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Research Article

# FORMULATION AND EVALUATION OF TASTE MASKED RAPID RELEASE TABLETS OF SUMATRIPTAN SUCCINATE

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**ABSTRACT**

The present study deals with the masking of intensely bitter taste of an antimigrainal drug, sumatriptan succinate and to formulate, a rapid release formulation of the taste masked drug. Taste masking was attempted by different approaches i.e. use of effervescent couple (ME), solid dispersion (MS), kneading (MK), polymer dispersion (MD), addition of flavour and sweetener (MF) and precipitation method (MP). The prepared mixture/granules were subjected for evaluation of taste masking, on 12 healthy human volunteers and it was reported that, mixture/granules prepared by ME, MK, MD and MP were found to be taste masked, but products prepared by MS and MF showed no taste masking. Prepared taste masked mixture/granules were mixed with other directly compressible excipients in various ratios and six tablets per batch (24 tablets) were prepared using direct compression technique. Prepared tablets were evaluated for wetting time, disintegration time, uniformity of dispersion, drug content and *in vitro* drug release at pH 6.8 and 7.4. Formulation ME1, formulated by using mixture/granules prepared by ME showed, minimum value for disintegration time (12sec) and wetting time (2sec) and maximum drug release i.e. 99.79% at pH 6.8 and 98.65% at pH 7.4 respectively, within 2 min. In a nutshell, ME1 has been selected as a best formulation and this is suggested that, it can be subjected for pilot plant scale up.

**Keywords**: Taste masking, Rapid release tablets, Sumatriptan succinate, Tartaric acid, β – Cyclodextrin, Eudragit E-100

## INTRODUCTION

In the present scenario, a variety of pharmaceutical research has been come in to focus to develop new dosage forms for effective therapy with increased safety. Considering value of life, most of these endeavors have been focused on patient compliance.[1] Palatableness of oral dosage form admits a key factor for achieving compliance especially in pediatric, geriatric, bedridden, nauseous or non-compliant patients[2] who find difficulty in swallowing or chewing solid dosage forms due to diseased state or are willingly reject to take solid dosage forms due to concern of choking. Hence, an oral disintegrating tablet seems a suitable alternative for them[3]. More than 50% of pharmaceutical products are orally administered for several reasons and bitter and unpleasant taste of drug is one of the important formulation problems that is encountered with such oral products.[4] The center for drug evaluation and research defines oral disintegrating tablet as a solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds when placed on the tongue.[5]

In mammals the ingestive response to sweeteners, amino acids and many bitter compounds is initiated by the interaction of chemical compounds with G – protein coupled receptor (GPCRs) on the apical membrane of taste cell. Two families of GPCR are known to mediate this detection process- the $T_2$Rs and $T_1$Rs. $T_2$Rs –respond selectively to compounds that elicit bitter taste sensation in humans.$T_1$Rs which appear to function predominantly as heterodimers are activated by amino acids and sweetener (artificial and natural).[6] In the development of orally dosage forms and product development taste is most important factor.[7] Taste masking of oral pharmaceuticals play a significant role to improve patient compliance; therefore taste masking technologies offer wide scope for innovation and invention in the development of patient friendly dose administration. Negligible perception of unpleasant taste of the drug two major strategies are commonly utilized, are reduction of drug solubility in saliva where balance between reduced solubility and bioavailability must be achieved, and secondly is to alter the ability of the drug to interact with taste receptor.[8]

Migraine is a neurobiological disorder affecting 10-15 percent of the younger generation in developed countries each year, approx 73% migraine patients mainly prefer oral therapy to treat the disorder. However gastric stasis is a common problem during a migraine attack, which adversely affect drug absorption and pharmacokinetics, resulting in delayed and inconsistent relief.[9] The mechanism employed for disintegration of the conventional tablets is basically dependent on surface erosion and gastric motility. However, gastric stasis is a well known occurrence during a migraine attack. Therefore, if the release properties of an oral migraine treatment could dissolve and disperse independent of gastric motility, it may allow for faster absorption into the systemic circulation. Sumatriptan succinate is a 5-HT 1D (5-hydroxy tryptamine 1D) receptor agonist, used as in the treatment of migraine and cluster headache, Sumatriptan succinate is generally administered by oral and parental routes.[10] On oral administration Sumatriptan succinate is found to be rapidly but incompletely absorbed, which undergoes hepatic metabolism, resulting in a low absolute bioavailability (14% in humans).[11] The main objects of efforts in the management of migraine are to provide patients with highly effective and rapid relief from during attack. Onset of action could be an important factor in selecting the best route of administration or formulation for a particular patient. Patient compliance and safe administration of the drug is also an important consideration to be kept in mind during migraine attack. Fast or effervescent oral medications are ideal for migraine attacks because they are rapidly absorbed and give fast action during attack.[12]

Sumatriptan succinate is bitter in taste so, taste masking is an extremely important factor for the formulation of rapidly release tablets.

## MATERIALS AND METHODS

### Materials

Sumatriptan succinate was a kind gift from Ranbaxy Ltd. Gurgaon, India. Eudragit E-100 purchased form Degussa India private Ltd (Mumbai, India), sodium starch glycolate purchased from Qualikems fine chemical Pvt. Ltd (New Delhi, India). All other chemical were of analytical grade.

### Methods

### Preparation of taste masked mixture/granules

### Effervescent method

Sodium bicarbonate and tartaric acid were preheated on a water bath to remove absorbed and residual moisture. The drug was poured in a mortar and sodium bicarbonate and tartaric acid were added, all the contents were thoroughly mixed and passed through sieve #44. Obtained blend was kept in a desiccator till further use.[13]

### Kneading method

Complex of drug and β – cyclodextrin was prepared by kneading. Required amount of drug (1g) and β – cyclodextrin (1g) was

transferred in a mortar and subjected to dry mixing; applying continuous stirring with pestle. The mixture of water and ethanol (3:1) was added to the above physical mixture and continuously stirred until the slurry was formed. Obtained slurry was poured in a tray and dried in hot air oven for 2 hr at 50°C, dried mass was collected and kept in desiccators to remove excess of residual solvent.[14]

**Solid dispersion method**

1g of sumatriptan succinate was accurately weighed and poured in a china dish. 10ml of methanol and 1g of mannitol (carrier) was added to the china dish and mixed properly. The above mixture was kept at room temperature to evaporate the solvent and dried in hot air oven at 50ºC for 4 hrs. After drying, resultant mass was passed through sieve no. 60 and mixture was stored in desiccators, till further use.

**Precipitation method**

Sumatriptan succinate (50mg) and Eudragit E-100 (25mg) complex was prepared applying precipitation method. Saturated solutions of sumatriptan succinate and Eudragit E-100 were prepared in absolute ethanol in 2:1 ratio. Above solution was incorporated into (0.1 N) sodium hydroxide with constant stirring at 500 rpm using mechanical stirrer (HICON, Grover Enterprises, New Delhi). The foamy matrix obtained on surface of the solution was separated and dried at room temperature for 24 hours under vacuum. The dried matrix was subsequently pulverized and finally stored in a tightly closed container.[15]

**Polymer dispersion**

Eudragit E-100 was dissolved in ethanol (10% v/v) to prepare a polymeric solution. 25 mg of drug was accurately weighed and mixed with prepared polymeric solution, until a uniform dispersion was obtained. The dispersion was spread in a tray and dried at room temperature, after drying the dried mass was scrapped with spatula. The scrapped product was stored in a desiccator till further use.

**Addition of flavour/ sweetener**

1g of sumatriptan succinate was accurately weighed and poured in china dish and 670mg of sucrose was added with drug, mix properly then add other excipients and blend was kept in a desiccator till further use.

**Characterization of prepared Mixture /Granules**

**In vivo evaluation of taste masking**

12 healthy human volunteers were selected to assess the degree of taste masking of prepared taste masked mixtures/granules, with their written consent. Prepared mixture/granules were separately placed at the posterior lobe of the tongue for 4-6 sec., spat out and mouth was rinsed with water. The perception of taste and grittiness of dispersion was then reported.

**Micromeritic Characterization**

**Determination of bulk density and tapped density**

1 gm of taste masked power/granules was poured into 25 ml graduated measuring cylinder and the bulk volume was noted down. Graduated cylinder was then subjected to 100 tapping, using tapped density apparatus (HICON, Grover Enterprises, New Delhi), until the change in volume approaches constant value. The bulk density was then obtained by dividing the weight of sample by the final volume in c.c. of the sample contained in the cylinder.[16]

$$\text{Bulk density (poured)} = \frac{\text{weight of powder}}{\text{bulk volume of powder}} \quad (1)$$

$$\text{Bulk density (tapped)} = \frac{\text{weight of powder}}{\text{tapped volume of powder}} \quad (2)$$

**Compressibility index**

The simplest way of measurement of free flow property of powder is compressibility, an indication of ease with which a material can be induced to flow given by % compressibility index (CI) which is calculated as follows:

$$\%\ CI = \frac{\text{tapped density} - \text{bulk density}}{\text{tapped density}} \times 100 \quad (3)$$

**Hausner's ratio**

Hausner's ratio is an index of ease of powder flow, it is related to interparticulate friction as such, could be used to predict powder flow properties. It is calculated by following formula.

$$\text{Hausner's ratio} = \frac{\text{tapped density}}{\text{bulk density}} \quad (4)$$

**Angle of repose**

Angle of repose was determined using fixed height cone method. The blend was poured through a funnel that can be raised vertically until a maximum cone height obtained. Radius of the heap was measured and angle of repose was calculated using the equation:

$$\tan \theta = h/ r \quad (5)$$

Where h is the height of the cone and r is the radius of the base of heap.

**Scanning Electron Microscopy**

The surface morphology of taste masked mixture prepared by the different methods was observed under scanning electron microscope (FEI Quanta™ 200 scanning electron microscope USA). Samples were previously sputter coated with a gold layer under an argon atmosphere in order to make them conductive. The coated samples were then observed and photomicrographs were taken at different magnifications.

**Preparation of taste Masked Rapid Release Tablets**

Taste masked rapid release tablets were prepared by mixing accurately weighed amount of taste masked granules (containing appropriate amount of drug as per the number of tablets to be compressed) prepared by different methods with directly compressible excipients to obtained a perfect blend with uniform drug content. The prepared blend was than subjected to hand operated single punch tablet press (HICON, Grover enterprises, New Delhi).

The $2^2$ factorial designs[17] were implemented for the preparation [Table 1] and optimization of taste masked rapid release tablets of sumatriptan succinate using mixtures/granules prepared by different methods. Two independent factors are concentration of tartaric acid and sodium bicarbonate (effervescent method) and the concentration of sodium starch glycolate and sodium benzoate in case of tablet batches formulated by using mixture/granules prepared by kneading, precipitation and polymer dispersion method (Table 1)

**Characterization of Tablet Properties**

**Friability**

Friability of taste masked fast disintegrating tablets was determined by using roche friabilator (Electolab, Mumbai). 10 tablets from each batch were selected at random and weighed accurately. Tablets were then placed in a plastic chamber that rotates at 25 rpm for 4 minute dropping tablets from a distance of six inches with each revolution. The friabilator was then operated for 100 revolutions after that tablets were dusted and reweighed.[18] Friability can be calculated using following equation

Friability = Initial weight – Final weight × 100/ Initial weight (6)

**Disintegration time**

The disintegration time of the prepared tablets was determined by placing the tablets of each batch separately in a beaker containing 250 ml of distilled water and the time of complete disintegration

was noted (for effervescent method). But in case of kneading, precipitation and polymer dispersion, disintegration test was carried out on 6 tablets using USP Disintegration Apparatus (HICON, Grover Enterprises, New Delhi), using distilled water as disintegration media at 37ºC ±0.5ºC was used as disintegration media and the time in second taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured in seconds.

**Table 1: Formulation design (factorial $2^2$) of taste masked rapid release tablet**

| Ingredients | Effervescent method | | | | Kneading method | | | | Polymer dispersion | | | | Precipitation method | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (mg) | ME1 | ME2 | ME3 | ME4 | MK1 | MK2 | MK3 | MK4 | MD1 | MD2 | MD3 | MD4 | MP1 | MP2 | MP3 | MP4 |
| Sumatriptan succinate | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | - | - | - | - | - | - | - | - |
| Tartaric acid | 25 | 50 | 50 | 25 | - | - | - | - | - | - | - | - | - | - | - | - |
| Sodium bicarbonate | 50 | 50 | 25 | 25 | - | - | - | - | - | - | - | - | - | - | - | - |
| β – cyclodextrin | - | - | - | - | 25 | 25 | 25 | 25 | - | - | - | - | - | - | - | - |
| Drug – polymer complex | - | - | - | - | - | - | - | - | 72.46 | 72.46 | 72.46 | 72.46 | 71.16 | 71.16 | 71.16 | 71.16 |
| Sodium starch glycolate | - | - | - | - | 3 | 12 | 12 | 3 | 3 | 12 | 12 | 3 | 3 | 12 | 12 | 3 |
| Mannitol | 47 | 22 | 47 | 72 | 88 | 83.5 | 79 | 92.5 | 65.54 | 61.04 | 56.54 | 70.04 | 66.84 | 62.34 | 57.84 | 71.34 |
| Sodium benzoate | 3 | 3 | 3 | 3 | 7.5 | 3 | 7.5 | 3 | 7.5 | 3 | 7.5 | 3 | 7.5 | 3 | 7.5 | 3 |
| Talc | - | - | - | - | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 |

**Wetting Time**

The wetting time of the tablet was measured by using the method described by Patel et al.[19] Five circular tissue papers of 5 cm diameter were placed in a petridish of 5cm diameter. 5ml of water containing methylene blue (0.1% w/v) was added to the petridish. A tablet was carefully placed on the surface of the tissue paper and the time required for the dye to reach the upper surface of the tablet was recorded. The measurements were done in triplicate and the mean value was recorded.

**Drug Content**

Three tablets were crushed and powder equivalent to 25 mg was taken and extracted with 10 ml quantity of phosphate buffer pH 6.8 and pH 7.4. Solutions were suitably diluted and the drug content was analyzed spectrophotometrically at 227 nm. Each sample was analyzed in triplicate.

**In vitro drug release**

*In vitro* drug release of sumatriptan succinate from rapid release tablets was determined using USP dissolution apparatus II (paddle type) (HICON Grover enterprises, New Delhi, India). The dissolution test was performed using phosphate buffer pH 6.8 and pH 7.4 as dissolution media, at 37±0.5ºC. The speed of rotation of paddle was set at 100 rpm. At predetermined time intervals 5 ml of sample was withdrawn and analyzed at a 227 nm. The procedure was similarly for dissolution studies of prepared taste masked rapid release tablets in phosphate buffer pH 7.4.

**Uniformity of dispersion**

Two tablets were kept in 100 ml water and gently stirred for 2 minute. The dispersion was passed through 22 #. The tablets were considered to pass the test if no residue remained on the screen.

**RESULT AND DISCUSSION**

**In vivo evaluation of taste masking**

By applying various method taste masked mixture/granules has been prepared and products were subjected to *in vivo* evaluation for taste masking. From the result [Table 2] obtained, it has been clearly observed that three methods – effervescent method, kneading method, precipitation method exhibit complete taste masking (+) while method employed namely polymer dispersion showed slight taste masking (0) but in case of addition of flavour /sweetener and solid dispersion no taste masking(-) was reported hence both the methods were rejected.

Blend containing drug and effervescent couple showed excellent taste masking, which due to presence of tartaric acid and sodium bicarbonate, which definitely contribute for efficient effervescent reaction and facilitate faster dissolution of the drug and produce lemony taste due to formation of carbonic acid results in negligible perception of unpleasant, taste of the drug. The granules prepared by kneading method, reflects the formation of drug entrapped β cyclodextrin complex which nullifies the perception of bitter taste of drug. Mixture/granules prepared by precipitation method also showed good taste masking which is the indicative of complete embedding of the drug with in a polymeric network formed by Eudragit E-100, while product of polymer dispersion exhibited slight taste masking may be due to increment in solubility of the drug in the system which may enhance the binding capacity of drug molecule to the taste receptor.

**Characterization of Selected Taste Masked Granules/ Powder**

Prepared granules were evaluated for various micromeritic parameters like bulk density, tapped density, Carr's index, Hausner's ratio and angle of repose. Bulk density (poured) of taste masked granules prepared by different methods was found to be in the range of 0.324-0.555 gm/cc while tapped density was found to be in the range of 0.441-0.714 gm/cc. Bulk density (poured and tapped) is inverse of bulk volume; hence lower values of bulk density support the porous structure which facilitate ingresment of water, result in rapid disintegration. From the results [Table 3] it has been observed that granules/mixtures prepared by various methods exhibited good flow property as angle of repose determined for all the powders lying in the range of 20-25º. Flow of all the powders was also determined by Carr's Compressibility index from the reported values it was concluded that all the mixtures/granules showed the % compressibility index between the range 11-21 suggested that all the powders are having good to fair flow properties. Hausner's ratio is another mean for defining the flow property, which was also implemented to determine the flow of powders. From the numerical values obtained it was observed that all the powders exhibited the value close to 1.2 or less that again proves that, all the mixtures/granules used had good to fair flow property.

**Table 2: Comparative results for taste masking of all formulations prepared by various methods**

| Volunteer code | Methods | | | | | |
|---|---|---|---|---|---|---|
| | Effervescent method | Kneading method | Addition of Fl-avour/sweetener | Polymer dispersion | Solid dispersion | Precipitation method |
| 1 | + | + | - | 0 | - | + |
| 2 | + | + | - | 0 | - | + |
| 3 | + | + | - | 0 | - | + |
| 4 | + | + | - | 0 | - | + |
| 5 | + | + | - | 0 | - | + |
| 6 | + | + | - | 0 | - | + |
| 7 | + | + | - | 0 | - | + |
| 8 | + | + | - | 0 | - | + |
| 9 | + | + | - | 0 | - | + |
| 10 | + | + | - | 0 | - | + |
| 11 | + | + | - | 0 | - | + |
| 12 | + | + | - | 0 | - | + |

Degree of taste masking: (-) No taste masking; (0) Slightly masked; (+) Complete taste masked

**Table 3: Comparative results for various micromeritic parameters used to evaluate powders /granules prepared by different methods**

| Method(s) Formulation Code | | $D_{Bulk}$ (g/cc) | $D_{Tapped}$ (g/cc) | Carr's compressibility index | Hausner's ratio | Angle of repose (θ) |
|---|---|---|---|---|---|---|
| Effervescent method | ME1 | 0.324 ± 0.20 | 0.452 ± 0.55 | 11.65 ± 0.12 | 1.13 ± 0.38 | 20 ± 0.45 |
| | ME2 | 0.545 ± 0.34 | 0.731± 0.38 | 25.44 ± 0.22 | 1.34 ± 0.44 | 25 ± 0.67 |
| | ME3 | 0.545 ± 0.43 | 0.697 ± 0.44 | 21.80 ± 0.31 | 1.27 ± 0.47 | 24 ± 0.33 |
| | ME4 | 0.555 ± 0.76 | 0.714 ± 0.25 | 22.26 ± 0.29 | 1.28 ± 0.58 | 28 ± 0.59 |
| Kneading method | MK1 | 0.357 ± 0.19 | 0.500 ± 0.71 | 28.6 ± 0.32 | 1.40 ± 0.61 | 25 ± 0.82 |
| | MK2 | 0.348 ± 0.23 | 0.454 ± 0.40 | 23.34 ± 0.56 | 1.30 ± 0.40 | 30 ± 0.32 |
| | MK3 | 0.348 ± 0.82 | 0.468 ± 0.27 | 25.64 ± 0.19 | 1.34 ± 0.55 | 24 ± 0.44 |
| | MK4 | 0.375 ± 0.32 | 0.468 ± 0.22 | 19.87 ± 0.70 | 1.24 ± 0.49 | 22 ± 0.49 |
| Polymer dispersion | MD1 | 0.340 ± 0.33 | 0.441 ± 0.82 | 22.90 ± 0.24 | 1.29 ± 0.28 | 30 ± 0.29 |
| | MD2 | 0.357 ± 0.37 | 0.454 ± 0.25 | 21.36 ± 0.33 | 1.27 ± 0.49 | 25 ± 0.68 |
| | MD3 | 0.348 ± 0.49 | 0.441 ± 0.70 | 21.08 ± 0.39 | 1.26 ± 0.72 | 24 ± 0.73 |
| | MD4 | 0.340 ± 0.37 | 0.454 ± 0.78 | 25.11 ± 0.27 | 1.33 ± 0.59 | 23 ± 0.48 |
| Precipitation method | MP1 | 0.483 ± 0.28 | 0.600 ± 0.42 | 19.5 ± 0.38 | 1.24 ± 0.23 | 25 ± 0.29 |
| | MP2 | 0.441 ± 0.59 | 0.555 ± 0.61 | 20.54 ± 0.43 | 1.25 ± 0.22 | 28 ± 0.51 |
| | MP3 | 0.441 ± 0.77 | 0.576 ± 0.28 | 23.43 ± 0.51 | 1.30 ± 0.47 | 30 ± 0.50 |
| | MP4 | 0.392± 0.37 | 0.476 ± 0.50 | 18.75 ± 0.24 | 1.23 ± 0.29 | 24 ± 0.61 |

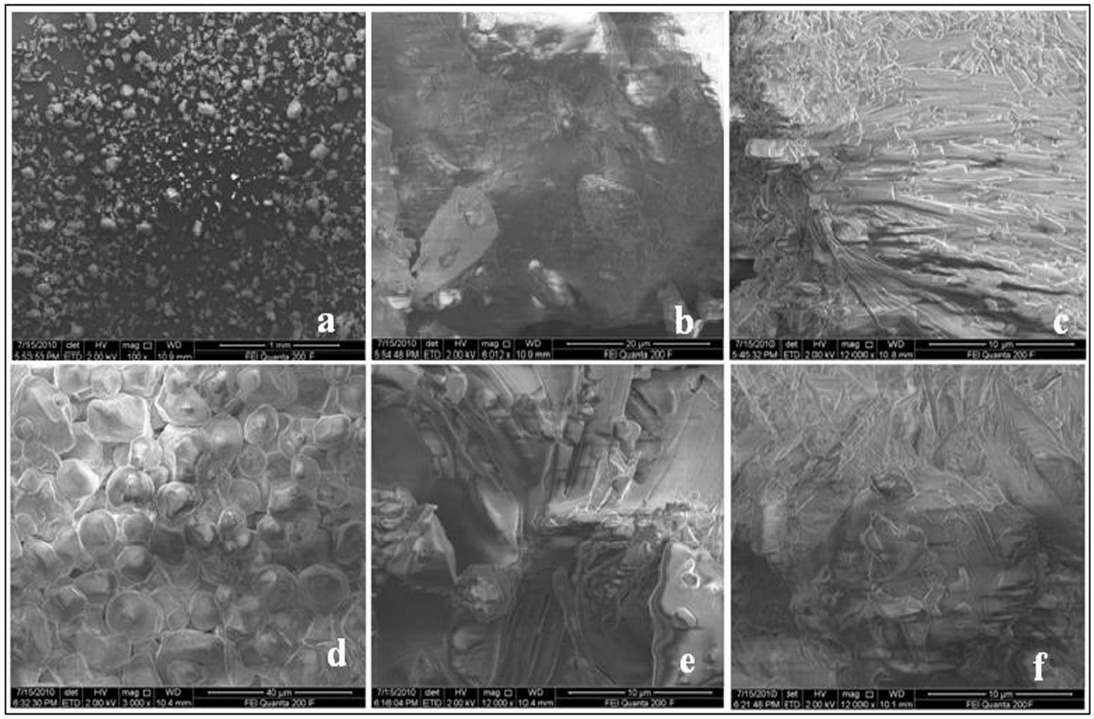


**Fig. 1: Scanning Electron Micrograph of (a) and (b) Pure drug (c) Effervescent method (d) Kneading method (e) Polymer Dispersion method (f) Precipitation method**

**Scanning Electron Microscopy**

Figure1 shows scanning electron micrographs of the pure sumatriptan succinate (a) and (b) and mixture/granules prepared by using effervescent couple (c) and by applying kneading method (d), polymer dispersion method (e) and precipitation method (f). From the micrographs it has been observed that pure drug exhibited in granular form when captured at the magnification of 100 X [Figure 1a], but at the magnified sight [Figure 1b] the drug exhibited a smooth texture without any pore or imperfection on the upper surface of the particle. Micrographs of the blend containing drug and effervescent couple [Figure 1c] appears like a network of irregular fine crystals with rough surface, which is the indicative of the perfect mixing of effervescent couple (tartaric acid and sodium bicarbonate) and drug, which definitely contribute for efficient effervescent reaction and facilitate faster dissolution of the drug and produce lemony taste due to formation of carbonic acid results in negligible perception of unpleasant taste of the drug.

The microstructure of the granules prepared by kneading method [Figure 1d] reflects the formation of drug entrapped irregular circle shape structure which may be due to pulverization of the kneaded mass containing drug and β cyclodextrin. These irregular circular agglomerates exhibit smooth surface and shiny texture which indicate the high extent of drug coating ensures better taste masking, along with pore like deep holes which permit high water uptake. On the other hand mixture/granules prepared by polymer dispersion and precipitation method [Figure 1e and f] showed rough surface with rigid texture and fractured linings, ascertained complete embedding of the drug with in a polymeric network formed by Eudragit E-100.

**Evaluation of Prepared Taste Masked Rapid Release Tablets**

Prepared tablets were evaluated for physical parameters such as friability, thickness, disintegration time, wetting time, uniformity of dispersion and drug content parameters and the results are tabulated [Table 4] for comparative assessment of tablet properties of the prepared formulations. In all the formulations friability value was found to be less than 1% indicating that the formulations are mechanically stable. The thickness was found to be between 2.1± 0.43 mm to 2.4 ±0.65 mm indicating that the tablets were of uniform size.

**In Vitro disintegration time**

The disintegration time(s) of the formulated tablets were evaluated as described and it was found that all the prepared tablets comply with the pharmacopoeial limit (European Pharmacopoeia, 2005) i.e. less than 60 sec. for *in vitro* disintegration time. The disintegration time of formulations ME1, MK4, MD4 and MP4 was found to be 12±0.31, 15±0.34, 15±0.28 and 22±0.42 sec respectively, those were found to be the formulations exhibited least disintegration time among their respective batches. In case of ME1 (effervescent method) stoichiometric ratio of acid and base was used which give good effervescence reaction (libration of $CO_2$) which increase the porosity of the tablet thus disintegration was faster. The results showed by formulation MK4, MD4 and MP4 revealed that low concentration of sodium starch glycolate showed faster disintegration due to its water ingresment property at optimum concentration, as compare to high concentration of sodium starch glycolate, which form a gel like structure in contact with water, hinder the disintegration of dosage form. The pre mentioned statement can be better experienced in case of formulation MP2 which exhibited the disintegration time of 35±0.29 sec. i.e. the maximum time taken to disintegrate among all prepared formulations.

**Wetting Time**

The wetting time of the tablets was measured by using the method described by Patel et al. This experiment mimics the action of saliva on the tablet in the oral cavity. From the table the wetting time of formulation ME1, MK4, MD4 and MP4 was 10±0.21, 12±0.45, 18±0.46 and 12±0.32 sec. respectively. Among the best formulations ME1 showed very less time, to get completely wet. It was concluded that the porous structure of the taste masked granules and sodium starch glycolate (superdisintegrant) used in the tablet formulation as it allowing water to enter the tablet matrix by means of capillary pores, were responsible for the faster water uptake.

**Estimation of Drug Content**

Percentage drug content was estimated and results were summarized in which showed that the percentage drug content of all formulations was found to be in the range of 94.4±0.77 % to 99.50±0.56 %.

On the basis of least disintegration and wetting time and highest drug content formulation ME1, MK4, MD4 and MP4 were selected as optimized formulations among all the prepared formulations and subjected for *in vitro* drug release study to assess the extent of drug release. A conventional formulation was formulated in laboratory without the addition of effervescent couple and superdisintegrants, and compared with the best formulations, on the parameter of drug release

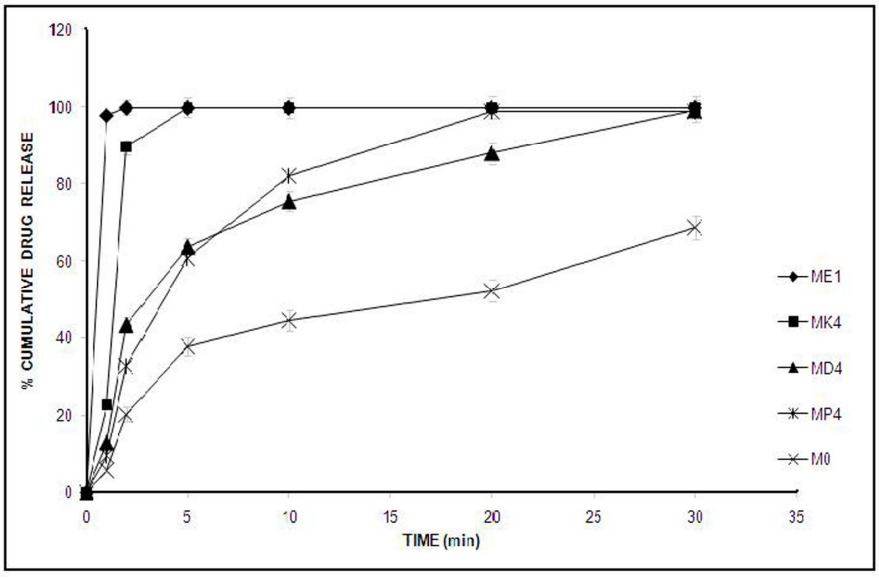


**Fig. 2: Comparative drug release profile of conventional tablet (M0) and optimized taste masked rapid release tablets (ME1, MK4, MD4 and MP4) at pH 6.8**

**In vitro drug release**

The data obtained from the drug release studies of prepared formulations in phosphate buffer (pH 6.8) was found to be increased, when compared to the data obtained from the release profile obtained in phosphate buffer (pH 7.4), indicates that the drug requires acidic medium for maximum dissolution. The conventional tablet (M0) exhibited the release of 68.56±0.32% in phosphate buffer (pH 6.8) where as 65.22±0.56 % in phosphate buffer (pH 7.4) showing more dissolution ability at pH 6.8. In case of tablets prepared by effervescent method, formulation ME1 showed highest drug release of 99.79±0.38 % and 98.65±0.45 % in phosphate buffer pH 6.8 [Figure 2] and 7.4 [Figure 3] respectively. Increase in drug release showed by ME1 may be due to optimum concentrations of tartaric acid and sodium bicarbonate (1: 2), which is required for efficient effervescent reaction.

Drug release pattern of the formulations prepared by using mixture/granules produced by kneading (MK4), polymer dispersion (MD4) and precipitation method (MP4) was comparatively studied and it was observed that the drug release for, MK4 was found to be 99.48±0.34% and 99.23±0.45%, from the formulation MD4 was 98.95±0.53 % and 98.10 ±0.71% and formulation MP4 exhibited the percentage drug release of 98.92±0.57% and 96.22±0.69% in phosphate buffer pH 6.8 and 7.4 respectively.

From the drug release profiles of MK4, MD4 and MP4, it can be said that the above mentioned pattern of drug release from the dosage form is may be due to low concentration of sodium starch glycolate (3% w/w) and sodium benzoate (3% w/w), allows maximum water uptake required for disintegration and provide high degree of hydrophilicity to the drug which facilitates the phenomenon of faster dissolution as compared to conventional tablet.

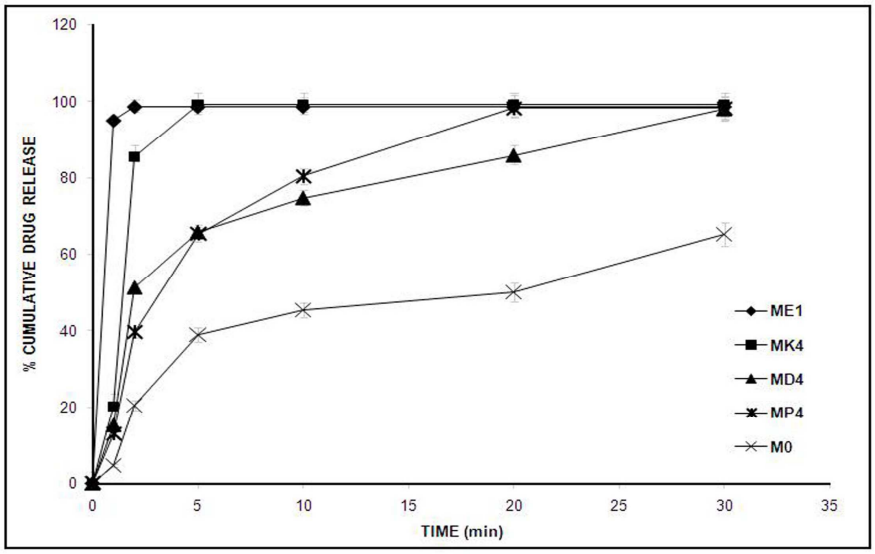


**Fig. 3: Comparative drug release profile of conventional tablet (M0) and optimized taste masked rapid release tablets (ME1, MK4, MD4 and MP4) at pH 7.4**

The high release of all the formulations in phosphate buffer pH 6.8 may be due to, the basic property of sumatriptan succinate exhibited by tertiary amine, along with the sulphonamide group which neutralize the acidic nature of methyl group, indicate that drug is more soluble at pH 6.8 as compared to pH 7.4.

**Model independent parameters**

The obtained drug release data was subjected to model independent drug release kinetics using PCP – DISSO Software and minimum time required to release maximum drug was calculated. Comparative analysis of the time required for 50% and 90% drug release ($t_{50\%}$, $t_{90\%}$) was conducted between conventional tablets and prepared optimized formulations. From the calculated results [Table 5] it has been observed that formulation ME1exhibited minimum time i.e. 0.92 and 0.52 min respectively to release 90% of drug at pH 6.8 and 7.4, among all the optimized formulations. On the other hand conventional tablet has taken 19.17 min to release 50% of the drug which was when compared with prepared optimized formulation, a clear demarcation in the difference in release was observed with the prepared taste masked rapid release tablet preparation.

**Table 4: Comparative Evaluation of Taste Masked Rapid Release Tablets of Sumatriptan Succinate**

| Method | Formulation code | Thickness(mm) | Friability (%) | Disintegration time(s) | Wetting time(s) | Drug content (%) | Uniformity of dispersion |
|---|---|---|---|---|---|---|---|
| Effervescent method | ME1 | 2.1 ± 0.43 | 0.56±0.32 | 12±0.31 | 02±0.31 | 99.50±0.56 | Pass |
| | ME2 | 2.2 ± 0.56 | 0.79±0.45 | 20±0.29 | 04±0.19 | 97.73±0.35 | Pass |
| | ME3 | 2.2 ± 0.33 | 0.58±0.35 | 25±0.38 | 05±0.45 | 94.60±0.40 | Pass |
| | ME4 | 2.2 ± 0.23 | 0.67±0.66 | 30±0.45 | 05±0.44 | 95.50±0.57 | Pass |
| Kneading method | MK1 | 2.2 ± 0.87 | 0.63±0.21 | 17±0.36 | 15±0.65 | 99.40±0.82 | Pass |
| | MK2 | 2.3 ± 0.46 | 0.65±0.47 | 24±0.29 | 17±0.25 | 98.80±0.19 | Pass |
| | MK3 | 2.3 ± 0.31 | 0.63±0.67 | 35±0.78 | 24±0.36 | 97.50±0.48 | Pass |
| | MK4 | 2.3 ± 0.56 | 0.59±0.73 | 15±0.34 | 12±0.45 | 99.30±0.44 | Pass |
| Polymer dispersion | MD1 | 2.3 ± 0.32 | 0.70±0.24 | 20±0.20 | 16±0.81 | 96.60±0.24 | Pass |
| | MD2 | 2.4 ± 0.65 | 0.76±0.29 | 28±0.38 | 24±0.32 | 94.40±0.77 | Pass |
| | MD3 | 2.2 ± 0.22 | 0.65±0.61 | 29±0.23 | 20±0.53 | 95.50±0.61 | Pass |
| | MD4 | 2.2 ± 0.40 | 0.61±0.34 | 15±0.28 | 14±0.46 | 98.80±0.27 | Pass |
| Precipitation method | MP1 | 2.3 ± 0.39 | 0.65±0.44 | 30±0.81 | 22±0.30 | 97.70±0.41 | Pass |
| | MP2 | 2.2 ± 0.28 | 0.66±0.30 | 35±0.29 | 25±0.47 | 96.60±0.63 | Pass |
| | MP3 | 2.4 ± 0.48 | 0.70±0.55 | 30±0.29 | 19±0.59 | 98.30±0.36 | Pass |
| | MP4 | 2.2 ± 0.12 | 0.62±0.32 | 22±0.42 | 16±0.32 | 99.20±0.44 | Pass |

**Table 5: Model independent parameters for drug release in phosphate buffer pH 6.8 and pH 7.4**

| Formulation Code | Phosphate buffer pH 6.8 | | Phosphate buffer pH 7.4 | |
|---|---|---|---|---|
| | $t_{50\%}$ (min) | $t_{90\%}$ (min) | $t_{50\%}$ (min) | $t_{90\%}$ (min) |
| M0 | 19.17 | - | 19.99 | - |
| ME1 | - | 0.92 | - | 0.52 |
| MK4 | 2.17 | 4.50 | 1.17 | 4.53 |
| MD4 | 2.31 | 27.28 | 1.94 | 20.95 |
| MP4 | 3.04 | 18.19 | 2.53 | 11.18 |

## CONCLUSION

The present study resulted complete taste masking of sumatriptan succinate and faster disintegration with high dissolution rate of prepared rapid release tablet formulation. All these methods are simple and easy to scale up in industry. Formulation ME1 prepared by effervescent technology was found to be best, exhibited highest dissolution rate 99.79 % and 98.65 % at pH 6.8 and 7.4 within 2 min, least *in vitro* disintegration time 12sec and wetting time of 2sec. which was found to be more superior in terms of performance as compared to marketed formulation. Conclusively, it can be said that taste masking and rapid disintegration of tablets formulated in this investigation may possibly help in administration of sumatriptan succinate in a more palatable form.

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