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# FORMULATION AND EVALUATION OF MOUTH DISSOLVING TABLET OF NARATRIPTAN HCl USING SUBLIMATION TECHNIQUE

**Syed S M*[1], Farooqui Z S[2], Mohammed M[1], Shaikh A Y[3]**

[1]Research Scholor Y B Chavan College of Pharmacy Dr. Rafiq Zakaria Campus Rauzabagh, Aurangabad 431001, Maharashtra, India.

[2]Seniour Lecturer Kamla Nehru Polytechnic Pharmacy Dr. Rafiq Zakaria Campus Rauzabagh, Aurangabad, India.

3Lecturer Kamla Nehru Polytechnic Pharmacy Dr. Rafiq Zakaria Campus Rauzabagh, Aurangabad, India.

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***Correspondence for Author:**
**Syed S M,**
Research Scholor Y B Chavan College of Pharmacy,
Dr. Rafiq Zakaria Campus
Rauzabagh, Aurangabad
431001, Maharashtra, India.

## ABSTRACT

The aim of current study was to formulate fast acting mouth dissolving tablet of Naratriptan HCl for the treatment of migraine in subject with a shortened time period for the onset and maximum peak concentration. Tablets were prepared by direct compression following sublimation camphor was used as a sublimating agent. Sodium starch glycolate and crospovidone were used as superdisintegrants in different concentrations. The prepared tablets were evaluated for thickness, uniformity of weight, content uniformity, hardness, friability, wetting time, water absorption ratio, in vitro disintegration time and in vitro drug release. The tablet disintegrates in vitro within 12-20 sec. Almost 90% of drug was released from most of the formulations within 15 min. The formulations containing 4% crospovidone was found to give the best results. From the results it was concluded that mouth dissolving tablet of Naratriptan by sublimation technique can be promising tool for delivery of Naratriptan in migraine.

**Keywords:** Naratriptan, Migraine, superdisintegrants, Sublimation.

## INTRODUCTION

Cluster headache is a relatively rare but extremely debilitating disorder that is characterized by the rapid onset of unilateral, periorbital headache that quickly escalates to maximum

intensity. Patients routinely report the pain of an attack as being the most severe they have ever experienced. By the definition of the International Headache Society, attacks typically last from 15 to 180 min when left untreated and are accompanied by one more cranial autonomic features such as ipsiletaral conjunctival injection, lacrimation and rhinorrhea or nasal congestion. In this case, a rapid onset of pharmacological effect is an often desired from drugs. This can effectively be achieved by parenteral administration, but this method may not always be convenient for the patient. Therefore, there is growing interest in developing new, non-parenteral, reliable and convenient dosage forms using administration routes where a rapidly dissolved drug is immediately absorbed into the systemic circulation Sublingual administration can offer an attractive alternative route of administration. The advantage of the sublingual drug delivery is that the drug can be directly absorbed into systemic circulation bypassing enzyme degradation in the gut and liver. In addition, the thin sublingual mucosa (about 190 μm compared to 500–800 μm of the buccal mucosa) and the abundance of blood supply at the sublingual region allow excellent drug penetration (absorption) to achieve high plasma drug concentration with a rapid onset of action. A well-established example is nitroglycerin, which is used for the treatment of acute angina. A fast dissolving system can be defined as a dosage form for oral administration, which when placed in the mouth, rapidly disperses or dissolves and can be swallowed in the form of liquid [1, 2].

Naratriptan is a triptan drug used for the treatment of migraine headaches. It is a selective 5-hydroxytryptamine1 receptor subtype agonist (5-HT1B/1D). Chemically it is N-methyl-2-[3-(1-methylpiperidin-4-yl)-1H-indol-5-yl] ethane-1-sulfonamide monohydrochloride. It is well absorbed (70% oral bioavailability), absorption is rapid with peak plasma concentrations after 2-5 hours. As migraine sufferers have markedly reduced functional ability, they would be benefited from acute treatment that helps them to resume their functional activities as quickly as possible [3].

In the present study mouth dissolving tablet of naratriptan was developed so as to achieve rapid disintegration in mouth systemic absorption and maximum peak concentration in less time. As tablet disintegrates in mouth this could enhance the clinical effect of the drug through pre-gastric absorption from the mouth, pharynx and oesophagus this leads to an increase in bioavailability by avoiding first pass liver metabolism.

## MATERIALS AND METHODS

Naratriptan HCl was obtained as a gift sample from Orchid Pharma Ltd. Aurangabad. Sodium starch glycolate and Crospovidone from Wockhardt limited, Waluj, Aurangabad. Strawberry Flavour from Cipla pharmaceuticals, Mumbai.

Mouth dissolving tablets of Naratriptan HCl were prepared using the superdisintegrants (Crospovidone, Sodium starch glycolate) in varying concentration. In this study Mouth dissolving tablet was prepared by sublimation technique camphor was used as a sublimating agent. Sodium starch glycolate and crospovidone were used as superdisintegrants in different proportions. Mannitol and microcrystalline cellulose were used as diluents. All the ingredients were passed through sieve no.60 separately. The drug and ingredients except mag. stearate were mixed uniformly and set aside. Finally mag. Stearate was added and the blended mixture was directly compressed using 6.5 mm punch in Karnavati tablet punching machine to form a tablet of 100 mg. The compressed tablets were subjected for drying at a temperature of 60°C to facilitate the volatilization of sublimable component i.e. camphor.

**TABLE 1: Composition of Mouth Dissolving Tablet of Naratriptan HCl (100 mg)**

| Ingredients | F 1 | F 2 | F 3 |
|---|---|---|---|
| Naratriptan HCl | 2.5 | 2.5 | 2.5 |
| Microcrystalline cellulose (MCC) | 50 | 50 | 50 |
| Mannitol | 24 | 22 | 20 |
| Camphor | 20 | 20 | 20 |
| Cross povidone | 2 | 4 | 6 |
| Straw-berry flavour | 0.5 | 0.5 | 0.5 |
| Magnessium stearate | 1 | 1 | 1 |

All quantities in milligram (mg).

**TABLE 2: Composition of Mouth Dissolving Tablet of Naratriptan HCL (100 mg)**

| Ingredients | F 1 | F 2 | F 3 |
|---|---|---|---|
| Naratriptan HCl | 2.5 | 2.5 | 2.5 |
| Microcrystalline cellulose (MCC) | 50 | 50 | 50 |
| Mannitol | 24 | 22 | 20 |
| Camphor | 20 | 20 | 20 |
| Sodium starch glycolate | 2 | 4 | 6 |
| Straw-berry flavour | 0.5 | 0.5 | 0.5 |
| Magnessium stearate | 1 | 1 | 1 |

All quantities in milligram (mg).

**Evaluation of Mouth Dissolving Tablets**

**Uniformity of Weight**

To study weight variation, 20 tablets were weighed individually using an electronic balance and the test was performed according to the official method. The average weight was calculated from the total weight of 20 tablets. The individual weights were compared with the average weight. Since the average weight of tablet is 100 mg, the percentage difference in the weight variation should be within the permissible limits (± 7.5 %). The tests requirements are met if not more than 2 tablet of individual weights are less than average percentage ie.7.5%.

**Hardness**

Monsanto hardness tester was used to check the hardness of the tablet. The tablet was placed vertically between the jaws of the tester. The two jaws placed under tension by spring and screw gauge. By turning the screw, the load was increased and at collapse the applied pressure from the spring was measured in $kg/cm^2$. Then mean ± SD was calculated.

**Friability**

Twenty tablets were weighed and placed in a Roche friabilator (Electrolab, India). Twenty preweighed tablets were rotated at 25 rpm for 4 min. The tablets were then dedusted and reweighed and the percentage of weight loss was calculated. The percentage friability of the tablets were measured as per the following formula,

$$\% \text{ loss} = \frac{\textit{Initial wt. of tablets - Final wt. of tablets}}{\textit{Initial wt. of tablets}} \textit{ x 100}$$

**Drug Content**

Ten tablets were powdered and the blend equivalent to 5mg of Naratriptan HCl was weight and dissolved in suitable quantity of 0.1M HCl solution was filtered and diluted and drug content analysed spectrophotometrically at 223 nm using Shimadzu UV- 1800, Japan.

**In-vitro Disintegration test**

The Test was carried out on 6 tablets using tablet disintegration tester Electrolab, Mumbai. Distilled water at $37^oC \pm 2^oC$ was used as a disintegration media and the time in second taken for the complete disintegration of the tablet with no palable mass remaining in the apparatus was measured in seconds.

**Wetting Time**

The wetting time of the tablet can be measured using a simple procedure. A piece of double folded tissue paper placed in a petridish containing 6 ml of water. One tablet was placed on this paper and time for complete wetting of tablet was noted.

**Thickness**

The uniformity of the diameter and thickness was measured using vernier caliper. The average diameter and thickness of the tablet was calculated. The test passed if none of the individual diameter and thickness value deviated by ± 5% of the average.

**Water absorption Ratio**

A piece of tissue paper folded twice was placed in a small Petridish containing 6ml of water. A tablet was put on the tissue paper and allowed to completely wet. The wetted tablet was weighted. Water absorption ratio, R was determined using following equation.

$$R = Wa-Wb / Wa \times 100$$

Where,

Wa = weight of tablet after water absorption

Wb= weight of tablet before water absorption

***In-vitro* Dissolution Study**

The release rate of Naratriptan HCl from mouth dissolving tablets was determined using USP dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of phosphate buffer pH 6.8 at 37°C ± 0.5°C and 50 rpm. Sample solution of 5 ml was withdrawn from the dissolution apparatus at regular intervals. The withdrawn samples were replaced with fresh dissolution medium of same quantity. The withdrawn samples were filtered through what man filter paper and analyzed spectrophotometrically (Shimadzu UV-1800, Japan) at 223 nm.

## RESULTS

**TABLE 3: Evaluation of Mouth Dissolving Tablets of Naratriptan HCl.**

| FORMULATIONS | F1 | F2 | F3 | F4 | F5 | F6 |
|---|---|---|---|---|---|---|
| Hardness ($Kg/cm^2$) | 3.2±0.20 | 3.3±0.15 | 3.2±0.11 | 3.1±0.20 | 3.0±0.10 | 3.3±0.25 |
| Friability | 0.55±0.02 | 0.60±0.03 | 0.49±0.01 | 0.74±0.04 | 0.70±0.04 | 0.65±0.03 |
| Drug content (%) | 99.01±1.10 | 99.45±0.19 | 101.95±0.64 | 98.96±1.2 | 101.25±1.12 | 99.39±1.5 |
| Thickness (mm) | 3.15±0.2 | 3.1±0.5 | 3.2±0.3 | 2.95±0.2 | 3.0±0.4 | 3.1±0.3 |
| Disintegration Time (sec) | 16 | 12 | 42 | 47 | 15 | 19 |
| Wetting time (Sec) | 13±1.9 | 10±0.59 | 21±1.2 | 24±1.83 | 16±1.5 | 14±0.98 |
| Water absorption ratio | 65.0±1.15 | 81.18±0.50 | 56.12±1.0 | 54.20±1.0 | 77.80±1.0 | 64.12±1.5 |

**TABLE 4: Drug Release Profiles of F 1 TO F 6**

| Time (minutes) | F 1 | F 2 | F 3 | F 4 | F 5 | F6 |
|---|---|---|---|---|---|---|
| 2 | 43.5±0.14 | 46.8±0.12 | 35.23±0.47 | 30.35±0.35 | 39.81±0.36 | 41.52±0.52 |
| 4 | 57.2±0.10 | 62.3±0.29 | 45.4±0.51 | 41.5±0.33 | 54.3±0.23 | 56.5±0.24 |
| 6 | 74.92±0.11 | 78.4±0.46 | 56.52±0.48 | 53.2±0.49 | 69.4±0.43 | 75.5±0.54 |
| 8 | 81.7±0.16 | 85.9±0.30 | 67.3±0.33 | 62.8±0.45 | 77.9±0.30 | 82.3±0.28 |
| 10 | 89.33±0.13 | 92.52±0.22 | 75.6±0.48 | 71.5±0.14 | 86.5±0.26 | 91.2±0.35 |
| 15 | 94.2±0.32 | 98.3±0.19 | 82.8±0.50 | 76.9±0.09 | 92.3±0.27 | 94.8±0.27 |

*All values are means ± SD, n=3

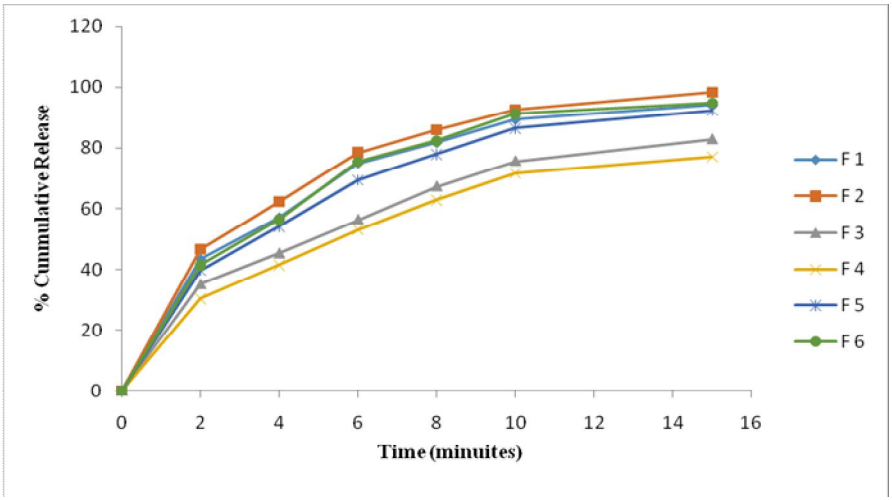


**Figure 1. Drug Release profile of F 1 to F 6**

## DISCUSSION

Mouth dissolving tablet of naratriptan hydrochloride was prepared by direct compression and sublimation technique. Cross povidone and sodium starch glycolate were used as superdisintegrant, camphor was employed as a sublimating agent, mannitol and MCC were used as diluents. Difeerent concentration of cross povidone and sodium starch glycolate were used from evaluation parameter it was found that cross povidone was effective disintegrant as compared to sodium starch glycolate, cross povidone was used in concentration as 2%, 4% and 6%, it was found that formulation containing 4% cross povidone has least disintegration time i.e. 12 seconds and more than 98% drug release within 15 minutes. From results it was found that cross povidone was efeective at a concentration of 2-4% further increase in concentration increases disintegration time and delays the drug release. Sodium starch glycolate was also used in different concentration, it was found that increase in concentration of SSG decreases disintegration time and increase rate of drug release.

Camphor was used as a sublimating agent leading to formation of porous structure there by helping in water absorption and easy disintegration. Among all the formulation the formulation F 2 was found to be more effective having shortest disintegration time i.e. 12 seconds and maximum drug release i.e. 98% within 15 minutes.

The prepared tablets were evaluated for thickness, uniformity of weight, content uniformity, hardness, friability, wetting time, water absorption ratio all parameters were found to be within compendial limits table 3.

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## REFERENCES

1. Ziya B, Cetin T, Umut T, Halil E, Cansel K, Ayhan, Yalcin O, Formulation of zolmitriptan sublingual tablets prepared by direct compression European Journal of Pharmaceutics and Biopharmaceutics 78 (2011) 499–505.
2. Sameer G.L, Yi-Ying Y, Ajay K. B Effects of disintegration-promoting agent, lubricants and moisture treatment on optimized fast disintegrating tablets International Journal of Pharmaceutics 365 (2009) 4–11.

3. Marcelo E. B, Carlos A. B, Ana L. A, Jose G. S. The Triptan Formulations A critical evaluation, Arq Neuropsiquiatr 2003;61(2-A):313-320
4. Bhardwaj V Bansal, M, Sharma P.K. Formulation and Evaluation of Fast Dissolving Tablets of Amlodipine Besylate Using Different Super Disintegrants and Camphor as Sublimating Agent American-Eurasian Journal of Scientific Research 5 (4): 264-269, 2010
5. Mahajan H.S., Kuchekar B.S., Badhan A.C., Mouth dissolving tablet of sumatriptan Succinate, Indian Journal of Pharmaceutical Sciences, March –April 2004, 238-240
6. Kumara Swamy.G, JMR.Kumar, J.V.L.N Sheshagiri Rao, U.Ashok Kuma1, Vidya sagar. P Spectrophotometric Determination Of Naratriptan Hydrochloride In Bulk And Pharmaceutical Dosage Form Indo American Journal of Pharmaceutical Research. 2011;1(4):253-256.
7. Sarasija, S., V.Pandit and H.P.Joshi, Mouth dissolving tablets of salbutamol sulphate. Indian J.Pharma.Sci 2007 69:467-
8. Parshu Ram Rai, A.K. Tiwary, Vikas Rana Superior disintegrating properties of calcium cross-linked Cassia fistula gumderivatives for fast dissolving tablets Carbohydrate Polymers 87 (2012) 1098– 1104.
9. Shukla D, Chakraborty S, Singh S, Mishradali B, Mouth Dissolving Tablets II: An Overview of Evaluation Techniques Sci Pharm. 2009; 77: 327–341
10. Chandira R, Venkataeswartlu B., Formulation and Evaluation of Mouth dissolving tablets of the Etoricoxib, P. J. Pharm. Science-2010, 23(2):178-181.
11. Lakshmi C, Akul S P, Totala A V, Chaudhary J J, Patel N J, Vedhavati S.V. Development And Characterization Of Melt-In-Mouth Tablets Of Atenolol By Sublimation Technique IJPRD, 2011; Vol 3(3);5: May 2011, 27 – 36.
12. Bala R, Khanna S, Pawar P Polymers In Fast Disintegrating Tablets – A Review Asian J Pharm Clin Res, Vol 5, Issue 2, 2012, 8-14.