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Preparation and Evaluation of Fast-Disintegrating Effervescent Tablets of Glibenclamide

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Fast-dissolving effervescent tablets (FETs) were prepared by the modification of nonreactive liquid-based wet granulation technique. Effervescent systems are not stable in the presence of trace amount of moisture, and elimination or inactivation of free water is the key to stability apart from manufacturing in controlled humidity environment. Our main objective of the project was to develop FETs of glibenclamide based on highly plastic granules that can be compressed at low pressure to form fast-melting pharmaceutical tablets. In this study, we have screened various acid and carbonate sources for the effervescent system. Citric acid was coated with plastic materials such as polyethylene glycol (PEG), which provide a physical barrier to the reaction. The inherent hygroscopic nature of PEG could decrease the affinity for moisture of effervescent mixtures and can provide a stabilizing effect. Sodium bicarbonate was blended with sugar alcohol like mannitol, which would give a protective coating. PEG 1000 melts at body temperature (~37°C) and thereby does not delay the reaction between the acid source and base. The present formulation using citric acid–sodium bicarbonate and citric acid–sodium glycine carbonate tablet with PEG and mannitol was found to have better reaction properties and reaction stability than does the standard citric acid–sodium bicarbonate tablet. FETs of glibenclamide might aid in dissolution due to increase in microenvironmental pH around the granules and saliva. Sensory study on disintegration time and mouth feel attributes ranked the present formulation based on grittiness, chalkiness, and overall preference as best.

Keywords fast effervescent tablet; balance test method; thermal stressing; effervescent stability; sensory test

INTRODUCTION

Fast-disintegrating tablet drug delivery is rapidly gaining acceptance as an important new drug delivery technology. Due to increased life expectancy, the elderly constitute a major portion of the world population today. These people will experience deterioration of their physiological and physical abilities like dysphagia (Dohney, 1993; Seager, 1998). This problem is also common in children because of their underdeveloped muscular and nervous system (Walid, Raj, & John, 2000). This dosage form can be achieved by a variety of technologies, including direct compression, wet granulation, and freeze-drying. Currently, seven fast-dissolving/-disintegrating technologies are in vogue in the world market (Khankari, Hontz, Chastain, & Katzner, 1999; Rong-Kun, Xiaodi, Beth, & Richard, 2000).

The major limitation associated with the usage of effervescent excipients in fast-dissolving tablet is their inability to prevent moisture absorption. Manufacturing requires a controlled environment of a low relative humidity and production of the final tablets with moisture impermeable blisters (Mohrle, 1989). As a consequence, the cost of fast-dissolving tablets is much higher when compared with standard tablets formulated by direct compression, despite having the more sophisticated technologies. Hence, the formulation scientists are focusing to exploit/utilize the direct compression technique in fabricating fast-disintegrating tablets. Mathematical regression studies have been done to determine the optimum combination of critical physical characteristics such as porosity and tensile strength and formulation component in tablets made of cellulosic compounds and saccharides (Barbel, Gerolf, & Peter, 1998). The bubble- or gas-generating reaction of the effervescent couple in the effervescent granule is most often the result of the reaction of an acidic agent and an alkaline agent. The reaction of these two general classes of compounds produces effervescence upon contact with water. A process for preparing fast-dissolving dosage form, comprising a blend of pharmaceutical

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active ingredient and effervescent mixture by controlled humidity and heating, has been described (Madan, Trehan, & Vinod Kumar, 2004). In another US Patent (6071539) effervescent granules having a controllable rate of effervescence are described. Such granules comprise an acidic agent, an alkaline agent, a plasticizer, and a hot-melt extrudable binder capable of forming a eutectic mixture with an acidic agent (Robinson & McGinity, 2000). An effervescent dosage form consisting of drug-encapsulated microparticles, which are adapted to provide immediate release of the pharmaceutical ingredients, is disclosed in another US Patent (5178878) by Wehling, Scheuhle, and Madmala, 1993. The aim of the present work is to develop a dosage form incorporating water- and/or saliva-activated effervescent granules having a controllable rate of effervescence and a therapeutic compound. This has been done by the modification of nonreactive liquid-based wet granulation technique. Another advantage of the present technique is that combination of the effervescent granules with the other ingredients can provide effective taste masking of particularly poor tasting compounds. Manufacturing of the fast effervescent tablets by the proposed method in this current study does not demand either sophisticated technology/instruments or stringent atmospheric conditions, which eventually reduces the cost of the prepared tablets.

MATERIALS AND METHODS

Materials

The following materials were used as received from commercial suppliers: polyethylene glycol (PEG) 1000 (Koch-Light Laboratories Ltd., Colnbrook, Bucks, UK), mannitol (Merck India Ltd., Mumbai, India), dextrose (SD Fine Chem, Mumbai, India), colloidal silicon dioxide, citric acid, sodium bicarbonate and sodium carbonate, sodium glycine carbonate, sodium hydrogen citrate, potassium hydrogen phosphate, sodium hydroxide (Nice Chemicals Pvt Ltd., Kochi, India), croscarmellose sodium (SD Fine Chem), Tween 80 (Merck, Hohengrunn, Germany), microcrystalline cellulose (Avicel® PH101 FMC Corporation, Philadelphia, PA, USA), Pink lake blend-LB1355 (Colorcon Inc., Philadelphia, PA, USA), and a gift sample of glibenclamide (Aristo Pharmaceuticals Ltd., Indore, MP, India).

Preparation of Effervescent Granules

Required quantities of citric acid, sodium hydrogen citrate or tartaric acid, and PEG 1000 (Table 1) were dissolved or dispersed in absolute alcohol (95%). Microcrystalline cellulose was granulated with the above solution. It was then spread on the trays and dried in a forced air oven at 55°C until the alcohol odor has gone (~4 h). The granules were then passed through 40-mesh screen. Stoichiometric quantity of sodium bicarbonate or sodium glycine carbonate was blended with mannitol for 15 min. Citric acid, sodium hydrogen citrate or tartaric acid granules, and sodium bicarbonate mixture was blended in a tumbler mixer (PM-1Cadmach Engineering, Ahmedabad, India) at 4 rpm until the mixture reaches uniformity. Various excipients like magnesium stearate, aspartame sodium, and flavoring agent were added and once again blended thoroughly. The blend was then passed through a sieve (80) to ensure homogeneity and fine particle size distribution. The blended materials were transferred into a polyethylene bag and stored in a desiccator until use.

Flowability of Granules

The static angle of repose was measured according to the fixed funnel method (Train, 1958). The bulk density of the mixed powders before compression was studied by determining the Hausner's ratio and Carr's index from the poured and tapped bulk densities of a known weight of sample using a measuring cylinder and the following formula (Carr, 1965; Hausner, 1967). Hausner's ratio = D_p/D_t, Carr's index = $[(D_p - D_t)/D_p] \times 100$, where D_p (poured density) = weight/V_p (poured volume) and D_t (tapped density) = weight/V_t (tapped volume).

TABLE 1
Composition of Various Effervescent Combinations

	Batch						
Ingredients (mg)	B1	B2	B3	B4	B5	B6	B7
Citric acid anhydrous	9.09	9.61	—	—	—	—	9.09
Sodium hydrogen citrate	—	—	11.19	10.44	—	—	—
Tartaric acid	—	—	—	—	10.00	9.61	—
Sodium bicarbonate	27.20	—	10.44	—	20.00	—	27.27
Sodium glycine carbonate	—	23.07	—	16.43	10.00	23.07	—
Polyethylene glycol 1000	9.09	9.61	11.19	10.44	20.00	9.61	—
Absolute alcohol	q.s	q.s	q.s	q.s	q.s	q.s	—
Mannitol	18.18	19.23	22.38	20.89	20.00	19.23	18.18
Microcrystalline cellulose	36.36	38.46	44.77	41.78	40.00	38.46	36.36

Preparation of Tablets

As given in Table 2 glibenclamide, croscarmellose sodium, and cornstarch were individually passed through sieve no. 60 and mixed thoroughly in a poly bag for about 5 min. Aspartame sodium, american mint, silicon dioxide, and magnesium stearate were sieved (80) and blended with the above mixture for about 2 min. The composition was compressed into flat tablets with 10 mm diameter using a single-punch tablet machine at a fixed compression force. The punches and die were lubricated with a small amount of magnesium stearate using a cotton swab preceding compression. The tablets were stored at 25°C and 34% relative humidity (saturated solution of magnesium chloride hexahydrate) for 1 week in a desiccator. The standard sodium bicarbonate–citric acid tablets in which PEG 1000 was excluded were used as control tablets.

Measurement of Tablet Tensile Strength and Friability

The tablet-crushing load, which is the force required to break a tablet into halves by compression in the diametric direction, was measured using a Pfizer tablet hardness tester. Tablet's friability was measured using Roche friabilator USP at 25 rpm for 4 min.

Measurement of Disintegration Time In Vitro and In Vivo

In vitro disintegration test was performed using a disintegration apparatus, with distilled water at 37 ± 0.5°C. All tablet property values are shown as averages of five determinations. The time required for complete disintegration in the mouth was measured in five healthy volunteers (Ethics permit PA 358). The end point was considered when there was no lump in the tongue. Further the volunteers kept the tablets motionless on their tongues during the test period as described by Koizumi, Watanabe, Morita, Utoguchi, and Matsumoto, 1997.

TABLE 2
Formulation Composition of Fast Effervescent Tablet Prepared by Direct Compression

Ingredients (mg)	Quantity (mg/tablet)
Glibenclamide	5.0
Croscarmellose sodium	25.0
Corn starch	25.0
Aspartame sodium	30.0
American mint	9.5
Silicon dioxide	3.5
Magnesium stearate	3.0
Color-Pink lake blend	q.s
Fast-dissolving granulation	250.0

Measurement of Tablet Porosity

The porosity of the tablet was calculated from bulk and true tablet volume. It is calculated from the measured tablet diameter, thickness, and true density of powder and was determined using the following equation $E = 100\,(1 - V_t/V_b)$ (Marshall, 1987). The diameter and thickness of the tablet were measured with a micrometer. The true density of the powder was determined using a helium pycnometer (AccuPyc 1330, Micrometrics Instrument Inc., Norcross, GA, USA).

Balance Test Method

A glass beaker with polyethylene cover was placed on an analytical balance. The cover had a rectangular shaft (2.9 × 0.6 cm), cut in the center through which the effervescent tablets were dropped into the beaker (Neil, Banker, & Peck, 1982a). Deionized distilled water (80 mL) was measured into the beaker and kept at room temperature. The weight of the reaction vessel and cover was tared. Weighed tablet was set on the edge of the slot in the cover. The tablet was then gently dropped through the slot into the beaker. Immediately after the tablet entered into water, the decrease in weight was noted down for 2 min. The final weight loss (W_F) measured 2 min after the reaction begins and the amount (mg) of carbon dioxide lost at any time (t) during an effervescent reaction were designated as W_a.

Water Uptake Studies

Moisture determinations for various excipients were carried out by their respective U.S.P.XXIII and/or N.F.XVIII methods (The United States Pharmacopoeia-24/National Formulary-19 2000). Loss on drying for compendial methods was performed in a hot air convection oven. Tablets were placed in desiccators containing saturated aqueous sodium chloride solution (75% RH). Samples were also kept at 50°C in capped glass bottles in a stability chamber for 4 weeks. At predetermined time intervals, samples were withdrawn. The water uptake was measured gravimetrically ($n = 3$).

Wetting Time and Water Absorption Ratio

A piece of tissue paper folded twice was placed in a small petridish (i.d. = 6.5 cm) containing 6 mL of water. A tablet was placed on the paper and the time required for complete wetting was then measured. Complete wetting can be taken as the time at which solvent front covers the entire tablet. Wetted tablets are transferred to a tissue paper to wipe off excess water and weighed immediately. The water absorption ratio was determined using following equation $R = (W_a - W_b)/(W_b \times 100)$, where W_b is the weight of the tablet before water absorption and W_a is the weight of the tablet after water absorption (Bi et al., 1996).

In Vitro Dissolution Studies

Dissolution test was carried out in 900 mL of pH 7.4 phosphate buffer containing Tween 80 (0.24%) and absolute alcohol (8.5%) at 37 ± 0.5°C in a dissolution tester USP with a paddle rotation at 50 rpm. Aliquot of dissolution medium was withdrawn at various time intervals up to 120 min, passed through 0.22-μm filter membrane (Millipore, County Cork, Ireland), and absorbance was measured at λ_{max} 300 nm using UV spectrophotometer. Dissolution was carried out for all designed formulations and conventional marketed tablets (El-Massik, Darwish, Hassan, & El-Khordagui, 1996). The dissolution studies were carried out in triplicate.

In Vivo Oral Absorption Test

In vivo test was performed to study the oral absorption of the prepared glibenclamide after each formulation was administered to three healthy volunteers (Ethics permit PA-323), keeping the tablet in the oral cavity until disintegration (Ishikawa, Watanabe, Utoguchi, & Matsumoto, 1999). The subjects were then rinsed their mouth with an aliquot of distilled water without ingesting the disintegrated particles. Aliquots of the above medium was passed through a 0.22-μm filter membrane (Millipore) and quantified by using UV spectrophotometer at 300 nm to determine the amount remaining in the oral cavity. The amount of drug absorbed through the oral mucosa was calculated by subtracting the amount from the initial amount.

Thermal Stressing of Packaged Tablets

The prepared tablets packed in an aluminum foil from various batches (five each) were placed in a 75°C convection oven (Baxter Scientific Products Model DN-63, Midland, Canada) for 3 h. It was then allowed to cool to room temperature. Once at room temperature, each of the aluminum foil was then peeled under controlled temperature and humidity conditions and assessed for the degree of tablet mottling. Because the tablets were colored, any effervescent reactions that occurred could easily be seen as darker spots or mottling on the tablet (Wells et al., 1997). Tablets were given a rating from 0 to 4 (least to most) for the degree of tablet mottling. Packaged tablets of each formula that had not been thermally stressed acted as controls. These tablets were given a mottling score of 0. All the stressed tablets were graded in a blinded fashion to minimize the variability and bias in the evaluation.

pH Determination

Tablets from various batches were put in a beaker containing distilled water (30 mL) and temperature was maintained at 25°C. The pH was measured after complete disintegration of the tablet using Mettler pH measuring apparatus. The consistent measurement of solution pH is a sign of uniform distribution of raw materials within the tablet.

Sensory Studies

Sensory study (Ethics permit PA-323; Institutional Ethical Committee) was carried out on disintegration time and mouth feel attributes like grittiness, chalkiness, and overall preference. The subjects ($n = 5$) were asked to record the time for the tablet to completely dissolve in the mouth and give scores for mouth feel attributes and overall liking of the product. Ranking is as follows: 1 = best, 2 = good, 3 = satisfactory, and 4 = worst.

RESULTS AND DISCUSSION

The reaction most often employed for tablet disintegration in an effervescent tablet formulation is that between a soluble acid source and an alkali metal carbonate to produce carbon dioxide gas. This reaction can also occur even in the presence of small amount of moisture. If this reaction does occur after the tablet is prepared and packaged, it will cause the product to become physically unstable and decompose. Once the reaction is initiated, the reaction will proceed even more rapidly because a byproduct of the reaction is additional water. For these reasons, the raw materials either in the anhydrous state, with little or no adsorbed moisture, or with water molecules in a stable hydrate are preferred. However, a lesser amount of water is inevitable for binding as the completely anhydrous granulation usually cannot be compressed into a physically stable product. Solubility, another raw material property, is equally important in the formulation of effervescent tablets and the materials used are expected to dissolve during the effervescent reaction (Mohrle, 1989).

Materials such as citric acid and sodium carbonate will form hydrates readily. Under low percent relative humidity conditions (<20%), the true equilibrium state is the anhydrous form; the hydrate must give up its water of hydration. If slight hygroscopic substance like PEG 1000 is incorporated into the effervescent formula, moisture present may preferentially be taken by it to prevent dissolution of the effervescent components, which will react to form carbon dioxide. Surface passivation is an important technique to achieve effervescent stability. This essentially involves pre-reacting the effervescent system in a closed vessel with heat to form a nonreactive coating around the effervescent granules (Swarbrick & Boylan, 2002). Other methods of improving effervescent stability include encapsulating the acid or base components of the formulation in an effort to provide a barrier to the reaction and producing a core tablet containing the effervescent system covered by a protective coating of a sugar alcohol (Lavie, 1986; Smith, 1961; Witzel & Clark, 1978).

Preparation of Effervescent Granules

In the present method, we have used the combination of above methods to improve the effervescent stability. Citric acid was coated with plastic materials such as PEG, which provide a physical barrier to the reaction. The inherent hygroscopic nature of PEG could decrease the affinity for moisture of effervescent mixtures and can provide a stabilizing effect. Sodium bicarbonate was blended with sugar alcohol like mannitol, which would give a protective coating. PEG 1000 melts at body temperature (~37°C) and thereby does not delay the reaction between the acid source and base. Bi, Sunada, Yonezawa, and Danjo (1999) have used microcrystalline cellulose as disintegrant to prepare rapidly disintegrating tablets. Microcrystalline cellulose has a high internal porosity and a large surface area due to randomly aggregated filamentous microcrystals. It provides highly absorbent, lubricant, and moisture retaining and distributing properties that are essential to the extrusion process as pelletization aid (Shah, Kabadi, Pope, & Augsburger, 1995). These beneficial properties of microcrystalline cellulose made us to use it as a suitable dispersant in the current formulations.

Balance Test Method

Quantification of an effervescent reaction to monitor the stability of selected effervescent tablet system has been studied by Neil, Banker, & Peck, 1982b. A simple, continuous, immediate response weight loss procedure by an adequately sensitive analytical balance offers the most direct and applicable technique to determine the total amount of carbon dioxide evolved, the reaction rate, and other characteristics of the reaction process. To study the rate of an effervescent reaction such as between sodium bicarbonate and citric acid in excess water, producing carbon dioxide, water, and sodium citrate, one can theoretically measure the increase in one reaction product or decrease in one reactant. The obvious element to measure continuously would be the carbon dioxide generated. The weight of carbon dioxide lost at any time during the effervescent reaction was given as W_a and final weight loss measured 2 min after the reaction was started was designated as W_F (Table 3). Citric acid in combination with sodium bicarbonate or sodium glycine carbonate has shown highest values compared with other acid and base sources. Plotting log ($W_F - W_a$) versus time graph will indicate the three events observed during the effervescent reactions. They are lag time (wetting period), actual time of the effervescent reactions, and latent period in which the effervescent reaction has stopped and carbon dioxide slowly comes out of the solution. From the slope of the first-order plot, reaction rate constant K can be calculated. Respective reaction rate constant values from various batches are given in Table 3. Highest value was observed by sodium glycine carbonate–citric acid batch (B2) followed by sodium bicarbonate–citric acid (B1). Control tablets of sodium carbonate–citric acid without PEG (B7) have shown similar reaction rate constant values as B1 and B2. The index of reactivity I_R, which combines both reaction rate and total carbon dioxide evolved (W_F), is the product of both reaction rate constant and final weight loss, and respective values were estimated and tabulated in the same table. After being stored in high relative humidity, tablets have not shown any significant physical changes like no significant swelling, and the surface was smooth in all the batches except control citric acid–sodium bicarbonate tablets (B7), which were highly porous and powdery, although slight swelling and little rough surface were observed with sodium hydrogen citrate and tartaric acid with sodium bicarbonate and sodium glycine carbonate (B3, B5, and B6), respectively.

Effervescent Stability Studies

The temperature had no influence on all the batches. This has been proved by the thermal stress study and mottling assessment of stressed tablets. Except control sodium carbonate–citric acid tablets, all other batches had showed zero mottling score. Investigation of the storage condition (75% RH) in the

TABLE 3
Final Weight Loss (W_F) of Carbon Dioxide, Reaction Rate Constant (K), Effect of Storage Time on the Index of Reactivity Values, and Porosity from Various Effervescent Formulations

Batch	W_F (mg)	$K \times 10^{-2}$/s	Index of Reactivity Values (mg/s) Storage Time (Weeks)			Porosity (%) Storage Time (Weeks)			Mottling Assessment
			0	2	4	0	2	4	
B1	550.0 ± 2.15	10.2 ± 1.23	56.10	55.90	55.80	18.00	20.00	22.00	0
B2	570.0 ± 4.54	11.0 ± 3.11	62.70	61.60	61.60	17.00	18.20	19.00	0
B3	470.0 ± 4.81	6.0 ± 6.12	29.40	27.30	26.70	14.00	15.60	16.00	0
B4	480.0 ± 7.32	6.5 ± 3.78	31.20	29.10	28.60	15.60	16.40	17.30	0
B5	485.0 ± 2.11	6.2 ± 5.33	30.07	28.90	28.70	16.80	18.90	19.70	0
B6	490.0 ± 2.65	6.4 ± 6.34	31.36	29.20	28.80	18.60	20.50	21.20	0
B7	560.0 ± 1.45	10.8 ± 7.34	60.48	10.21	5.26	21.45	35.76	45.87	2

Average of 15 values.

I_R showed that a maximum weight loss was with the control citric acid–sodium bicarbonate compared with other tablets. The losses of reactivity have occurred in all the formulations with maximum loss within first 2 weeks, but were insignificant (Table 3). Temperature has less pronounced effect on the stability of the tablets than relative humidity as shown by the I_R values. This shows the strong correlation between humidity and storage condition (Parrot, 1981). The PEG coating has significantly reduced the spontaneous reactivity and loss of carbon dioxide during the storage condition especially at 75% relative humidity. Therefore, stability measurements at 75% RH could be useful as a worst-case check to select the appropriate effervescent combinations. The actual relationship between the various levels of ingredients and its stability on long-term storage can be identified.

In Vitro Evaluation of Tablets

In Table 4, we have compared the friability, hardness, porosity, wetting time, water absorption ratio, and in vivo disintegration time of granules and prepared tablets. Except the control sodium bicarbonate–citric acid tablets (B7) in which PEG 1000 was excluded, granules of all other batches were uniform and free flowing. Control tablets also showed low hardness, high friability, and high compressibility. This might be due to poor binding due to total absence of binding agent like PEG. High porosity is essential for immediate water penetration and fast disintegration. Batches B1 and B2 showed high porosity compared with other batches. This was proved by shorter wetting time, water absorption ratio, and in vivo disintegration time. As expected control batches showed maximum porosity compared with all other batches when stored for 2 and 4 weeks (Table 3). This might be due to the increase in reactivity in presence of moisture, which would have resulted in increase of pore radius. This method was used in the assessment of aspirin stability by Gucluyildiz, Banker, and Peck, 1977. In short, the stability studies of selected effervescent systems have shown that the described experimental procedure has significantly improved the stability of the effervescent tablets. The index of reactivity has been used as a successful experimental tool for the effervescent tablet reactivity combining both the amount of carbon dioxide generation and the reaction rate of the effervescent reaction. The study of the effervescent system showed that the stability of the effervescent tablet was dependent on the tablet formulation, storage conditions, and length of time the tablet was stored. The present formulation using citric acid–sodium bicarbonate and citric acid–sodium glycine carbonate tablet (B1 and B2) coated with PEG and mannitol is found to have better reaction properties and reaction stability than does the standard citric acid–sodium bicarbonate tablet. The other tablets containing sodium hydrogen citrate and tartaric acid combinations have inferior reaction properties and reaction stability like the control tablet of sodium bicarbonate and citric acid.

In Vitro Dissolution and Sensory Studies

Glibenclamide is insoluble in water and only 45% of the oral dose is absorbed through gastrointestinal tract (Davis & Granner, 1996). The absorption of glibenclamide is dissolution rate limited. Fast-disintegrating effervescent tablets of glibenclamide might aid in the dissolution due to increase in microenvironmental pH around the granules and saliva. Pregrastric absorption could even decrease the t_{max} compared with conventional tablets. As shown in Table 4, the percentage glibenclamide absorbed from oral cavity ranges from 6 to 8%. Pregrastric absorption could even decrease the t_{max} compared with conventional tablets as proved by in vivo oral absorption test. The dissolution profiles of conventional tablet and fast-dissolving effervescent glibenclamide tablet were determined in phosphate buffer pH 7.4 in 120 min (Table 4). This medium containing Tween 80 and absolute alcohol has better discriminating power than borate buffer and showed that fast-dissolving tablets have slight improvement in the dissolution rate than the

TABLE 4
Evaluation of Glibenclamide Granules and Tablets

Properties	B1	B2	B3	B4	B5	B6
Angle of repose (θ)	23.86 ± 0.72	22.94 ± 0.62	23.54 ± 0.52	24.76 ± 0.37	23.74 ± 0.43	25.94 ± 0.16
Compressibility (%)	22.63 ± 0.45	24.46 ± 0.32	23.52 ± 0.22	22.32 ± 0.43	22.98 ± 0.19	30.93 ± 0.21
Hardness (N)	4.1 ± 0.80	4.8 ± 0.78	5.1 ± 0.76	5.0 ± 0.34	4.56 ± 0.67	2.12 ± 1.65
Friability (%)	0.665 ± 0.10	0.689 ± 0.13	0.701 ± 0.18	0.767 ± 0.11	0.623 ± 0.11	1.94 ± 0.13
Porosity (%)	18.32 ± 0.01	22.13 ± 0.01	16.18 ± 0.01	15.98 ± 0.01	15.76 ± 0.02	14.95 ± 0.01
Wetting time (s)	29.0 ± 5.25	27.0 ± 4.44	35.0 ± 3.45	33.0 ± 2.27	38.0 ± 3.17	38.0 ± 3.56
In vivo disintegration time (s)	31.0 ± 3.67	32.0 ± 4.68	38.0 ± 3.13	36.0 ± 4.56	38.0 ± 4.92	42.0 ± 3.87
pH	9.2 ± 0.22	9.3 ± 0.18	9.7 ± 0.88	9.8 ± 0.92	10.2 ± 0.118	9.3 ± 0.98
Buccal absorption	6.72 ± 0.68	7.48 ± 0.85	7.57 ± 1.19	8.43 ± 0.98	8.26 ± 0.99	7.49 ± 1.26
In vitro dissolution (%)	90.72 ± 1.28	92.18 ± 0.95	88.57 ± 0.79	89.87 ± 0.15	87.26 ± 0.49	86.49 ± 0.77

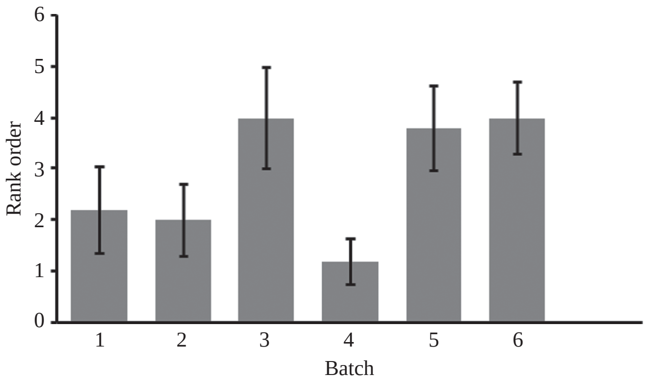

FIGURE 1. Sensory study and overall preferences between various batches.

conventional tablets. Therefore, fast-dissolving effervescent glibenclamide tablet could increase the bioavailability of glibenclamide (Blume, Ali, & Stewart, 1993). Determination of pH from different batches showed consistent values thereby indicating that raw materials are uniformly distributed. Although grittiness and chalkiness are similar in all the batches the time to dissolve in the mouth might be the reason between the differences among the overall preferences between various batches. It has been shown that although there is a close similarity between the batches from B1 to B6, the batches B1, B2, and B4 are superior as given in Figure 1. Sensory study on disintegration time and mouth feel attributes ranked the present formulation based on grittiness, chalkiness, and overall preference as best.

CONCLUSION

It can be concluded from this work that coating the acidic materials with lower melting point PEG and blending with sugar alcohol-coated alkaline material could significantly improve the stability of effervescent tablets without compromising dissolution rate. Fast effervescent tablets provide an excellent mouth feel and good physical stability because it melts at about 37°C. This dosage form is convenient, economically feasible, and needs only a modification of the conventional tableting method. Manufacturing of the fast effervescent tablets by the proposed method does not demand either sophisticated technology/instruments or stringent atmospheric condition, which eventually reduces the cost of the fast-dissolving tablets and ultimately benefits the patient population.

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