned similar values for the HR of natural powders, [13] reported values of HR of 1.30 and 1.43 for green and ripe mango respectively. These values have been compared with other supplement powders where similar properties were identified; green mango powder (HR= 1.30 ± 0.01 ; CI%= 22.91 ± 0.14) and ripe mango powder (HR= 1.32 ± 0.01 ; CI%= 24.45 ± 0.29) [13], pithaya powder (HR =1.53; CI%=

34.87) and guava powder (HR =1.37; CI%= 27.19) [12], *Ficus deltoidea* extract powder (HR =1.43±0.03; CI%=30±1.43) [14].

Particle size has also a great influence on powder flowability [15]. Generally, particle size influences the powder compaction behaviour of powders and thus is directly related to final product quality. Fitzpatrick et al. [18] also reported that particle size has a strong influence on powder segregation. The materials used presented a particle size of 42 and 57 µm for *Chlorella* spp. and Cactus respectively. These values are lower than some others reports from literature. Adiba et al. [11] reported particle sizes of 271 and 202 µm for date fruit and Spirulina powders. Zea et al. [12] founded particle size values higher than those here reported for pitaya and guava powder. Recently, Ong et al. [13] developed fast dispersible fruit tablets from green and ripe mango, reporting particle sizes for green mango fruit powder higher than those found for *Chlorella* spp. and Cactus. However, ripe mango fruit powder values were closer to the values here reported. The small particle size of our materials could indicate a poor medium flowability [18]. Also, it could be assumed that due to the particle sized obtained *Chlorella* spp. and Cactus can behave as cohesive powders and caking problems could be presented. Zea et al. [12] also observed that particle size in mixed fruit powders was larger than individual powders, assuming that was an agglomeration phenomenon.

3.2 Initial tableting results

Cactus and *Chlorella* spp. powders were formulated into tablets individually by direct compression without high-shear wet granulation. In direct compression tableting, dry powder must flow uniformly into the tablet dies to obtain a uniform

product if this is not the case it will represent the main problem encountered in direct compression tableting. Physical properties of the powder are found to have more impact on its flowability as compared to chemical properties. However, it is important to mention that powder flowability also depends on the handling, storing or processing of the material. It was found that Cactus powder presented poor ability to flow into the die and produced thin tablets and with a low value of hardness, this could be related to its physical properties. *Chlorella spp.* powder was freely flowable and the tablets presented acceptable properties such as weight uniformity. Overall, this demonstrated the need for a granulation operation to take place prior to tableting.

Wet granulation was selected to take place prior to tableting, since the main objective is to produce natural tablets with these two powders. The granulation process improves flow and cohesion reduces the dust and cross contamination and permits the handling of powder blends without loss of homogeneity [20, 21, 23].

The granulation process was conducted using a powders ratio of 70:30 % (w/w) (Cactus and *Chlorella spp.*) and distilled water to maintain the purity of the product as a natural health supplement. After some tests, a trial was performed using the following controlled parameters: impeller speed of 100 rpm, chopper speed of 500 rpm, wetting rate of 10 mL/min and 65 % (w/w) total amount of water. Two batches were evaluated using two different milling settings with a final particle size of 447.79 μm and 425.12 μm . The tablets produced had a nominal thickness of 5.5 mm and mass of 500 mg. These results showed that with the use of HSWG the flowability and particle size distribution of the granules increased in reference to the *Chlorella spp.* and Cactus powders (previously discussed). It was shown that the above settings for the granulation parameters would give viable tablets though not

with optimum properties (in particular tablet hardness was low); however these settings were taken as a datum position.

3.3. Effect of granulation process parameters on tablet properties

An L9 Taguchi DOE experimental design was conducted to assess whether the granulation process parameters of impeller speed, chopper speed, wetting rate and mixing time had an influence on the three quality attributes (hardness, friability and disintegration time) of the tablets. Results are shown in tables 3 and 4. All four granulation parameters indicated statistically significant effects at the 95% level ($p < 0.05$) on tablet properties (data not shown) i.e. all four granulation factors have a meaningful influence on all three tablet quality parameters. Tensile strength was defined as the most important parameter of the tablet for the present study. Table 3 indicates the experimental values obtained according to the L9 design showing the responses obtained for each set of experimental conditions tested. Examining Table 3, it can be observed that the factor with the highest impact on the tablet properties was wetting rate, even all the other factors presented statistical significance.

An improvement of hardness was observed for all experimental trials with exception of 1, 6 and 8 runs, where the same wetting rate (12 mL/min) was used.

The tensile strength was calculated in order to take into account the variation in tablet size between the experimental runs. The tensile strength was in a range between 0.40 to 0.91 MPa. Prakash et al. [17] reported similar results using fruit powders, showing that granulation method can build tablets with a higher strength than the direct compression formulation.

The disintegration time varied from 8.09 to 28.36 minutes; these values are in accordance with the ranges reported by several authors. Soares et al. [30] reported disintegration time in a range of 6-12 min for tablets from *Mayterus ilicifolia*; Lefevre and Dupas [31] found values in a range of 0.31 to 11.28 min for paracetamol tablets.

According to the official quality control tests for tablets (Compendial), the disintegration time range obtained at all conditions complies within specified limit for uncoated release tablets [26].

The friability values of the tablets formulated were in the range of 0.16 to 0.81%. All tablets presented a weight loss lower than the acceptable level of <1% during the friability test, as it can be observed in Table 4. Adida et al. [11] reported a range of friability of 0.07 to 0.80% for tablets formulated from *Spirulina*-date powder. Also, Mohamad-Zen et al. [35] reported friability values of 0.94-3.27% of okara tablet formulation.

Table 4 illustrates the results of the main effects ANOVA of the tensile strength of the formulated tablets. The *F* ratio calculated show that factors analysed had a statistically significant effect on tablets tensile strength. Wetting rate showed the most significant impact on tensile strength (77.3 %) followed by chopper speed (4.9 %), mixing time (1.5 %) and impeller speed (1.0 %).

Data analysis (Data not shown) for other physical characteristics such as particle size and bulk density showed that the evaluated parameters presented similar effect on bulk density values. Therefore, it is assumed that tensile strength is correlated to bulk density. On the other hand, no correlations were found between tensile strength and particle size.

3.4 Tablet property correlation studies

In general, the tensile strength of the tablets presented a direct correlation with friability and disintegration time (Figure 2). Tablets with high tensile strength presented low friability values (Figure 2a), while disintegration time increased as tablet tensile strength increased (Figure 2b). With respect to the disintegration time, formulations with high tensile strength presented long disintegration time (22.30 ± 0.32 min.) (Figure 2b). This disintegration time behaviour might be due to the highly hygroscopic nature forming a gel on the surface, preventing water penetrate into the tablet. The disintegration time of our tablets was approximately 22 minutes, indicating an appropriate value. These results indicated that HSWG wet granulation influenced the tablet quality parameters; allow obtaining tablets with characteristics ranged in the recommended levels. Zuurman *et al.* [36] observed that tablet strength is related to the porosities of the granules, mentioning that porous granules increase the deformation during compression.

In Figure 2a, a linear correlation is observed between tensile strength and friability, however, a poor fitting coefficient can be observed. Friability decreases as tensile strength increase, showing a more compacted structure of tablets at high tensile strengths. Figure 2b illustrates the correlation between tensile strength and disintegration time, where a good fitting coefficient was obtained. Zuurman *et al.* [36] developed lactose-starch tablets and also observed a positive correlation between tablets hardness and disintegration time.

3.5 Optimisation of the process to improve the quality attributes of tablets

The Taguchi methodology enables the settings of the four granulation parameters that will give the optimum tablet properties to be found.

It is critical to predicting the outcome of combinations not used in the design (especially the one considered to be the best, if it is not one of those used) and the confidence interval of the prediction, and then run a validation test with those conditions. If the experimental outcome of the validation set of conditions is within the confidence interval of the predicted responses, then neglecting interactive effects is approved.

The optimal values of the parameters are showed in Table 5. Experiments were repeated in triplicates under optimised conditions i.e. the impeller speed 50 rpm, the chopper speed 500 rpm, the wetting rate 10 mL/min and the mixing time 2 min. The tensile strength, critical attributes and variability were obtained under these conditions (Table 5). The value of tensile strength (0.91 ± 0.05 MPa) corresponds very well to the values predicted by the model (0.97 MPa), providing a good validation of the model. After the statistical optimisation, critical attribute such as disintegration time (24.67 ± 2.03 min) was increased and friability (0.05 ± 0.02 %) was decreased compared to the resulted obtained without any optimisation.

4. Conclusions

This research shows that food powders as Cactus and microalgae (*Chlorella* spp.) can be successfully used to produce health supplement. The tablets formulation was performed by the wet granulation method without the addition of an excipient. Tablets presented comparable quality attributes including tensile

strength, disintegration time and friability in comparison to off-the-shelf commercial natural tablets. This study demonstrated a process route leading to the development of new nutritional tablets in the natural market including new and healthily ingredients.

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List of Figures

Figure 1. Tablet shape and dimensions.

Figure 2. Correlation between tensile strength and a) friability; b) disintegration time of the *Chlorella* spp. and Cactus tablets.

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Table 1. Design of experiment for controlled high shear wet granulation process.

Run	Impeller speed, rpm	Chopper speed, rpm	Wetting rate, mL/min	Mixing time, min
1	50	500	12	4
2	50	700	14	6
3	50	900	10	2
4	100	500	14	2
5	100	700	10	4
6	100	900	12	6
7	150	500	10	6
8	150	700	12	2
9	150	900	14	4

Table 2. Powder properties of raw materials.

Material properties	<i>Chlorella</i> spp.	Cactus
Moisture content (%)	5.55±0.31	5.00±0.59
Water activity a_w	0.22±0.05	0.44±0.01
Bulk density (kg/m ³)	596.32±44.87	407.66±31.00
Tap density (kg/m ³)	737.42±21.23	472.79±41.47
Carr index, CI (%)	19.18±4.28	13.71±1.25
Hausner ratio, HR	1.24±0.06	1.15±0.01
Mean particle size D_{50} (μm)	42.21	57.48

Table 3. Physical characteristics of tablets obtained according the experimental design.

Run	Wet granulation factors				Responses		
	Impeller speed (rpm)	Chopper speed (rpm)	Wetting rate (mL/min)	Mixing time (min)	Tensile strength (MPa)	Disintegration time (min)	Friability (%)
1	50	500	12	4	0.54±0.04	10.54	0.37
2	50	700	14	6	0.88±0.05	22.20	0.16
3	50	900	10	2	0.87±0.03	19.54	0.32
4	100	500	14	2	0.80±0.04	16.56	0.32
5	100	700	10	4	0.91±0.05	22.30	0.32
6	100	900	12	6	0.40±0.03	8.09	0.81
7	150	500	10	6	0.86±0.05	28.36	0.19
8	150	700	12	2	0.53±0.02	11.53	0.32
9	150	900	14	4	0.74±0.03	16.20	0.23

Table 4. Analysis of variance of main effects on the tablets tensile strength.

Factors	SS	df	F	p
Impeller speed, rpm	6.565	2	5.508	0.0048
Chopper speed, rpm	32.699	2	27.413	0.0000
Wetting rate, mL/min	516.855	2	433.583	0.0000
Mixing time, min	10.374	2	8.703	0.0002
Error	101.920	171		
Total	668.413			

Table 5. Optimised conditions for *Chlorella* spp. and Cactus tablets.

Factors	Value
Impeller speed, rpm	50
Chopper speed, rpm	700
Wetting rate, mL/min	10
Mixing time, min	2
Tensile strength, MPa	0.91±0.05
Friability, %	0.05±0.02
Disintegration time, min	24.67±2.03

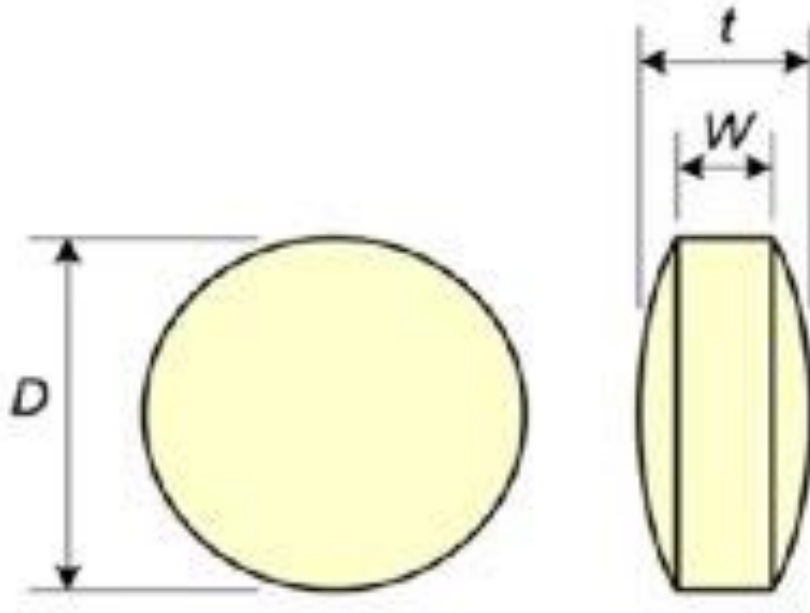


Fig. 1

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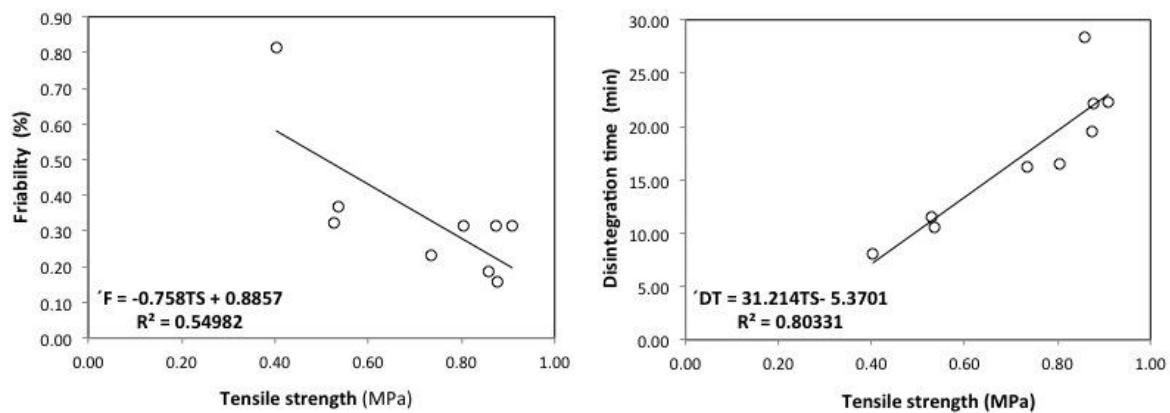
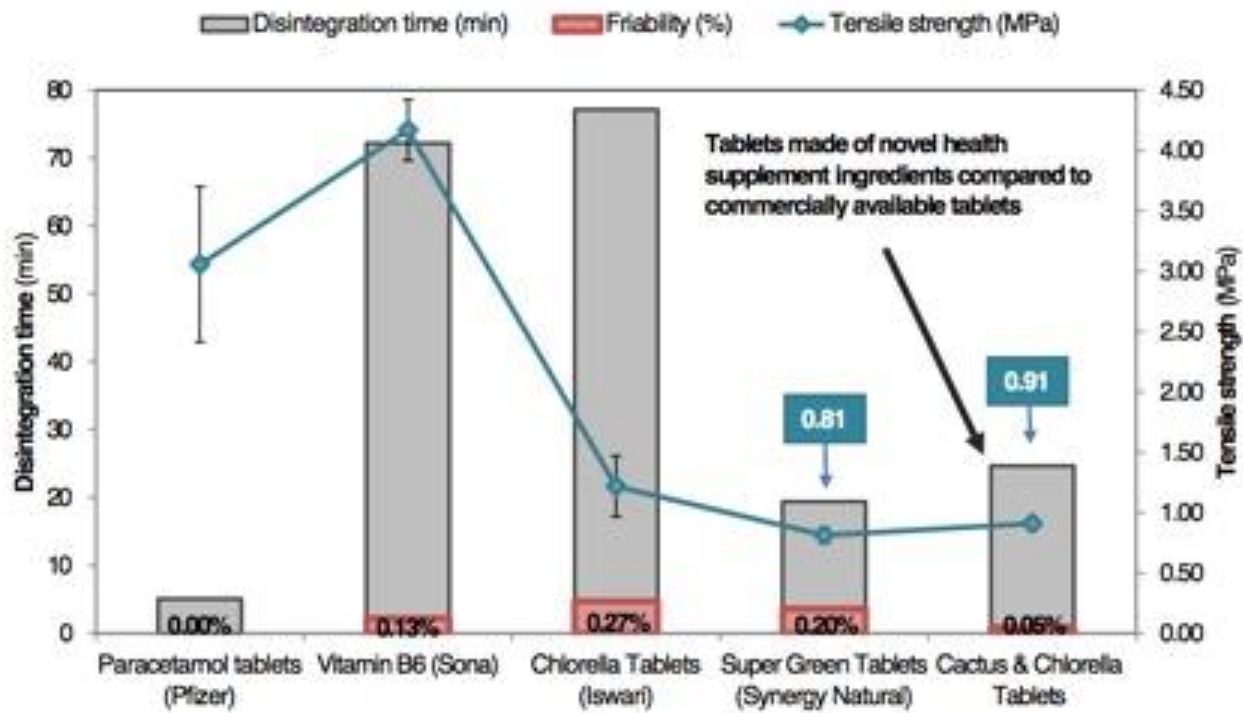


Fig. 2



Graphical abstract

Highlights

Food tablets were formulated from cactus and microalgae (*Chlorella* sp.) powders.

Wet granulation method was successfully performed without the addition of excipients.

The quality attributes of tablets were improved by the optimum levels of the controlled process parameters by Taguchi design.

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