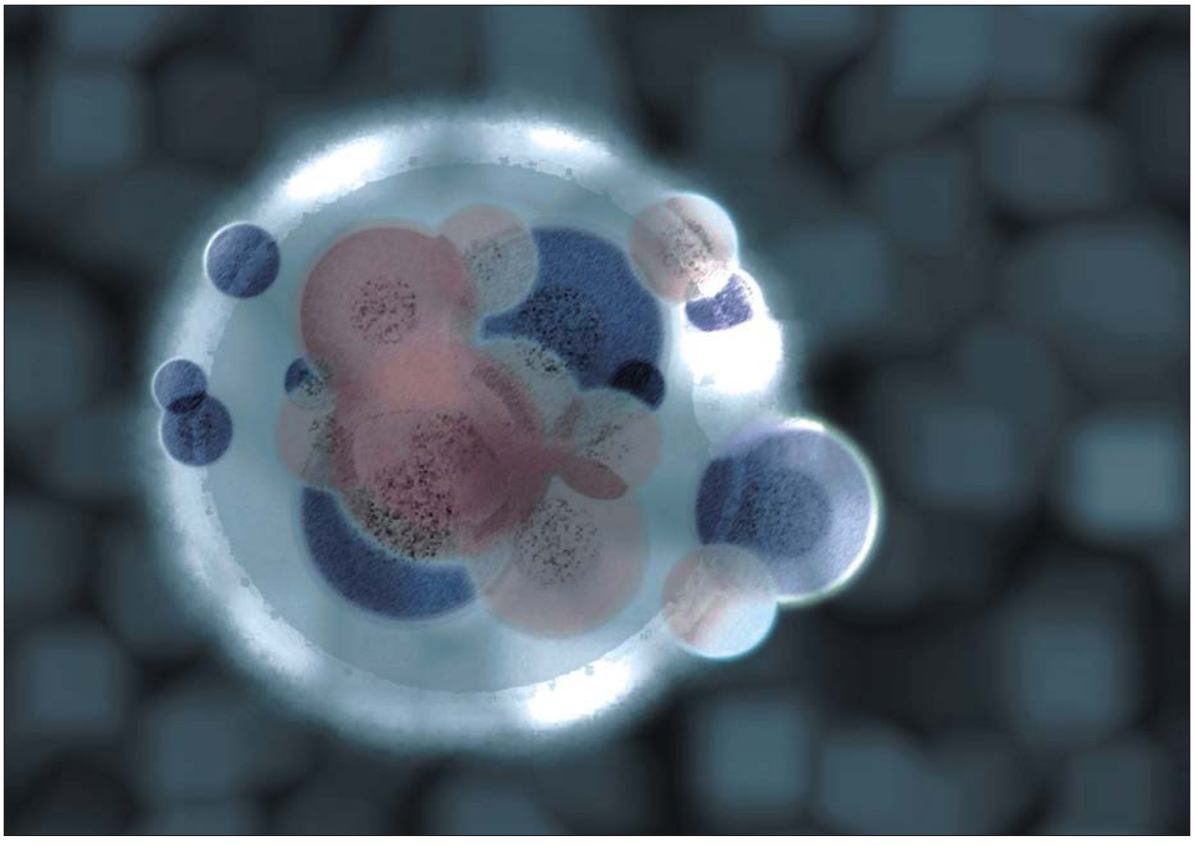

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Research Article
Optimisation of an Effervescent Pineapple Tablet

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Abstract
This study is mainly undertaken to design and optimize an effervescent tablet formulation of Josapine pineapple by using the D-optimal experimental design methodology. Josapine pineapple powder, citric acid, sodium carbonate and stevia were used in the formulations as independent variables. Tablets were prepared by the direct compression method and evaluated for their disintegration time and sensory properties which were regarded as responses in a D-optimal design. Formulation V3 was selected as the optimum formulation with pineapple powder, citric acid, sodium carbonate and stevia at 49.59, 20.00, 11.96 and 18.45%, respectively. In addition, V3 has a very fast disintegration time and quite high overall acceptability which represents the consumer approval. The observed values of the responses obtained from the optimized formulation were very close to the predicted values where the euclidean distance calculated for V3 was equal to 0.26. In conclusion, this study reveals that the effervescent pineapple tablet has a wide potential for future development and can be enhanced for commercialization.

Key words: D-optimal, effervescent tablet, stevia, josapine pineapple powder

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Now a days, people in the world are moving towards a healthy lifestyle. They are focused more on exercise and also the food that they take every day. Fruits are one of the foods that are rich in minerals, vitamins, phytochemical and also enzymes that simply suit the current trends of a healthy lifestyle[1]. Fruits not only can be consumed fresh but also after processing and preserving in different forms and types[2]. For example juices, beverages, jams, jellies or fruit punch. Fruit juice is a very popular form of fruit representation because it can be simply consumed as a drink that can benefit the health by its nutritional value. Fruit juices from different fruits vary in their flavour and composition, mainly sugar and acid content[3].

Nevertheless, fruit juice has a high water content which makes it susceptible to decomposition by microorganisms, chemical and also enzymatic reactions. Consequently, the idea of an effervescent fruit tablet can overcome the weakness of fresh fruit products. Effervescent fruit tablets can prolong the shelf life while minimizing the packaging requirements and reducing shipping weight. During preparation of the effervescent fruit tablet, various factors such as colour, sugar and natural acid need to be balanced in order to obtain a desirable fruit drink flavour and taste after mixing with water. The development of an effervescent fruit tablet needs to be optimized for their disintegration time and sensory attributes to obtain maximum acceptability. *Stevia rebaudiana* or known as stevia is chosen to replace sugar since it gives an excellent sweetness plus it is natural so that a very small amount of stevia can satisfy the role of sugar itself. Steviol glycoside extracts from stevia having up to 300 times the sweetness of sugar and stevia has attracted attention with the rise in demand for low carbohydrate and low sugar sweeteners. This is because stevia has a negligible effect on blood glucose therefore it is attractive to people on carbohydrate-controlled diets.

Optimisation is a special technique developed to increase the desirable quality parameters by analyzing the various components of individual factors such as disintegration time, sweetness and flavour required in relation to sensory evaluation of detailed descriptors. Optimisation consists of few steps for obtaining the optimum condition or result under a given set of constraints. Optimisation is very useful especially in food research with different systematic experimental designs for product process or formulation[4]. Expected high desirable scores and low disintegration time in an effervescent fruit tablet are computed by using an integrated approach such as analysis of variance (ANOVA) and response surface modelling. There is still no report of an optimisation study on effervescent fruit tablets in Malaysia.

Usually for experiments that involve a formulation, a two-level factorial is utilized as an alternative for the design of experiment (DOE) method. The two-level factorial consists of all combinations of each factor at its high and low range of levels. By using a two-level factorial this can decrease the number of experiments required because only a fractions of runs need to be completed to produce estimates of the main effects and simple interactions. In pharmaceutical, nutraceutical and food formulations where the conditions need the response to be dependent on the proportions of the ingredients, factorial designs may not make much sense. Therefore, mixture design is much more suitable in this study because it accounts for the dependence of response on the proportionality of the ingredients used. In mixture experiments, the factors are the components or ingredients of a mixture and consequently their levels are not independent[5].

The objective of this study is to develop a formulation for an effervescent pineapple tablet by adapting the effervescence effect as an advantage to dissolve quickly in water. Moreover, the aim is extended to develop a formulation of effervescent pineapple tablet that is acceptable to consumers by using an optimisation technique through mixture design. In addition, the mixture design facilitated by Design Expert 7.0 is used to develop a series of formulations. In the context of the effervescent pineapple tablet formulation process, a study of the effect of the mixture of the composition on the sensory properties and disintegration time is performed. The amount of pineapple powder, citric acid, sodium carbonate and stevia are manipulated in this study and denoted as independent variables.

MATERIALS AND METHODS

Selection of fruits: Pineapple fruits were bought from the Pasar Borong Selangor, Malaysia which sourced the fruits from a pineapple plantation in Simpang Renggam, Johor. The variety chosen was Josapine with an average size, attractive bright orange red colour fruits with good quality and fully ripe. These were picked in batches of five for the appropriate laboratory determinations. After purchase, the fruits were immediately transported to the laboratory.

Preparation of freeze-dried powders: The working area, cutting board, knife, plastic containers and other utensils used

were washed and sanitized with sodium hypochlorite solution at pH 7 for the maximum sanitizing effect prior to processing. After the removal of the crown and skin, the whole fruits were crushed into pulp using a domestic blender. The pulp was added with 20 % maltodextrin. Some preliminary experiments to produce pineapple powder were undertaken. From the result, the pure pineapple pulp without the addition of a drying agent gave a powder that was very hygroscopic which had a tendency to become sticky and agglomerate. Corn maltodextrin DE 10 was added to the pulp in order to help decrease the hygroscopicity of the freeze-dried pineapple powder. The treated pulp was put into an airtight plastic container and kept in a freezer at 20°C for 8 h. After freezing, the samples were transferred to a vacuum freeze dryer (Ben Hay, United Kingdom) and dried at 35°C for 48 h at 0.25 m bar. In this freeze drying process, the moisture was removed from the freezing pineapple pulp by sublimation and this helped in minimising the deterioration of quality during the drying process. The pineapple powder obtained was collected and sealed in a plastic container and stored in a refrigerator (4°C) until required for further tests.

Experimental design: D-optimal mixture design was used to evaluate the effect of changes in mixture compositions on dependent variables and statistical optimisation of the formulation with the least number of experiments[6]. D-optimal design is straight optimisation based on a chosen optimality criterion and the best model that will fit. Four independent variables, namely freeze-dried pineapple powder, stevia, citric acid and sodium carbonate were taken into account in the experimental design. However, due to some limitations of the Design Expert software, only three independent variables could be taken into account for experimental design at any one time. The parameters selected are freeze-dried pineapple powder, citric acid and sodium carbonate while stevia remains as an actual component. The main purpose of this experimental design is to maximize the consumer acceptability and minimize disintegration time through optimisation of the dependent variables. Some 20 formulations with different levels based on minimum and maximum ranges of the independent variables were prepared. The range of maximum and minimum percentages of independent variables affects the experiments whereby the levels of each variable are restricted and dependent on each other since the level of a single component cannot be changed independently[7]. Hence, the amount of each variable in the mixture[8,9] should total to 100%. Table 1 shows the restrictions imposed on the mixture component proportions. Constraints were applied based on the applicable amounts of the components in pharmaceutical formulations. Disintegration time and overall acceptability were considered as dependent variables (responses) in this study.

Table 1: Mean particle size diameter, 11 m of the ingredients

Ingredients	Mean particle size diameter (11 m)
Pineapple powder	261±1.0
Sodium carbonate	233±1.0
Citric acid	266±1.0
Stevia sugar	727±1.0

Data represents Mean±SD of triplicate analysis

Tablet preparation: Each ingredient was weighed according to the generated formulation by using an electronic balance (A and D company, Tokyo). The powders were mixed by using a tumbler mixer and slowly poured into a uniaxial die using a steel funnel. Tablets were directly compressed by a universal testing machine (Instron 5566 machine, USA) equipped with a 21 mm flat-faced punch and die set. Then, the die was tapped 20 times to achieve homogeneous density distribution of the mixed powder. The compression speed was fixed at 0.5 mm sec^{-1} and the force applied was fixed at 7 kN. Compacted tablets were ejected by removing the bottom punch and with a constant force of 1 mm sec^{-1} applied to the upper punch. Tablets were stored in a desiccator for 24 h to allow the binder to react and improve the interparticle bonding.

Sensory analysis: The effervescent pineapple tablet drinks were prepared according to the mixture design formulation and evaluated for their acceptance. The samples were coded with random letters. One effervescent pineapple tablet was dissolved in 50 mL water to make each drink. Thirty panellists aged between 19-48 years were served with an effervescent pineapple tablet drink and asked to compare with those prepared from pulp. The panel measured selected critical attributes such as aroma, flavour, colour, sweetness and total acceptability. All product samples were evaluated in order to obtain liking scores (7-point hedonic scale). A higher rating reflected good quality attributes (dislike very much-like very much). The panellists were instructed to rinsae their mouth with water and eat a puffed biscuits between samples in order to minimize the residual flavour effect. All the critical attributes were calculated based on 100% overall acceptability.

Modified disintegration time: The disintegration time of the tablets was measured by using a beaker and stirrer. Some 50 mL of distilled water was used per tablet with a constant

speed magnetic stirrer. The disintegration time was recorded when the tablet was totally dissolved in the water.

Quality control tests for tablets: The prepared effervescent tablet made using pineapple fruit powder via direct compression was subjected to the standard tablet quality control tests[10]. Weight variation, tensile strength test, friability and particle size and shape were determined for the quality control of the optimum tablet formulations.

Weight variation: Weight variation was determined by weighing 20 tablets individually and the average weight was recorded and the percentage of variation for each tablet was determined.

Tensile strength test: The tensile strength of the tablet was determined 24 h after manufacture by testing six tablets from the optimum formulation using a universal testing machine (Instron 5566 Machine, USA). The time was constant so as to have consistent elastic recovery of the tablets. Radial tensile strength of the pharmaceutical tablets was measured using a diametral compression test known as the Brazilian disc test[11]. In the Brazilian disc test, the cylindrical tablets were placed between two plates and the tablets are compressed along their central lines until they break. The compression force was applied at the top of tablet diametrically (Fig. 1). The radial tensile strength, T of the tablets was calculated using following formula[11]:

$$T = \frac{2P}{\pi Dt} \quad (1)$$

Where:

T = Tablet tensile strength (N)
P = Fracture load (N)
D = Tablet diameter(m)
t = Thickness of the tablet (m)

Friability: Ten tablets was placed in a friability tester (Electrolab Model EF-2, Mumbai) and exposed to rolling and repeated shocks at 25 rpm for 4 min. The weight loss was recorded. A maximum weight loss of no more than 1% during the friability test is generally considered acceptable[10].

Particle size and shape: Particle size and shape is an important characteristic during the particle formation and processing as it greatly affects the quality of the final product[12]. Particle size and shape influence the contact surface area as a greater size distribution is caused by finer particles, while a large contact surface area between the particles results in a high angular particle shape[13,14]. The particle shape was analysed by using a Hitachi S-3400N Scanning Electron Microscope, SEM (Hitachi High Technologies America Inc., California USA).

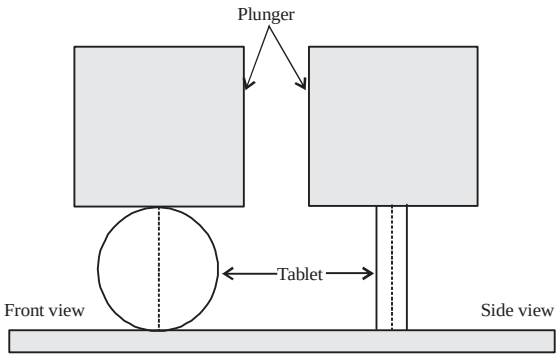

Fig. 1: A schematic diagram of tablet tensile strength evaluation through Brazilian disc test

Statistical analysis: An experimental table was constructed by using D-optimal mixture design. The data was analysed by one-way analysis of variance (ANOVA), followed by optimisation through a special cubic model by using Design Expert version 7.0 software. The differences were defined as statistically significant at $p<0.05$.

RESULTS AND DISCUSSION

Analysing the mixture data: The percentage range of ingredients used to prepare the 20 formulations and the respective observed responses are given in Table 2. From the preliminary statistical analysis (ANOVA) of the experiments it is suggested that a non-linear response function is expected. Based on statistical significance ($p<0.05$) of data fitting to possible models (linear, quadratic, cubic and special cubic) and the insignificance of lack of fit, the special cubic model was chosen for interpreting the results. The special cubic model was fitted to the data for response Y_1 (disintegration time, min) and Y_2 (overall acceptability, percentage). The mathematical models generated for responses Y_1 and Y_2 are as follows:

$$Y_1 = 1.37\,X_1+1.38\,X_2+8.29\,X_3+2.64\,X_4+0.61\,X_1X_2-9.56\,X_1X_3-3.07\,X_1X_4-9.34\,X_2X_3-1.60\,X_2X_4-11.78\,X_3X_4+108.76\,X_1X_2X_3+0.51\,X_1X_2X_4+9.44\,X_1X_3X_4-4.43\,X_2X_3X_4$$

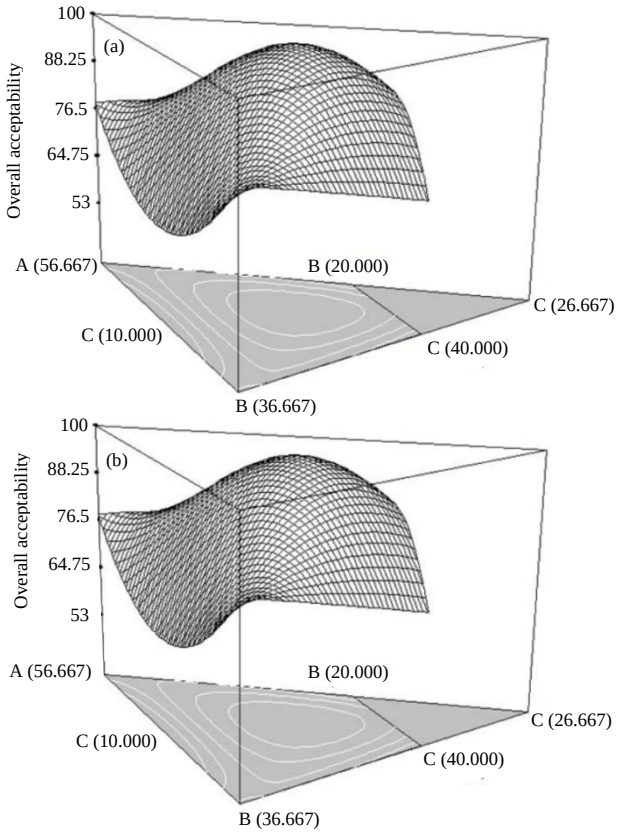

Fig. 2(a-b): 3D response surface plots for (a) Disintegration time and (b) Overall acceptability as affected by the percentages of A: Pineapple powder, B: Citric acid, C: Sodium carbonate

Table 2: Mixture design, disintegration time and overall acceptability of the effervescent pineapple tablets

					Response			
	Vm "iable factor"				Disintegration time (ruin) (Y_1)		Overall acceptability (%) (Y2)	
Formulation	X_1 (%)	X_2 (%)	X_3 (%)	X_4 (%)	[b]Pred	[d]Obs	[b]Pred	[d]Obs
V_1	40.00	31.24	10.81	17.95	1.36	1.31±0.03	93.33	94.01±0.78
V_2	40.00	33.66	10.00	16.34	1.44	1.42±0.05	93.33	93.95±0.70
V_3	49.59	20.00	11.96	18.45	1.22	1.22±0.06	89.42	89.67±0.16
V_4	49.23	20.00	12.44	18.33	1.24	1.23±0.01	89.59	89.01±0.66
V_5	43.33	23.33	13.58	19.76	1.90	1.83±0.08	84.11	83.84±0.54
v_6	41.29	34.74	13.97	10.00	2.32	2.29±0.01	81.89	82.94±0.73
V_7	55.19	21.80	13.01	10.00	2.36	2.39±0.01	81.65	81.06±0.40

X_1: Pineapple powder, X_2: Citric acid, X_3: Sodiurn carbonate, X_4: Stevia sugar, [b]Predicted values, [b]Observed values [d]Mean±SD

$$Y_2 = +65.78\ X_1+62.50\ X_2+45.36\ X_3+64.49\ X_4+4.54\ X_1X_2+28.43\ X_1X_3+90.56\ X_1X_4+56.91\ X_2X_3+139.44\ X_2X_4+79.21\ X_3X_4+1447.85\ X_1X_2X_3-729.47\ X_1X_2X_4+162.01\ X_1X_3X_4-329.33\ X_2X_3X_4$$

In the present study, pineapple powder (X_1, %), citric acid (X_2, %), sodium carbonate (X_3, %) and stevia (X_4, %) had significant effects on the disintegration time and overall acceptability of the effervescent pineapple tablet. Figure 2a and b show the response surface plots predicted from the special cubic model for the disintegration time and overall acceptability. In these graphs, the response is shown as a function of the pineapple powder, citric acid and sodium carbonate, having fixed stevia to a value of 13.33% with respect to the total of 100%. These plots are very useful to illustrate the interaction effects of the factors on the responses. From Table 3, X_1X_3, X_2X_3, X_3X_4 and $X_1X_2X_3$ were significant model terms for disintegration time ($p<0.05$).

Table 3: Analysis of variance (ANOVA) of dependent variables

Source of variation	Sum of square	Degree of square	Mean	F-value	p-value square prob>F
Y_1 (Disintegration time)					
Model	9.50	13	0.730	80.01	<0.0001
Linear mixture	5.96	3	1.987	217.64	<0.0001
X_1X_2	0.03	1	0.031	3.40	0.1145
X_1X_3	0.21	1	0.215	23.53	0.0028
X_1X_4	0.04	1	0.038	4.14	0.0881
X_2X_3	0.25	1	0.249	27.23	0.0020
X_2X_4	0.02	1	0.015	1.65	0.2465
X_3X_4	0.19	1	0.194	21.22	0.0037
$X_1X_2X_3$	0.75	1	0.747	81.83	0.0001
X_1X_2	0.00	1	0.000	0.02	0.9044
$X_1X_3X_4$	0.03	1	0.031	3.34	0.1173
$X_2X_3X_4$	0.01	1	0.008	0.90	0.3802
Residual	0.05	6	0.009		
Lack of fit	0.00	1	0.003	0.30	0.6089
Pure error	0.05	5	0.010		
Cor total	9.55	19			
Y_2 (Overall acceptability)					
Model	2165.44	13	166.57	11.83	0.0031
Linear mixture	1060.24	3	353.41	25.09	0.0009
X_1X_2	1.71	1	1.71	0.12	0.7391
X_1X_3	1.90	1	1.90	0.14	0.7259
X_1X_4	32.97	1	32.97	2.34	0.1769
X_2X_3	9.24	1	9.24	0.66	0.4489
X_2X_4	114.29	1	114.29	8.12	0.0292
X_3X_4	8.76	1	8.76	0.62	0.4602
$X_1X_2X_3$	132.39	1	132.39	9.4	0.0221
X_1X_2	293.79	1	293.79	20.86	0.0038
X_1X_3	8.99	1	8.99	0.64	0.4549
$X_2X_3X_4$	45.20	1	45.20	3.21	0.1234
Residual	84.50	6	14.08		
Lack of fit	47.92	1	47.92	6.55	0.0507
Pure error	36.57	5	7.31		
Cor total	2249.93	19			

Figure 2a shows that increasing the percentage of citric acid and sodium carbonate and decreasing the amount of pineapple powder in the tablet formulation may result in a reduced disintegration time. This situation was predictable since both citric acid and sodium carbonate are effervescent agents where the reaction between these two will produce the effervescence in the form of carbon dioxide through bubble form and help the tablet to disintegrate quickly[15]. The fastest disintegration times throughout all the formulation were 1.16 and 1.24 min which resulted from the reaction of the citric acid and sodium carbonate in a 2:1 ratio. For the overall acceptability response, X_2X_4, $X_1X_2X_3$ and $X_1X_2X_4$ were significant model terms ($p<0.05$) in the Y_2 equation. Figure 2b shows an area with the highest overall acceptability that can be observed in the response surface plot. Pineapple powder gives the greatest flavour effect and incorporation with a suitable amount of stevia gives a satisfactory amount of sweetness in the effervescent tablet formulation which might lead to a desired overall acceptability.

Optimisation results: The aim of optimisation is to achieve the defined targets for all three responses simultaneously with respect to the predefined constraints. Suitable balancing between the levels of components is essential to acquire optimal responses. Table 4 shows seven optimum check-point formulations with higher desirability and thus selected for numerical optimisation. All the proposed optimized formulations were prepared and analysed for the responses. Table 4 shows the comparative values of the predicted and observed responses. All formulations show an acceptable disintegration time and good consumer acceptability. Among the formulations V_1-V_7, the highest correlation (lowest difference) between the predicted (Pred) and observed (Obs) values for both the two responses was detected for formulation V_3. This was confirmed by calculating the euclidean distance (Ed) using the following equation[16]:

Table 4: Validation step: Optimized levels for independent variables and comparative values of predicted and observed responses for numerically optimised formulations

		Cornp 1	Cornp 1	Cornp 1	Cornp 1	Response 1	Response 2
Std	Run	A: Pineapple powder (%)	B: Citric acid (%)	C: Sodiurn carbonate (%)	D: Stevia (%)	Disintegration time (rnrn)	Overall time acceptability (%)
10	1	40	30	20	10	2.51	38.89
12	2	50	20	15	15	4.43	38.89
19	3	40	20	20	20	1.48	25.00
20	4	40	20	20	20	1.57	25.00
17	5	40	26.67	13.33	20	1.30	77.78
8	6	50	20	20	10	1.59	22.22
15	7	50	20	10	20	1.24	77.78
5	8	40	40	10	10	1.38	75.00
6	9	40	40	10	10	1.19	80.56
2	10	60	20	10	10	1.40	86.11
18	11	45	20	15	20	2.55	44.44
11	12	43.33	23.33	20	13.33	3.96	69.44
7	13	40	35	15	10	1.56	88.89
14	14	40	33.33	10	16.67	1.44	83.33
16	15	45	25	10	20	1.48	80.56
4	16	50	30	10	10	1.21	91.67
13	17	40	30	15	15	1.16	75.00
3	18	50	30	10	10	1.35	88.89
9	19	50	20	20	10	2.29	22.22
1	20	60	20	10	10	1.34	75.00

$$Ed = (\Sigma_i (Pred_i\text{-}Obs_i)^2)^2 \quad (2)$$

where, $Pred_i$ and Obs_i are predicted and observed values, respectively of response I and the summation was over all responses. The euclidean distance calculated for V_3 was equal to 0.26. In addition, V_3 has a very fast disintegration time and quite high overall acceptability which represents consumer acceptance. Therefore, V_3 was selected as the optimum formulation for further studies.

Tablet quality control tests: All of the tablets that were used for the tests were produced under similar conditions to avoid processing variations. The weight of the optimum effervescent pineapple tablet is 2.5±0.015 g. The tensile strength value is 4.1±0.18 kN while for the friability of the tablet is 0.75±0.12%. The acceptable tensile strength value for the standard effervescent tablet is 3 kN[17]. The acceptable value of tensile strength of the optimum effervescent pineapple tablet may be due to the irregular shape of the ingredients (refer to the ingredients particle shape in Fig. 3) as the plastic deformation material is fundamentally affected by differences in the particle shapes[18]. Irregular particle shape tended to interlock with each other. After passage of time, the particle interlocking may result in strong mechanical bonds between particles.

The friability of the tablets is one of the important factors to be considered where the low friability percentage is a must to avoid the formation of dust and also to ensure that the tablet is hard and flexible in preventing crushing and also breakage. According to Gennaro[10], the acceptable friability based on the weight loss of a powder and the upper level of acceptability is generally regarded as being less than 1% for pharmaceutical products. The friability value for the optimum effervescent pineapple tablet is less than the 1% standard. Hence, this suggests that the optimum effervescent pineapple tablet can survive future packaging and transportation and thus reduce the amount of weight loss.

Table 5 shows the particle size of each ingredient of effervescent pineapple tablet. Particle size is one of the most important physical properties and may influence the disintegration time[19]. Table 5 shows that the mean diameter of the particle size of the sodium carbonate powder is the smallest compared to the pineapple powder, citric acid and stevia. Particle size and shape influenced the contact surface area where a greater size distribution is caused by the fine particles and large contact surface area between the particles caused by an angular particle shape[20].

Figure 3a and d show SEM images of the main ingredients; citric acid, sodium carbonate, stevia powder and pineapple powder. The pineapple particles appear to have a more solid and smoother surface than the others, with rough and porous surfaces as revealed through high magnification. The presence of porous particles is expected after the sublimation of ice crystals during the freeze drying process[21].

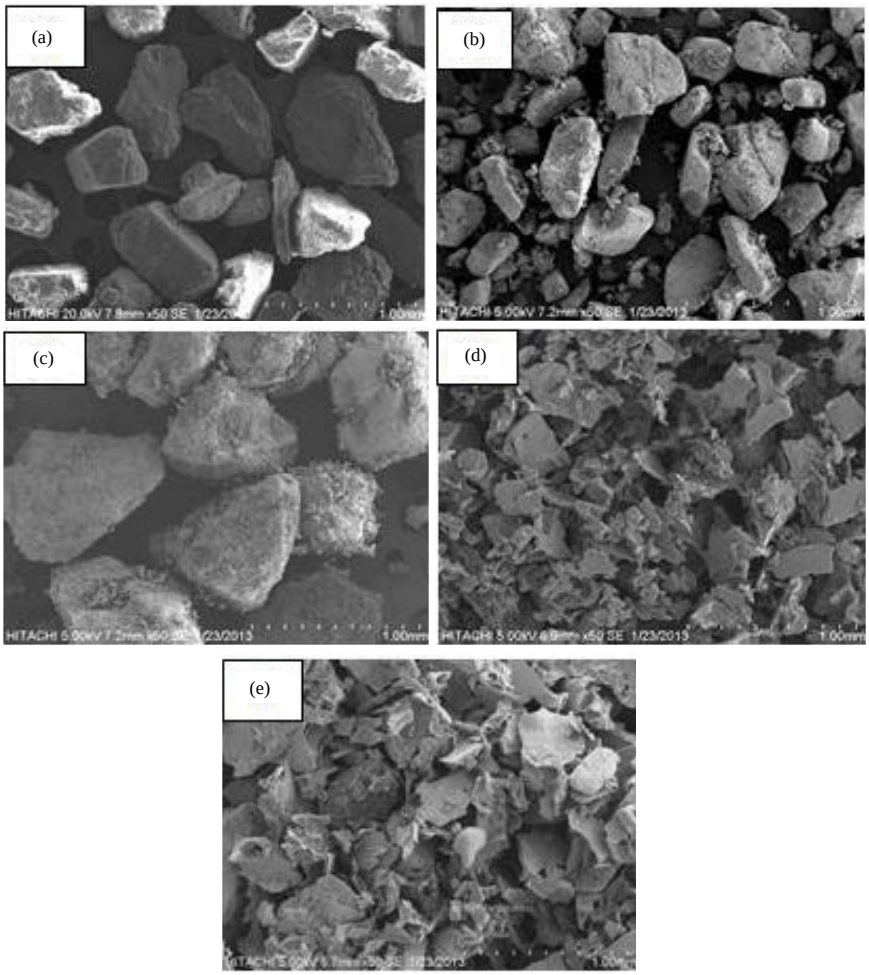

Fig. 3(a-e): Scanning electron microscope images of effervescent agent (a) Citric acid, (b) Sodium carbonate and natural sweetener, (c) Stevia powder and fruit powder, (d) Pineapple powder and (e) Mixture of all the ingredients under 50x magnification

Table 5: Mean particle size diameter of the ingredients

	Experimental range		
Factors	Low value (%)	High value (%)	Constraint
X_1 (Pineapple powder)	40	60	$X_1+X_2+X_3+X_4 = 100$
X_2 (Citric acid)	20	40	$X_1+X_2+X_3+X_4 = 100$
X_3 (Sodium carbonate)	10	20	$X_1+X_2+X_3+X_4 = 100$
X_4 (Stevia sugar)	10	20	$X_1+X_2+X_3+ = 100$

The shapes of citric acid, sodium carbonate and stevia particles have a typically irregular shape. However, there are differences between the surface morphology of the particles as the citric acid particles have a smoother surface compared to the rougher surfaces of sodium carbonate and stevia particles. Figure 3e showed SEM images of the compressed tablet. The irregular particle shape for each ingredients interlocked with each other after compression, this explain the high tensile strength result of the tablet.

CONCLUSION

Effervescent tablets of Josapine pineapple with citric acid, sodium carbonate and stevia as variable components were prepared and optimized using D-optimal mixture experimental design. The quantitative and qualitative effect of these factors on tablet disintegration time and overall acceptability can be predicted by the special cubic model. Formulation V3 was selected as the optimum formulation with pineapple powder, citric acid, sodium carbonate and stevia at 49.59, 20.00, 11.96 and 18.45%, respectively. In addition, V_3 has a very fast disintegration time and quite high overall acceptability which represents the consumer approval. The observed values of the responses obtained from the optimized formulation were very close to the predicted values where the Euclidean distance calculated for V_3 was equal to 0.26. The

results have confirmed that the D-optimal technique can be successfully employed for designing an effervescent tablet with the desired physical properties.

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