IJPSR (2017), Vol. 8, Issue 5 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 18 October, 2016; received in revised form, 12 December, 2016; accepted, 16 December, 2016; published 01 May, 2017

ORALLY FAST DISINTEGRATING TABLETS OF SUMATRIPTAN LOADED EUDRAGIT E MICROPARTICLES: A PROMISING CHOICE FOR TASTE MASKING

Soliman Mohammadi Samani [1, 2], Neda Zolfaghari [2], Elahehnaz Parhizkar [2] and Fatemeh Ahmadi [*1, 2]

Research Center for Nanotechnology in Drug Delivery [1], School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran.
Department of Pharmaceutics [2], School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran.

Keywords:

Sumatriptan succinate, Eudragit E, Fast disintegrating tablet, Microparticles, Taste masking

Correspondence to Author:
Dr. Fatemeh Ahmadi

School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran.

E-mail: ahmadi_f@sums.ac.ir

ABSTRACT: Sumatriptan succinate, a selective 5-hydroxytryptamine-1 receptor agonist, is an antimigraine drug with bitter-taste. The present study was performed to prepare and evaluate eudragit-E microparticles containing sumatriptan and formulate fast disintegrating tablets of drug microparticles to increase patient-compliance and improve the efficacy of drug. Microparticles were prepared by solvent-evaporation method using water-dichloromethane/PVA and water-dichloromethane/liquid paraffin systems. The effect of different variables (polymer:drug ratio, PVA concentration and solvents combination ratios) on particle size and encapsulation efficiency of the microparticles was investigated. The final microparticles were evaluated for particle size, loading percent, taste-masking, thermal analysis and in-vitro release profile. The drug loading were higher in w/o/o emulsion than w/o/w. Mean particle size was not statistically different for different formulations. Sumatriptan release rate from eudragit-E microparticles was very fast in HCl 0.1 N medium and release profile was acceptable for fast disintegrating tablets. The prepared tablets were evaluated for in-vitro disintegration time, weight variation, hardness, friability and in-vitro drug release. The optimized formulation (F6) (provided a pleasant taste and mouth-feel) disintegrated within 20 seconds and released more than 70% of drug within 15 minutes. Tablets formulated by drug loaded eudragit-E microparticles could be a promising formulation for taste-masking and decreasing failure in triptans therapy.

INTRODUCTION: Microparticles are one of the novel drug delivery systems and are prepared to obtain controlled drug delivery, improve bioavailability, target drug to specific sites, reduce side effects or manipulate onset of action and improve patient compliance.[1] Multiparticulate systems were entered the field of dosage form design when the application of polymers in pharmacy was introduced.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.8(5).2003-12

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.8 (5).2003-12

Polymers are being increasingly used in drug delivery systems as drug carriers, solubility enhancers and formulation excipients especially in tablet dosage forms. There are a variety of polymers that are now being used for preparation or coating of microparticles. Choice of the polymer depends on the ultimate goal of designing the delivery system. Eudragit E is a cationic copolymer based on dimethylaminoethyl methacrylate, butyl methacrylate, and methyl methacrylate. Region of drug release from eudragit E polymer is in stomach and this polymer is dissolved at pH values less than 5. [2, 3] Moreover, it is not dissolved in buccal cavity (pH 5.8-7.4) and keeps the coated drug intact, therefore, it could be a suitable candidate for taste masking of bitter taste drugs such as sumatriptan, a

drug which is used in palliative treatment of migraine. [4] Migraine is a chronic and mostly unilateral headache that its symptoms are often started with nausea, vomiting and light and sound sensitivity.[5] Migraine headaches require proper treatment in a short time. Sumatriptan succinate, a selective 5-hydroxytryptamine-1 receptor agonist, is an effective antimigraine drug which is effective for acute treatment of migraine via oral route.[6] Dosage forms of sumatriptan which are now available in the market include oral tablets, injection and nasal spray.

Injections are formulations of choice for emergency situations, but pain at the site of injection and need to a trained person for administration limits their use. [7] Conventional tablets present some limitations such as difficulty in ingestion of drug where the patients have little or no access to water. Moreover, for patients with severe nausea or vomiting during migraine headache, ingestion of tablet may aggravate vomiting. [8] Indeed, regular tablets are disintegrated in the stomach, so absorption and onset of action is a little bit delayed and treatment efficiency may be decreased. [9] Therefore, the orally fast disintegrating tablets (ODTs) of sumatriptan succinate could be a valuable alternative for current formulations. [10, 11] The advantages of ODTs mainly include ease of administration to patients who suffer from swallowing problems such as elderly, pediatrics and bedridden patients, [12, 13] taste masking and good mouth feel, fast dissolving with less or no water and rapid absorption. [14, 15] Sumatriptan succinate is a highly water soluble and bitter drug. If it is used directly in to ODTs, patient compliance and rapid action of drug would not be achieved.

Our aim was to develop orally fast disintegrating tablets of eudragit E microparticles containing sumatriptan succinate to mask bitter taste, improve efficacy of drug and increase patient compliance. The microparticles were prepared by double emulsion solvent evaporation technique and the ODTs were prepared by direct compression method. Characterization of particles and tablets were performed based on particle size, loading percent, drug release profile, disintegration time, weight variation, hardness, friability and thermal analysis.

MATERIALS AND METHODS:

Materials: Sumatriptan succinate was a gift sample from Osve Pharmaceutical Company (Tehran, Iran). Eudragit E, crosspovidone (polyplasdone), Ac-Di-sol were obtained as gift samples from Exir Pharmaceutical Company (Borujerd, Iran). Poly vinyl alcohol (PVP) was purchased from Fluka (Germany). Dichloromethane, hydrochloric acid (HCl 37% w/w), disodium hydrogen phosphate, potassium dihydrogen phosphate, sodium chloride, sodium hydroxide, methanol, microcrystalline cellulose (Avicel), sodium saccharin, magnesium stearate, Tween 80, Span 60, paraffin and n-hexane were purchased from Merck (Germany).

Preparation of sumatriptan succinate microparticles: Sumatriptan succinate microparticles were prepared by double emulsion solvent evaporation technique reported before with some modifications. [16, 17]

w/o/w emulsion solvent evaporation: For w/o/w emulsion, constant amount of sumatriptan succinate was dissolved in deionized water by vortexing (VELP, Spain) and bath sonicator (TECNO-GAS, Italy). Eudragit E was also dissolved in dichloromethane and then aqueous solution of drug was added to dichloromethane solution under probe sonicator (Hielscher, Germany) to prepare a w/o emulsion. The new emulsion (1ml) was added to 10 ml aqueous solution of PVA under homogenizer at 10000 rpm (Heidolph, Germany) for 10 min and the final mixture was stirred for 24 h to solidify particles by complete evaporation of dichloromethane. Different drug: polymer ratios of 1:2, 1:3 and 1:4 and different percentages of PVA; 0.5%, 1% and 2% were examined to obtain particles with suitable size and higher drug loading. After evaporation of dichloromethane, the microparticles were collected by centrifuge at 10000 rpm and washed 3-4 times with deionized water and stored at -72 °C and lyophilized. All microparticles were prepared in triplicate.

w/o/o emulsion solvent evaporation: The formulation with 1:3 drug to polymer ratio and highest loading percentage from the previous step was prepared with paraffin as the external phase of the emulsion. In this method deionized water containing 0.25% Tween 80 and dichloromethane as for previous section at ratios of 1:3 and 1:5 were

used to dissolve drug and polymer, respectively and the primary w/o emulsion was prepared. The resulting emulsion was then added to 50 ml liquid paraffin containing 0.05% Span 60 in 10 min and stirred for 24h. After evaporation of dichloromethane and formation of microparticles, the microparticles were centrifuged at 1500 rpm and washed 3-4 times with n-hexane and water and finally stored at room temperature to dry microparticles. All microparticles were prepared in triplicate.

Determination of particle size of microparticles: Particle size measurements were performed using a particle size analyzer SALD 2100 (Shimadzu, Japan). Microparticles were dispersed in water and sonicated for 5-10 min using bath sonicator to disperse particles and prevent aggregation. Samples were analyzed in triplicate.

Determination of drug loading and encapsulation efficiency percentage:

Microparticles prepared by w/o/w method: Five mg of microparticles was dissolved in dichloromethane and then sonicated to dissolve the polymer. Dichloromethane was then evaporated under nitrogen stream and 5 ml deionized water was added to precipitate the polymer and the resulting mixture was sonicated to dissolve the drug. Further, the solution was centrifuged at 5000 rpm and the clear supernatant was analyzed by UV/Visible spectrophotometer 1650 PC (SHIMADZU, Japan) at 284 nm. Encapsulation efficiency and drug loading percentage were calculated using following equations:

$$\text{Loading percent} = \frac{\text{encapsulated drug weight}}{\text{microparticle weight}} \times 100$$

$$\text{Encapsulation efficiency} = \frac{\text{encapsulated drug weight}}{\text{weight of drug used for encapsulation}} \times 100$$

Microparticles prepared by w/o/o emulsion: Five mg of microparticles was dissolved in methanol and then sonicated to dissolve the polymer. Subsequently, deionized water was added to precipitate polymer and the mixture was sonicated to dissolve the drug. The final mixture was then centrifuged at 5000 rpm and supernatant was analyzed by UV/Visible spectrophotometer at 284 nm. Encapsulation efficiency and drug loading percent were calculated using above mentioned equations.

Determination of emulsion type: Type of the emulsion formed in the method would determine the size and encapsulation efficiency of the particles. Therefore, the type of emulsion prepared was determined by measuring the conductivity of the solutions. Conductivity of deionized water, a 0.9% NaCl solution and the prepared emulsion was measured by conductometer. Theoretically, for w/o emulsion conductivity should be near to zero while the o/w emulsion would show some conductivity.

***In vitro* taste masking:** Fifteen mg of microparticles and an equivalent amount of mixture of sumatriptan succinate (3 mg) with eudragit E (12 mg) were weighed and then 5 ml phosphate buffer (pH 6.8) was added and the mixture was kept for 60 sec. Phosphate buffer was used to mimic the pH and conditions of saliva. After this time, the suspension was filtered. The filtrate was analyzed for drug content with UV spectrophotometer at 284 nm. The experiment was run in triplicate.[18]

Thermal analysis: Thermal behavior of drug, polymer and microparticles was evaluated by Differential Scanning Calorimetry (DSC) (302, Bahr Thermoanalyse, Germany). 5 mg of each sample was accurately weighed and sealed in aluminum pans and was heated from 30 to 300 °C at the rate of 10 °C/min. An empty pan was used as the reference.[19]

***In vitro* release studies of microparticles:** The drug release profile of the microparticles with maximum loading percent (20%) was studied. Accurately weighed samples of microparticles were added to 50 ml HCl 0.1 N and kept in shaker incubator at 37 °C with a speed of 70 rpm. At predetermined time intervals a 5 ml sample was withdrawn and replaced by an equal volume of fresh medium to keep the volume constant. The concentration of drug in samples was analyzed by UV spectrophotometer at 284 nm.

Microscopic analysis: Morphology of the microparticles was studied using optical microscope Novex µSmart (Euromex, Netherlands) with a magnification of 100.

Preparation of tablets: The orally disintegrating tablets were prepared by direct compression method. The ODTs (formulation F1 to F6) consisted of 50 mg of the selected microparticles (with maximum loading), avicel, crosspovidone, sodium saccharin and vanillin as shown in **Table 1**. Magnesium stearate was added as lubricant before compression. The powder was compressed on a tableting machine (AR400, ERWEKA, Germany). The tablets weight was kept at 215-228 mg and hardness was maintained in the range of 4-5 kg.

TABLE 1: FORMULATION COMPOSITION OF ODTS

Ingredients (mg)	F1	F2	F3	F4	F5	F6
Microparticles	50	50	50	50	50	50
Sorbitol	80	50	-	-	-	-
Avicel	30	60	100	100	100	100
Crosspovidone	25	25	25	50	25	50
Ac-Di-Sol	25	25	50	25	25	25
Na Saccharin	1	1	1	1	1	1
Mg Stearate	4	4	3	3	3	3
Vanillin	-	-	1	1	1	-

Evaluation of tablets:

Weight variation, hardness and friability: Twenty tablets were selected randomly to weigh individually using a digital balance (Sartorius, Germany) and then average and standard deviation of weight were calculated. [20] Hardness of the tablets was assessed using an ERWEKA hardness tester (Germany). The mean hardness of 10 tablets was obtained. To measure the friability of the tablets, 10 tablets were weighed and placed in friability test apparatus rotated at 25 rpm for 4 min. Thereafter, tablets were weighed again and friability (%) was calculated using following equation:

$$F = \frac{Weight\ initial - Weight\ final}{\text{Weight initial}} \times 100$$

***In vitro* disintegration time:** 10 tablets were individually placed in 10 ml distilled water and the time to disintegrate completely was recorded.

***In vitro* dissolution study:** The dissolution profile of the selected formulation of tablets (formulation F6) with in vitro disintegration time less than 60 sec was studied in 250 ml HCl 0.1 N and in phosphate buffer (pH 6.8) using USP dissolution apparatus type II (ERWEKA, Germany). Dissolution medium temperature was 37 ± 0.5 °C and paddle speed was set to 50 rpm. Samples were withdrawn and analyzed as reported for microparticles.[21, 22]

Determination of tablets taste by volunteers: The optimized formulation (F6) and a non taste-masked formulation of sumatriptan succinate were tested by 10 healthy human volunteers. The taste was rated on a scale of 1 (very bitter), 2 (bitter), 3 (fair) and 4 (pleasant).

RESULTS: Taste masking of bitter taste sumatriptan succinate along with fast disintegration and release were two important goals in this study. Firstly, w/o/w emulsion was used to prepare microparticles. Although many formulations with different polymer: drug ratios and PVA percent were tried, suitable amount of loading percentage was not achieved. Therefore, w/o/o emulsion was used to improve maximum drug loading percentage. Results of conductometry showed that for the first emulsion prepared and deionized water, conductivity was zero while for NaCl solution 25.1 millisiemens was recorded. These results show that the continuous phase of the emulsion is not conductive and therefore the emulsion is w/o. Table 2 shows the details of different combinations of variables tested for optimization of size and loading of particles.

Evaluation of microparticles:

Particle size: The mean particle size of microparticles in w/o/w emulsion when stirrer and homogenizer used as external force are shown in **Table 2**. The mean particle size of microparticles prepared by w/o/o emulsion method was 1 µm.

TABLE 2: COMBINATION OF DIFFERENT VARIABLES USED FOR OPTIMIZATION OF PARTICLES

Formulation	Eudragit E (mg)	Sumatriptan succinate (mg)	polymer/drug ratio	PVA% (mg/100ml)	Homogenizer rate (rpm)	Mean particle size	stirrer rate (rpm)	Mean particle size
1	40	20	2	0.5	10000	*	1500	3.11 ± 2.08
2	60	20	3	0.5	10000	*	1500	5.70 ± 1.65
3	80	20	4	0.5	10000	*	1500	5.30 ± 0.99
4	40	20	2	1	10000	1.04 ± 0.06	1500	3.76 ± 1.78
5	60	20	3	1	10000	1.41 ± 0.10	1500	1.54 ± 0.58
6	80	20	4	1	10000	5.78 ± 1.78	1500	4.90 ± 1.15
7	40	20	2	2	10000	1.08 ± 0.18	1500	4.42 ± 0.99
8	60	20	3	2	10000	1.43 ± 0.11	1500	3.87 ± 1.46
9	80	20	4	2	10000	3.79 ± 0.33	1500	5.92 ± 1.45

* No particle was formed.

Encapsulation efficiency and drug loading percent: Polymer: drug ratio was an important factor in drug loading. Encapsulation efficiency and drug loading were decreased by increasing polymer: drug ratio from 2 to 4. By increasing PVA%, 0.5 to 2, drug loading was increasing but effect of this increase in PVA percent of 1 and 2 was not significant. Therefore, formulations 4 to 9 were also prepared with homogenizer as external force to increase drug loading. Results showed that formulation 5 and 8 with homogenizer provided maximum drug loading. **Table 3** summarizes the results of drug loading and encapsulation efficiency of different formulations prepared by w/o/w method.

TABLE 3: ENCAPSULATION EFFICIENCY AND DRUG LOADING OF FORMULATIONS PREPARED BY W/O/W METHOD

Formulations	Stirrer		Homogenizer	
	Encapsulation Efficiency%	Drug Loading%	Encapsulation Efficiency%	Drug Loading%
1	–	–	–	–
2	12.95	3.23	–	–
3	14.83	2.96	–	–
4	13.8	4.6	–	–
5	12.9	3.2	17.31	4.32
6	8	1.6	13	2.6
7	24.7	8.2	16.31	5.38
8	19	4.75	22.6	5.65
9	7	1.4	11.7	2.34

Comparsion of drug loading in w/o/w and w/o/o methods: Sumatriptan succinate encapsulation efficiency was higher in w/o/o emulsion (drug/polymer ratio of 1:3) than w/o/w. Drug loading in microparticles when paraffin was used as external phase was 20 ± 1.8%, which was 5-fold higher than w/o/w method.

***In vitro* taste masking of microparticles:** Taste masking ability of the selected formulation with the highest loading percentage was tested and the results are shown in **Table 4**.

TABLE 4: RESULTS OF TASTE MASKING ABILITY OF MICROPARTICLES

Samples	Calculated concentration of physical mixture of drug and polymer µg/ml	Release percentage of physical mixture of drug and polymer	Calculated concentration of microparticles µg/ml	Release percentage of microparticles
1	464.2	77.36	101.4	11.93
2	437.5	72.92	76.6	12.76
3	481.9	80.32	71.6	16.9

Thermal analysis: Fig. 1 shows the characteristic endothermic peaks of Eudragit E, sumatriptan succinate and microparticles with their melting points. The reported sumatriptan succinate melting point is 169-171°C. DSC analysis of microparticles revealed no major peak in the range 30-300°C.

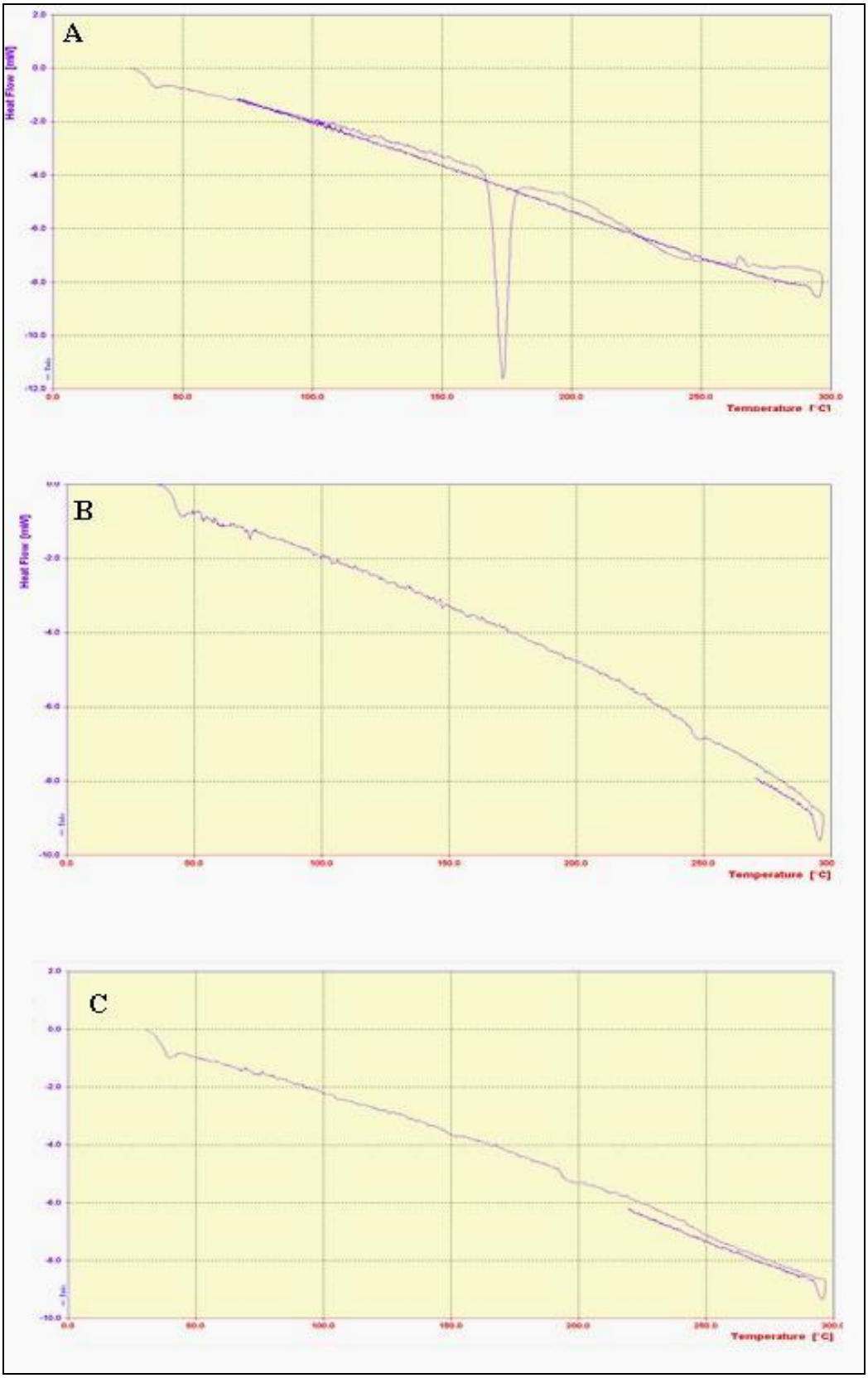

FIG. 1: DSC THERMOGRAMS OF A) SUMATRIPTAN SUCCINATE, B) EUDRAGIT E AND C) MICROPARTICLES PREPARED BY W/O/O METHOD

Morphological characteristics of microparticles: **Fig. 2** shows the microscopic image of the micoparticles prepared by w/o/o method by magnification of 100. As see in the figure, particles are spherical with smooth surface.

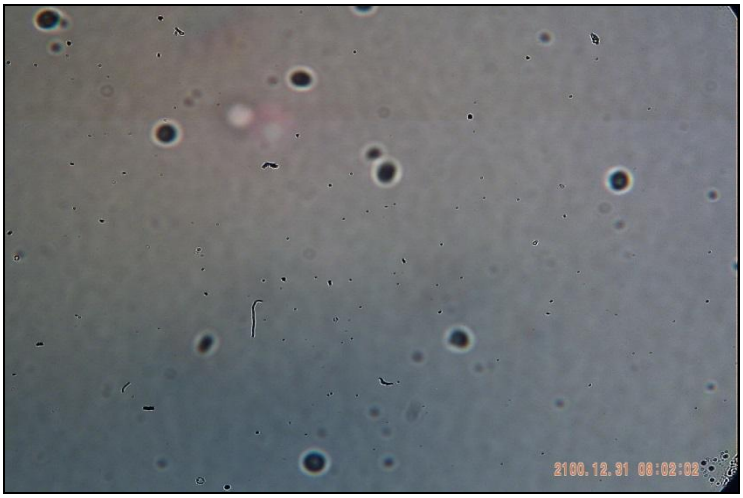

FIG. 2: MICROSCOPIC IMAGE OF MICROPARTICLES PREPARED BY W/O/O METHOD

Evaluation of tablets: The disintegration time of formulations F1 and F2 of tablets was 360 and 240 sec, respectively which was reduced to 60 and 30 sec for formulations F3 and F4. Formulations F5 and F6 were disintegrated in 20 sec and formulation F6 was selected for further characterizations. The average weight of tablets of formulation F6 was 228.98 ± 2 and the mean of hardness of 10 tablets was 4.83± 0.19 kg, and the friability for 20 tablets was found within the acceptable limits (<1%). All these physical characterization of tablets were within the acceptable limits suggested by the pharmacopoeia.[20]

***In vitro* dissolution studies:** The microparticles released more than 70% of the drug content in 15 min in HCl 0.1 N as shown in **Fig. 3a.** The release profiles of formulation F6 in HCl 0.1 N and phosphate buffer pH 6.8 are also presented in **Fig. 3b** and **3 c,** which demonstrates the faster drug release in acidic media.

.

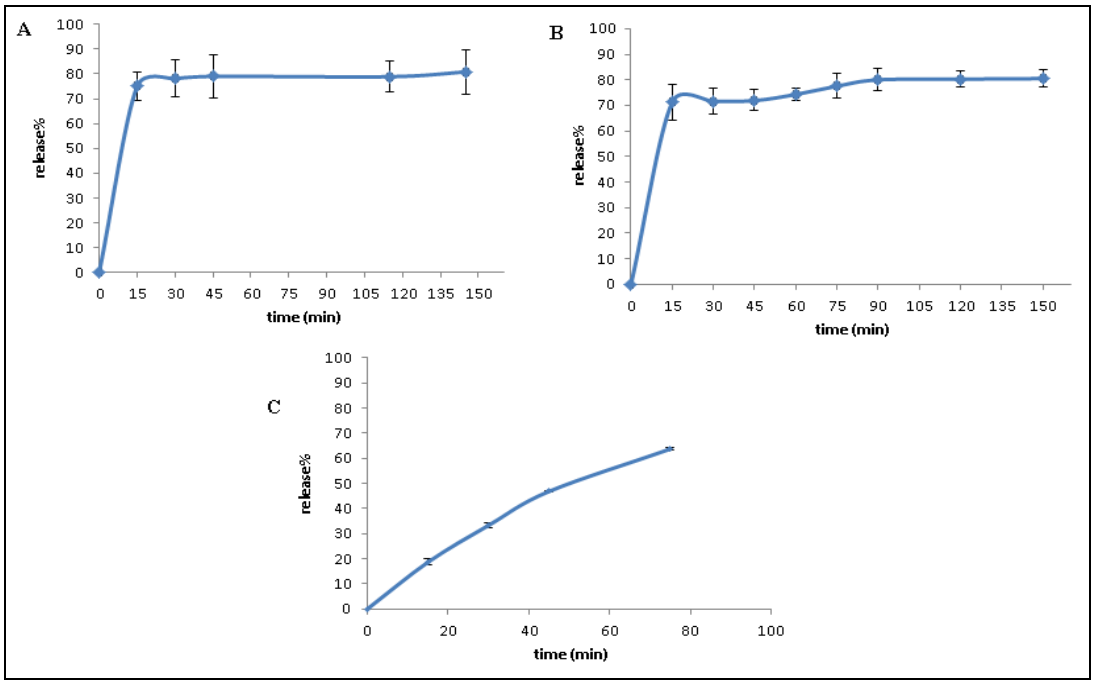

FIG. 3: DRUG RELEASE PROFILES OF a) MICROPARTICLES PREPARED BY W/O/O METHOD TESTED IN HCL 0.1 N, b) F6 IN HCL 0.1 N AND c) F6 IN BUFFER PHOSPHATE pH 6.8

***In vivo* taste masking of ODTs:** As presented in **Table 5**, all the volunteers reported that the control formulation which was prepared by compression of the physical mixture of drug and polymer without microencapsulation was very bitter but the optimized formulation (F6) was found pleasant to almost all of them.

TABLE 5: RESULTS OF *IN VIVO* TASTE MASKING TESTED BY THE VOLUNTEERS

	Taste score	
Volunteers	**control**	**F6**
1	1	3
2	1	3
3	1	3
4	1	3
5	1	3
6	1	2
7	1	3
8	1	3
9	1	3
10	1	3

DISCUSSION: Migraine is a common impairment of the vascular network of the nervous system which causes severe headaches. In most situations this headache is associated with nausea, vomiting, sensitivity to light and in some cases autonomic dysfunction. [5] Treatment of migraine with simple solid oral formulations needs extra time for disintegration of the dosage form in the stomach which may delay the onset of action. Indeed, nausea associated with most cases of migraine may impair the swallowing reflex in the patients. Therefore, designing novel oral delivery systems such as fast disintegrating tablets which are disintegrated rapidly in the presence of little amount of water seems necessary. [9] Sumatriptan succinate is an anti-migraine drug which is now available in the market as oral, injection and nasal formulations. Development of a fast disintegrating formulation of sumatriptan would be beneficial in increasing the efficacy and patient compliance. [23] By these formulations disintegration time in the stomach would be saved and the chance of mucosal absorption in oral cavity would also be increased. [7] Sumatriptan succinate is a highly water soluble and bitter drug.

A suitable polymer is required to coat the drug particles in order to mask the unpleasant taste of the drug in the oral cavity as well as controlling the release until the drug reaches to the stomach.[19] Eudragit E is a golden choice in this case as it is dissolved at pH values less than 5 and keeps the coated drug intact in the oral cavity. Therefore, the contact with taste buds is prevented and the drug will be released in the stomach. By coating drug particles with this polymer through microencapsulation method, our main goals were obtained. [4] Sumatriptan succinate loaded Eudragit E microparticles were prepared using w/o/w emulsion solvent evaporation method.[16, 17] Drug: polymer ratio, PVA% and type of the external force (stirrer or homogenizer) were important factors to obtain microparticles with higher drug loading percentage.

Although by this method, microparticles of suitable size were formed, sufficient drug loading percent was not achieved. This is because of high water solubility of sumatriptan which is rapidly diffused out of the particles to the external phase (PVA). Therefore, w/o/o emulsion solvent evaporation method was used to prepare microparticles with maximum drug loading percentage. [24] Water: dichloromethane ratio, water: dichloromethane: paraffin ratio and percentage of span 60 in paraffin were important factors to obtain microparticles with suitable size and loading percentage.

These observations have been confirmed in similar situations studying water soluble drugs in lipid soluble polymers, for example acetazolamide loaded Eudragit E microparticles[25]. Higher concentrations of span 60 resulted in aggregation of microparticles and decreased drug loading percentage. The encapsulation efficiency and drug loading were very high for all microparticles obtained in water: dichloromethane ratio of 1:3.

DSC analysis showed that by encapsulation of drug in polymer, endothermic peak of melting was disappeared which may be due to the formation of amorphous drug in the particles. The amorphous drug would be more soluble with higher dissolution rate in the stomach. In vitro taste masking studies showed that in 60 sec, less than 15% of drug is released from microparticles in average, while this amount was about 77% for physical mixture of drug and polymer. Evaluating the taste of microparticles confirmed that the drug is not release in salvia (pH 6.8). Therefore, unpleasant taste of the drug would not be sensed when the formulation is placed on the tongue. This effect has also been proved previously for sumatriptan loaded particles made by spray drying technique.[19]

The dissolution studies showed that the release of drug from microparticles in HCl 0.1N medium was fast and the drug could be readily available in the stomach.

ODTs containing taste masked sumatriptan microparticles were prepared by the direct compression method using different combinations of superdisintegrants. The optimized formulation (F6) was disintegrated very fast within 20 sec and weight variation, friability and hardness of ODTs of formulation F6 were in acceptable range of pharmacopeia. More than 70% of drug was released within 15 min in HCl 0.1 N (stomach) while this amount was significantly lower when the tablets were tested in similar time in phosphate buffer pH 6.8 (oral cavity). The results was suitable in comparison with sumatriptan loaded Eudragit E microparticles prepared by spray drying which released 90% of the drug in different media studied (HCl 0.1 N, phosphate buffer pH 6.8 and acetate buffer pH 4.5) [19].

This finding shows that microencapsulation of sumatriptan in eudragit E by solvent evaporation method using paraffin as the external phase could be more desirable for taste masking of sumatriptan.

In summary, sumatriptan loaded Eudragit E microparticles formulated into ODTs could be a useful oral dosage form with suitable taste masking, fast release rate and higher patient compliance in children and other patients versus conventional formulations.

ACKNOWLEDGEMENTS: The authors thank Dr. Saeed Daneshamouz for his kind scientific comments to improve the quality of tests and data presentation.

FUNDING: The present article was extracted from a Pharm D thesis grant No. 92-01-05-6556 written by Neda Zolfaghari and was financially supported by Vice Chancellery for Research of Shiraz University of Medical Sciences, Shiraz, Iran.

CONFLICT OF INTERESTS: The Authors declare that there is no conflict of interest.

REFERENCES:

1. Anselmo AC, Mitragotri S. An overview of clinical and commercial impact of drug delivery systems. J Control Release. 2014;190:15-28.
2. Priemel PA, Laitinen R, Grohganz H, Rades T, Strachan CJ. In situ amorphisation of indomethacin with Eudragit® E during dissolution. Eur J Pharm Biopharm. 2013;85(3):1259-1265.
3. Cho Y, Ha E-S, Baek I-H, Kim M-S, Cho C-W, Hwang S-J. Enhanced supersaturation and oral absorption of sirolimus using an amorphous solid dispersion based on Eudragit® E. Molecules. 2015;20(6):9496-9509.
4. Xu J, Bovet L, Zhao K. Taste masking microspheres for orally disintegrating tablets. Int J Pharm 2008;359(1-2):63-69.
5. Heyer MD G, Rose MD S, Merison MD K, Perkins BS S, Lee CNP G. Specific Headache Factors Predict Sleep Disturbances Among Youth With Migraine. Pediatr Neurol. 2014;51(4):489-493.
6. Fujita M, Sato K, Nishioka H, Sakai F. Oral sumatriptan for migraine in children and adolescents: A randomized, multicenter, placebo-controlled, parallel group study. Cephalalgia. 2013:0333102413510213.
7. Carpay J, Schoenen J, Ahmad F, Kinrade F, Boswell D. Efficacy and tolerability of sumatriptan tablets in a fast-disintegrating, rapid-release formulation for the acute treatment of migraine: Results of a multicenter, randomized, placebo-controlled study. Clinical Therapeutics. 2004;26(2):214-223.
8. Malke M, Shidhaye S, Kadam V. Formulation and evaluation of Oxacarbazine fast dissolve tablets. Ind J Pharm Sci. 2007;69(2):211-214.
9. Milton K, Scott N, Allen M, Abel S, Jenkins V, James G, et al. Pharmacokinetics, pharmacodynamics, and safety of the 5-HT(1B/1D) agonist eletriptan following intravenous and oral administration. J Clin Pharmacol. 2002;42(5):528-539.
10. Tayel SA, El Nabarawi MA, Amin MM, Abou Ghaly MH. Sumatriptan succinate sublingual fast dissolving thin films: formulation and in vitro/in vivo evaluation. Pharm Dev Technol. 2016;21(3):328-337.
11. Chaurasia V, Kumar V, Jain D. Sumatriptan Succinate Loaded Microspheres Containing Compressed Core Tablets For Effective Treatment Of Migraine. Bull Pharm Res. 2016;6(2):56-67.
12. Bandari S, Mittapalli RK, Gannu R. Orodispersible tablets: An overview. Asian Journal of Pharmaceutics (AJP). 2014;2(1).

13. Adchitre Vaishali B, Khadbadi S, Patil PR, Shaikh M. Fast Dissolving Tablets–A Novel Approch To Drug Delivery. American Journal of Pharmaceutical Research. 2016;6(04).
14. Mahajan U, Parashar B, Sharma N, Jadhav Y, Musasvad S, Patil V. Fast Dissolving Tablet- An Overview of Formulation Technology. Indo Global Journal of Pharmaceutical Sciences (IAJPS). 2012;2(2):157-166.
15. Bhattarai M, Gupta AK. Fast Dissolving Oral Films: A Novel Trend to Oral Drug Delivery System. Sunsari Technical College Journal. 2016;2(1):58-68.
16. Joshi A, Patil C, Shiralashetti S, Kalyane N. Design, characterization and evaluation of Eudragit microspheres containing glipizide. Drug Invention Today. 2013;5(3):229-234.
17. Hombreiro-Pe´reza M, Siepmannb J, Zinuttia C, Lamprechtc A, Ubricha N, Hoffmana M, et al. N on-degradable microparticles containing a hydrophilic and/or a lipophilic drug: preparation, characterization and drug release modeling. J Control Release. 2003;88(3):413-428.
18. Shukla D, Chakraborty S, Singh S, Mishra B. Fabrication and evaluation of taste masked resinate of risperidone and its orally disintegrating tablets. Chem Pharm Bull. 2009;57(4):337-345.
19. Sheshala R, Khan N, Drawis Y. formulation and optimization of orally disintegrating taqblets of sumatriptan succinate. Chem Pharm Bull. 2011;59(8):920-928.
20. APA. British pharmacopeia. london: stationary office2009.
21. Dang T, Cui Y, Chen Y, Meng X, Tang B, Wu J. Preparation and Characterization of Colon-Specific Microspheres of Diclofenac for Colorectal Cancer. Trop J Pharm Res. 2015;14(9):1541-1547.
22. Trivedi P, Verma A, Garud N. Preparation and characterization of aceclofenac microspheres. Asian Journal of Pharmaceutics (AJP). 2014;2(2).
23. Gugulothu D, Desai P, Pandharipande P, Patravale V. Freeze drying: exploring potential in development of orodispersible tablets of sumatriptan succinate. Drug Dev Ind Pharm. 2015;41(3):398-405.
24. Freitas S, Merkle H, Gander B. Microencapsulation by solvent extraction/evaporation: reviewing the state of the art of microsphere preparation process technology. J Control Release. 2005;102(2):313-332.
25. Haznedar S, Dortunc B. Preparation and in vitro evaluation of Eudragit microspheres containing acetazolamidE. Int J Pharm 2004;269(1):131-140.

How to cite this article:
Samani SM, Zolfaghari N, Parhizkar E and Ahmadi F: Orally fast disintegrating tablets of sumatriptan loaded eudragit e microparticles: a promising choice for taste masking. Int J Pharm Sci Res 2017; 8(5): 2003-12.doi: 10.13040/IJPSR.0975-8232.8(5).2003-12.