e-ISSN: 2349-1329 www.ijarrp.com
Article Statistics:
Received on: 05-10-2015
Accepted on: 22-11-2015
Published on: 16-12-2015
Volume: 2 Issue: 1 2015
Page Numbers: 265-280
Research Article
Total Pages: 16

International Journal for Advanced Review and Research in Pharmacy (IJARRP)

Formulation and Evaluation of Oral Disintegrating tablets of Zolmitriptan

Kudupudi Venkateswarlu[1], Kusuma D[2]

1. Department of Pharmaceutics, Sri Sai Aditya Institute of Pharmaceutical Sciences and Research, Surampalem, Andhra Pradesh India.
2. Department of Pharmaceutical Technology, Sri Sai Aditya Institute of Pharmaceutical Sciences and Research, Surampalem, Andhra Pradesh India.

ABSTRACT

Zolmitriptan is widely used as Anti migraine agent. They are formulated as oral disintegrating tablets which show better patient acceptability and compliance with improved efficacy when compared with conventional dosage forms. Based on various studies carried out we have arrived at the following conclusions: Direct compression was used for the preparation of oral disintegrating tablets of Zolmitriptan Based on the preliminary studies various formulation trials (F1-F9) were carried out with different concentrations of superdisintegrants and diluents. From the various formulations it was concluded that the formulation F9, the reproducibility batch of F8 was finalized as the optimized formula. Formulation F9 showed satisfactory results with various physicochemical evaluation parameters like Hardness, Percentage weight loss, Disintegration time, Dissolution profile, Assay and Moisture content when compared with the marketed product. When subjected to accelerated stability studies the tablets were found to be stable.

Key Words: Zolmitriptan, Oral Disintegrating Tablets.

1. INTRODUCTION

Oral disintegration tablets are the novel technology for administration of the drug through the oral route. ODT's are solid unit dosage forms, which disintegrate or dissolve rapidly in the mouth without chewing and water. Oral administration is the most popular route due to ease of ingestion, pain avoidance, versatility to accommodate various types of drug candidates and most importantly patient compliance [1]. A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue [2]. Many patients find it difficult to swallow like pediatric and geriatric and those people who are travelling or little access to water and some patients who are mentally ill like schizophrenia they are also did not take medicine, oral disintegrating tablets solve these problems. An Oral disintegration tablets is a solid dosage form that disintegrates and dissolves in the mouth without water. ODTs disintegrates and dissolves in the mouth in less than 60 seconds and hence produce a rapid action [3]. Orally disintegrating tablets provide an advantage particularly for pediatric and geriatric populations who have difficulty in swallowing conventional tablets and capsules. Additionally, pediatric patients may suffer from ingestion problems as a result of underdeveloped muscular and nervous control. ODTs may show increased oral bioavailability. It provides good stability, accurate dosing, easy manufacturing, small packaging size, and easy to handle by patients. Over a decade, the demand for development of orally disintegrating tablets (ODTs) has enormously increased as it has significant impact on the patient compliance. Orally disintegrating tablets offer an advantage for populations who have difficulty in swallowing. It has been reported that Dysphagia (difficulty in swallowing) is common among all age groups and more specific with pediatric, geriatric population along with institutionalized patients and patients with nausea, vomiting, and motion sickness complications. ODTs

Corresponding Author:
Kudipudi Venkateswarlu. M.Pharm, Ph.D
Department of Pharmaceutics, Sri Sai Aditya Institute of Pharmaceutical Scieences and Research, Surampalem

Email: kudupudi72@gmail.com

with good taste and flavor increase the acceptability of bitter drugs by various groups of population. ODT products have been developed for numerous indications ranging from migraines (for which rapid onset of action is important) to mental illness (for which patient compliance is important for treating chronic indications such as depression and schizophrenia) [4]. Orally disintegrating tablets have been found to be the choice for Psychiatric as well as patient suffering from stroke, thyroid disorder, Parkinson's diseases and multiple sclerosis, patients with nausea, vomiting and motion sickness[5]. These systems may offer superior profile with potential mucosal absorption thus increase the drug bioavailability. These systems are also called melt-in-mouth tablets, Rapimelts, porous tablets, Orodispersible, quick dissolving or rapidly disintegrating tablets[6].

2. MATERIALS AND METHODS

2.1. LIST OF CHEMICALS USED

Refer Table 1 in Page 272

2.2. LIST OF EQUIPMENT USED

Refer Table 2 in Page 272

2.3. EVALUATION OF ORAL DISINTEGRATING TABLETS

Evaluation of blend properties of Zolmitriptan.

2.3.1. PREFORMULATION STUDIES

2.3.1.1. DRUG EXCIPIENT COMPATIBILITY STUDIES

Drug-excipient compatibility studies lay the foundation for designing a chemically stable formulation for clinical and commercial development. Drug excipient compatibility studies are conducted during preformulation to select the most appropriate excipients.

Objective

To study compatibility of the active ingredients with selected excipients and to prove that the selected excipients are compatible with the active ingredient.

Design Plan

The active ingredients and the excipients were mixed in the selected ratios in the polybag. The mixtures are transferred into glass vials and sealed. The samples were placed as first set of initial samples and second set of samples were kept at 40°C±2°C/75%±5 % RH for 4 weeks. The samples were analyzed for physical parameters.

2.3.2. PRE-COMPRESSION PARAMETERS

2.3.2.1. ANGLE OF REPOSE

The internal angle between the surface of the pile of blend and the horizontal surface is known as the angle of repose.

Method

The Angle of repose was known by passing the blend through a funnel fixed to a burette stand at a particular height (4 cm). A graph paper was placed below the funnel on the table. The height and radius of the pile was measured. Angle of repose of the blend was calculated using the formula.

$$\theta = \tan^{-1}(h / r)$$

h = Height of the pile
r = Radius of the pile

2.3.2.2. BULK DENSITY

Bulk density is used as a measure to describe packing materials or granules.

Method

Bulk density is the ratio of given mass of powder and its bulk volume. It was determined by transferring an accurately weighed amount of powder sample to the graduated cylinder with the aid of a funnel. The initial volume was noted. Ratio of weight of the sample to the volume it occupied was calculated.

Bulk density = W/V0 g/ml
W= Mass of the blend
V0 =Untapped volume

2.3.2.3. TAPPED DENSITY

Method

Tapped density was measured by transferring a known quantity of blend into a graduated cylinder and was placed on the tapped density apparatus. The initial volume was noted. The apparatus was set for 500 taps. The tapped density was determined as the ratio of mass of the blend to the tapped volume.

Tapped density=W/Vf g/ml
W= Mass of the blend
Vf = Tapped volume

2.3.2.4. COMPRESSIBILITY INDEX

It is the propensity of a powder to be compressed

Method

It is measured by tapped density apparatus for 500 taps for which the difference should be not more than 2%. Based on the apparent bulk density and tapped density the percentage compressibility of the blend was determined using the following formula.

% Compressibility = [(V0 – Vf) / V0] X 100

OR

% Compressibility = [(Tapped density – Bulk density) / Tapped density] X 100

2.3.2.5. HAUSNER RATIO

Galley Proof

It indicates the flow properties of the powder. The ratio of tapped density to the bulk density of the powders is called Hausner ratio.

Hausners ratio= Tapped density / Bulk density

Refer Table 3 in Page 272

2.3.2.6. LOSS ON DRYING

The Loss on drying test is designed to measure the amount of water and volatile matters in a sample when the sample is dried under specified conditions. The loss on drying of the blend (1.5g) was determined by using electronic LOD (helium lamp) apparatus at 105°C.

2.3.3. POST COMPRESSION PARAMETERS

2.3.3.1. PHYSICAL APPEARANCE

The physical appearance of the compressed tablets involves the measurement of a number of attributes like tablet shape, smoothness, chipping, cracks, surface texture, colour, embossing, debossing etc.

2.3.3.2. THICKNESS

Thickness was determined for 20 pre-weighed tablets of each batch using a digital vernier scale and the average thickness was determined in mm. The tablet thickhness should be controlled within a ± 5% variation of a standard.

2.3.3.3. WEIGHT VARIATION

20 tablets were selected randomly from a batch and were individually weighed and then the average weight was calculated. The tablets meet the USP specifications if not more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limits

Refer Table 4 in Page 272

2.3.3.4. HARDNESS TEST

The crushing load which is the force required to break the tablet in the radial direction was measured using a Schluenzier hardness tester. The hardness of 10 tablets was noted and the average hardness was calculated. It is given in kp or kg/cm^2.

2.3.3.5. PERCENTAGE FRIABILITY

In friability testing the tablets are subjected to abrasion and shock. It gives an indication of the tablets ability to resist chipping and abrasion during transportation and shipping [27].

Method

If the tablet weight is ≥ 650 mg 10 tablets were taken and initial weight was noted. For tablets of weight less than 650 mg the number of tablets equivalent to a weight of 6.5 g were taken. The tablets were rotated in the Electrolab Friabilator for 100 revolutions at 25 rpm. The tablets were dedusted and reweighed. The percentage friability should be not more than 1%w/w of the tablets being tested.

The percentage friability is expressed as the loss of weight and is calculated by the formula:

$$\% \text{ Friability} = [(W0 — Wf) / W0] \times 100$$

W0 = Initial weight of tablets

W f = Final weight of tablets

2.3.3.6. DISINTEGRATION TIME

Disintegration time is the time taken by the tablet to breakup into smaller particles. The disintegration test is carried out in an apparatus containing a basket rack assembly with six glass tubes of 7.75 cm in length and 2.15 mm in diameter, the bottom of which consists of a #10 mesh sieve. The basket is raised and lowered 28-32 times per minute in a medium of 900 ml which is maintained at 37±2°C. Six tablets were placed in each of the tubes and the time required for complete passage of tablet fragments through the mesh # 10 was considered as the disintegration time of the tablet. The disintegration time that patients can experience for oral disintegrating tablets ranges from 5 to 30seconds [28, 29].

2.3.3.7. PERCENTAGE WATER CONTENT

Karl Fischer reagent (sulphur dioxide and iodine dissolved in pyridine and methanol) is used to determine the water content of the tablets using Karl Fischer Titrator.

2.3.3.8. DISSOLUTION STUDIES

Dissolution is a process by which the disintegrated solid solute enters the solution. The test determines the time required for a definite percentage of the drug in a tablet to dissolve under specified conditions.

Method

The dissolution test was carried out in USP Apparatus Type II (paddle) with 0.1 N Hydrochloric acid as the dissolution medium. The samples were drawn at 5, 10, 15, 20 30, min. Fresh volume of the medium were replaced with the withdrawn volume to maintain the sink conditions. Samples withdrawn were analyzed for the percentage of drug released.

Dissolution Parameters

Dissolution Apparatus	:	USP Apparatus Type II (Paddle)
Dissolution Medium	:	0.1N Hydrochloric acid
Volume	:	500 ml
Temperature	:	37±2° C
Rpm	:	50
Sampling Intervals (min)	:	5, 10, 15,20, 30

Galley Proof

2.3.3.9. MOISTURE UPTAKE STUDIES

Moisture uptake studies for ODT should be conducted to have an insight into the stability of the formulation, as several excipients used are hygroscopic. Moisture uptake studies were carried out by weight method.

Method

- Clean and dry petriplates were taken and their empty weights were recorded.
- 10 tablets were placed into each petriplates and the total weight of each petriplate with the test substance was recorded.
- Finally the petriplates were placed in desicators saturated to 29, 43 and 75% relative humidities at 25°C using various standard salt solutions.
- The weights of all the petriplates were recorded at the end of 1, 2, 4, 6, 8, 24, 48, 72 h.
- The petriplates were carefully wiped with tissue paper to remove any adhering moisture before the weight was recorded.
- The percentage of moisture absorption was determined using the formula

% Moisture absorption = (Observed weight – Initial weight X 100) / Initial weight

2.3.3.10. STABILITY STUDIES

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors, such as temperature, humidity etc.

Galley Proof

Objective

To generate documented evidence that the tablets manufactured comply with the finished product specifications under accelerated and long term stability conditions as per ICH guidelines.

Design Plan

Accelerated study

The product is subjected to accelerated stability studies at 40°C ± 2°C / 75% ± 5% RH for 6 months.

Long term study

The product is subjected to long term studies at 25°C±2°C/60% ± 5% RH for 12 months.

Package type

The tablets were packed as 30's count in HDPE containers, induction sealed with adsorbent cotton and silica gel.

Stability Sampling

Refer Table 5 in Page 272

2.4. EXPERIMENTAL WORK

2.4.1. Direct Compression

Direct compression is one of the popular techniques for preparation of these dosage forms. The advantages of this method include easy implementation, use of conventional equipments along with commonly available excipients, limited number of processing steps and cost effectiveness. Disintegration and solubilization of directly compressed tablets depend on single or combined action of disintegrants, water-soluble excipients and effervescent agents. The basic principle involved in development of these dosage forms using this technique is addition of superdisintegrants in optimum concentrations so as to achieve rapid disintegration along with pleasant mouth feel. It is considered as the best method to prepare orally disintegrating dosage forms since the prepared tablets offer higher disintegration due to absence of binder and low moisture contents. This approach is also considered as disintegrant addition technology. Some formulations were developed using microcrystalline cellulose and low substituted hydroxy propyl cellulose as disintegrating agents and also D-mannitol and crospovidone.

2.5. STANDARD CALIBRATION CURVE OF ZOLMITRIPTAN

Solutions ranging from 5 to 25 µg/ml were prepared using 0.1 N Hcl); separately, absorbance was measured for each solution at λ max of 220 nm using Shimadzu UV/ visible 1700 spectrophotometer, graph was plotted for absorbance versus concentration of Zolmitriptan.

Standard graph of Zolmitriptan in 0.1 N Hcl Solution at λ max 220nm

Refer Table 6 in Page 273

Standard graph of Zolmitriptan in 0.1N Hcl at 220 nm: ***Refer Figure 1 in Page no 276***

2.6. NARRATIVE DESCRIPTION OF MANUFACTURING PROCESS

Formulation of oral disintegrating tablets of Carbidopa-Levodopa 25mg/250 mg were carried out by direct compression technique. The procedure followed for each of the trial has been described as follows:

As the drug substances are hygroscopic the amount of drug substance weighed may not be equivalent to the desired weight (because of the presence of moisture). Therefore the quantity of substance to be weighed was calculated as follows

Quantity of substance = Strength X Assay purity X LOD purity

Assay of substance X (100 – LOD of substance)

Procedure for F1:

- Zolmitriptan, Supertab11SD, Avicel ph 102, Crospovidone, Aspartame & peppermint were weighed, sifted through #40 mesh and blended in the polybag for 10 min.
- Mg stearate passed through #80 mesh which was added to the above blend and lubricated for 5 min in the poly bag
- From the final blend tablets were compressed using 6.4 mm round flat shaped punches.

Procedure for F2& F3

In this trial the concentrations of Crospovidone were increased gradually and was evaluated for the parameters

- Zolmitriptan, Supertab11SD, Avicel ph 102, Crospovidone, Aspartame & peppermint were weighed, sifted through #40 mesh and blended in the polybag for 10 min.
- Mg stearate passed through #80 mesh which was added to the above blend and lubricated for 5 min in the poly bag
- From the final blend tablets were compressed using 6.4 mm round flat shaped punches.

Procedure for F4

In this trial superdisintegrant was changed from Crospovidone to croscarmellose sodium initially low concentrations of disintegrant were used

- Zolmitriptan, Supertab11SD, Avicel ph 102, croscarmellose sodium, Aspartame & peppermint were weighed, sifted through #40 mesh and blended in the polybag for 10 min.
- Mg stearate passed through #80 mesh which was added to the above blend and lubricated for 5 min in the poly bag
- From the final blend tablets were compressed using 6.4 mm round flat shaped punches.

Procedure for F5 & F6

In this trial superdisintegrant croscarmellose sodium concentrations were increased gradually and evaluated for tablet parameters

- Zolmitriptan, Supertab11SD, Avicel ph 102, croscarmellose sodium, Aspartame & peppermint were weighed, sifted through #40 mesh and blended in the polybag for 10 min.
- Mg stearate passed through #80 mesh which was added to the above blend and lubricated for 5 min in the poly bag
- From the final blend tablets were compressed using 6.4 mm round flat shaped punches.

Procedure for F7:

In this trial superdisintegrant was changed from croscarmellose sodium to sodium starch glycolate initially low concentrations of disintegrant were used

- Zolmitriptan, Supertab11SD, Avicel ph 102, sodium starch glycolate, Aspartame & peppermint were weighed, sifted through #40 mesh and blended in the polybag for 10 min.
- Mg stearate passed through #80 mesh which was added to the above blend and lubricated for 5 min in the poly bag
- From the final blend tablets were compressed using 6.4 mm round flat shaped punches.

Procedure for F8 & F9

In this trial superdisintegrant sodium starch glycolate concentrations were increased gradually and evaluated for tablet parameters

- Zolmitriptan, Supertab11SD, Avicel pH 102, sodium starch glycolate, Aspartame & peppermint were weighed, sifted through #40 mesh and blended in the polybag for 10 min.
- Mg stearate passed through #80 mesh which was added to the above blend and lubricated for 5 min in the poly bag
- From the final blend tablets were compressed using 6.4 mm round flat shaped punches.

Galley Proof

FORMULATION DEVELOPMENT OF ZOLMITRIPTAN ORALDISINTEGRATING TABLETS

Refer Table 7 in Page 273

3. EXPERIMENTAL RESULTS

3.1 Solubility Studies

3.1.1 Solubility studies of Zolmitriptan: Refer Table No. 9 in page 274

3.1.2 Dissolution studies of Reference product ZOMIG-ZMT 5 mg tablets: Refer Table No. 11 in page 274

3.1.3 Cumulative percentage of drug release (ZOMIG-ZMT-5 mg) : Refer figure no 2 in page no 277

3.2 Drug-Excipient compatibility studies

3.2.1 Fourier Transform Infrared Spectroscopy (FTIR): Refer figure no 3 in page no 277

3.2.2 FTIR Spectra Of Zolmitriptan: Figure no 4 in page no 277

3.2.3 FTIR Spectra of Avicel PH 102: Figure no 5 in page no 278

3.2.4 FTIR Spectra of Supertab 11SD: Figure no 6 in page no 278

3.2.5 FTIR Spectra of Ssg: Figure no 7 in page no 278

3.2.6 FTIR Spectra of Mg Stearate: Figure no 8 in page no 279

3.2.7 FTIR Spectra of Final Mixture: Refer figure no 9 in page no 279

3.2.8 Purity Index of Zolmitriptan And Final Mixture: Refer figure no 10 in page no 280

3.3 Results of Precompression Parameters

3.3.1 Pre compression Parameters: Refer table No. 12 in page 274

3.4 Results of Postcompression Parameters

3.4.1 Post Compression Parameters: Refer Table no 13 in page 274

3.5 Cumulative % drug release of Zolmitriptan oral disintegrating tablets

3.5.1 % drug release of Zolmitriptan oral disintegrating tablets F1, F2 and F3: Refer Table no 14 in page 275

3.5.2 % drug release of Zolmitriptan oral disintegrating tablets F4, F5 and F6: Refer Table no 15 in page 275

3.5.3 % drug release of Zolmitriptan oral disintegrating tablets F7, F8 and F9: Refer Table no 16 in page no 275

3.6 Comparison of Dissolution Studies OF 5 mg ODT

3.6.1 Comparison of reference product (ZOMIG-ZMT) with F1, F2 and F3

3.6.2 Comparison of reference product (ZOMIG-ZMT) with F4, F5 and F6

3.6.3 Comparison of reference product (ZOMIG-ZMT) with F7, F8 and F9

3.7 RESULTS OF MOISTURE UPTAKE STUDIES Condition: 29%RH

3.7.1 Moisture uptake observations at 29% RH Condition: 75%RH: Refer Table no 17 in page no 275

Gross weight (drug + petridish) : 38.105 g

3.7.2 Moisture uptake observations at 75% RH: Refer table no 18 in page no 276

3.8 RESULTS OF STABILITY DATA

3.8.1 Stability study data: Figure no 10 in page no 280

3.9 Dissolution data of stability study sample: Refer figure no 11 in page no 280

3.9.1 Dissolution data of stability sample: Refer figure no 12 in page no 280

4. BIBLIOGRAPHY

1. Srikonda Venkateshwara sastry, Janakiram Nysnadam and Joshna .A Recent technological advances in oral drug delivary a review PSST 2000;3(4):138-145
2. Sudhir Bharawaj, Vinay Jain, Shailesh Sharma, Jat CR, Suman Jain. orally Disintegrating Tablets: A Review. Drug Invention Today 2010; 2(1):81-88
3. Mahaveer Khinchi P. Orally Disintegrating Tablets: A future prospectus. International Journal Pharmaceutical science And Biotechnology 2010;1(2):71-79
4. Jaysukh Harini J, Dhaval Rathod A, Khantilal Vadalia R. orally disintegrating Tablets: A Review. Tropical Journal of pharmaceutical Research 2009;8(2):161-172
5. Sastry SV, Nyshdham JR, Fix JA. Recent Technological Advances in oral drug delivery: An overview. Pharm. Sci Technol Today.2000;3:138-145
6. Rakesh Pahwa,Mona Piplani,Prabodh C, Sharma, Dhirender Koushik, Sanju Nanda. Orally Disintegrating Tablets friendly to Pediatrics Gediatrics. Archives of Applied science Research 2010;2(2):35-48
7. Debjit Bhowmik, Chiranjib B, Krishnakanth, Pankaj, Margeret Chandira R. Fast dissolving Tablets: An overview. Journal of chemical and pharmaceutical Research 2009; 1(1):163-177
8. Vijay Kumar Chauhan. Mouth dissolving Tablets: An overview. Journal of Pharm & Biomedical Sciences 2011;5(8)
9. Rangasamy Manivannan. Oral disintegrating tablets: A future compaction International Journal of pharma Research & Development online 2009;1(10)
10. Brown D.orally disintegrating tablets: Taste over speed. Drug delivery Tech,2001;3(6):58-61
11. Reddy LH, Gosh BR, Fast dissolving drug delivery systems: A review of literature. International Journal Pharm Sci, 2002;64(4):331-336
12. Chang RK, Guox, Burnside BA, couch RA Fast dissolving tablets Pharm Tech 2000;24:52-58
13. Aurora J, Pathuk V. oral disintegrats technologies:oral disintegrates dosage forms:An overview. Drug delivery technology 2005;5(3):50-54
14. Hamilton EL, Luts E M. Advanced orally disintegrating tablets brings special benefits to patients and product Life cycle. Drug delivery Technology 2005;5(1):34-37
15. Habib W, Khankari R, Honts J. Fast dissolving drug delivary systems. crt rev ther Drug carrier system 2005 17(1):61-72
16. Gosh TK, Chaterjee DJ, Pfister W. Quick dissolving oral dosage forms. Drug delivers to the oral cavity: Molecules to market NY,USA:CRC press,2005;337-356
17. Seager H. Drug delivery products and Zyclis fast dissolving doses form. Journal of pharm pharmacology, 1998;50:375-382

Galley Proof

18. Lies MC, Atherton AD, Copping NM. freeze dried dosage forms and methods for preparing same us patent 1993; 5:188-825

19. Sugihara M, Hidaka M, Saitou A. Discriminatory features of dosage form and package JPN Journal of Hospital pharmacy 1986; 12: 322-328

20. Tarique Khan, Sayeed Nazeem, Siraj Shaik, Afsar Shaik, Ashish Kairnar, Aezaj Ahmed. An approach for Rapid disintegrating tablet. A Review International Journal of Pharmaceutical Research and Development 2011;3(3):170-183

21. Suresh Bandari, Rajendhra Kumar Mittapalli, Ramesh Gannu, Yamsani Madhusudhan Rao. Oro dispersible tablets: An overview. Asian Journal of pharmaceutics 2008;2(1):2-11

22. Sandeep Divete, Kunchu Kavitha, Ganesh Nanjan Sockan. Fast disintegrating Tablets: An emerging Trend. International Journal of pharma sciences Review & Research 2011; 6(2):18-22

23. Tarun Kumar Satpathy, Different Approaches of fast-melts tablets:A review" pharmainfo.net 2007;5(5)

24. Avani R, GosaiSanjay B, Patel, Karthika K, Sawanth Formulation & Evaluation of Oral Disintegrating Tablets of Ondesetron Hcl by Direct compression using super disintegrats. International Journal of pharmaceutical sciences and Nanotechnology,2008;1(1):1-6

25. Honey Goel, Parshuram Raj, Vikas Rana, Ashok Tiwary K. Orally disintegrating system: Innovations in formulation and Technology. Recent trends on Drug delivary & formulation 2008; 2:258-274

26. Prashant Khemariya. Preparation & evaluation of mouth dissolving tablets of Meloxicam: International Journal of Drug delivary 2010;2: 76-80

27. Dali shukla, Subhasis chakrabory, Sanjay Singh Brahmeshwar Mishra Mouth Dissolving Tablets: An Overview of evaluation Techniques. Scientia Pharmaceutica 2009;(77):327-341

28. Bi Y, Sunanda H, Yonezawa V, Danjo K,otsuka A, Lidak preparation and evaluation of a compressed tab rapidly disintegrating in oral cavity. chem pharm bull.1996;44:2121-2127

29. Narazaki R, harada T,Takami N,Kato Y,ohwaki T. A new method for disintegration studies of rapid disintegrates tablets. chem pharm bull. 2004;52:704-707

30. Ramesh J, Prabhakar Reddy V, Chandrasekhar Rao G Formulation and evaluation of oral disentegratity tablets of Labetalol hydrochloride. International journal of pharmaceutical sciences 2010;2(2):488-495

31. Ashok Kumar, Agarwal AG. Formulation, development & of evaluation of orally disintegrating tablets by sublimation technique. International Journal of Pharm Tech Research 2009;1(4):997-999

32. Ravi Kumar, Patil M.B, Sachin Patil.R, Mahesh S, Mahalaxshmi.R. Development and characterization of orodispersible Tablets of Aceclofenac by sublimation technique. International Journal Pharm Tech Research 2009;1(2):210-214

33. Bhupendra, Prajapathi.G, Bhaskar Patel. Formulation, Evaluation & optimization of orally Disintegrating Tablet of Piroxicam. International Journal Pharm Tech Research 2010;2(3):1893-1899

34. Basani G, Reddy S, Somagoni JM, Rao YM. Formulation & Evaluation of orally Disintegrating Tablets of Baclofen. Journal of Global Pharma Technology 2010;2(3):137-145

35. Sandeep Kumar D Formulation and evaluation of mouth Dissolving Tablets of Felodipine. Asian Journal of pharmaceutical of clinical Research 201;1(4)

36. Sumantha Malakar, Someshwara Rao B, Ashok Kumar P,Suresh Kulakarni. Formulation and Evaluation of Fast Dispersible Aceclofenac Tablets: Effect of Functionality of Super disintegrates. Journal of Global Pharma technology 2010;2(5):90-96

37. Suresh Kulakarni V, Ranjit Kumar P, basavaraj, Someshwara Rao, Ramesh B, Ashok Kumar P. Effect of superdisintegrats on formulation of Taste masked fast disintegrating Lisinopril Tablets. International Journal of current Pharmaceutical Research 2011;1(3)

38. Prateek Gandhi P, Kumar Vaidya A, Guru Shelake T, Priyanka Kulakarni R. Formulation & evaluation of Met formin Hydrochloride fast Disintegrating Tablets By using polacrilin Potassium NF from different from different Sources as Superdisintegrants International Journal of pharmacy & pharmaceutical sciences 2010; 2(2)

39. Prashant Khemariya etal Preparation & evaluation of mouth dissolving tablets of Meloxican. International Journal of Drug delivary 2010;2: 76-80

40. Swamy PV, Gada SN, Shirsand B, Kinag M.B, Shilpa H Design and evaluation of cost effective oro dispersible tablets of Diethyl carbomazine citrate By efficient Method. International Journal Pharma Sciences & Research 2010;1(6):258-264

41. Pandey Shivanand, Viral Devmurari, Manish Goyani. Formulation & evaluation of Task masked fast disintegrating Tablets of Lisinopil International Journal of pharm Tech Research. 2010; 2(2):1639-1643

42. Suhas kakade M,Vinod mannur S, Ravindhra Kardi V,Ketan Ramani B, Avaz Dhada V. Formulation and evaluation of orally Disintegrating Tablets of sertraline. International Journal of Pharma Research

Galley Proof

& Development-online 2010; 1(12).

43. Kanakadurga devi N, Prameela Rani A, Sai Mrudula B, formulation & evaluation of ODT of Montelukast Sodium: effect of functionality of evaluation of Superdisintegrats Journal of pharmacy Research 2010;3(4):803-808

44. Patil C, Das effect of various superdisintegrats on the drug release profile and disintegrating time of Homolengine ODT. African Journal of pharmacy and pharmacology 2011;5(1):76-82

45. Bhupendhra G,Prajapathi, Bhaskar Patel. Fomulation and optimization of orally disintegrating tablet of piroxicam. International Journal of Pharm Tech Research 2010; 2(3):1893-1899

List of Tables

Table No. 1: List of Chemicals Used

S.No	Name	Supplier
1	Zolmitriptan	SMS pharmaceuticals ltd, Hyderabad
2	Super Tab 11 SD	DMV-Fonterra, France
3	Avicel Ph 102	Signet, Mumbai
4	Aerosil 200	Signet, Mumbai
5	Aspartame	Globalchem, Mumbai
6	peppermint	Powdarome chemicals, Goa
7	Magnesium stearate	Signet, Mumbai

Galley Proof

Table No. 2: List of Equipments used

S no.	Equipment Name	Make
1	Top load balance	Sartorius, Mumbai
2	Compression machine(17 station press)	Cadmach, Ahmedabad
3	Disintegration apparatus	**Electrolab, Mumbai**
4	**Friability apparatus**	**Electrolab, Mumbai**
5	**Hardness tester**	**Dr. schleuniger, USA**
6	**Digital screw guage**	**Fischer scientific**
7	**Sieve shaker**	**Electrolab, Mumbai**
8	**Tap density apparatus**	**Electrolab, Mumbai**
9	**Dissolution testing apparatus**	**Electrolab, Mumbai**
10	**UV-VIS Spectrometer**	**Shimadzu, Japan**
11	**FTIR Spectrometer**	**Shimadzu, Japan**
12	**Stability Chamber**	**Thermo Lab, Mumbai**

Table No. 3: Table of Flow properties and Compressibility index

S no.	Flow properties	Angle of repose (θ)	Compressibility index (%)	Hausner ratio
1	Excellent	25-30	<10	1.0-1.11
2	Good	31-35	11-15	1.12-1.18
3	Fair	36-40	16-20	1.19-1.25
4	Possible	41-45	21-25	1.26-1.34
5	Poor	46-55	26-31	1.35-1.45
6	Very poor	56-65	32-37	1.46-1.59
7	Very very poor	>66	>38	>1.60

Table No. 4: Acceptance criteria of weight variation USP

Average weight of tablet (mg)	% difference
130 or less	10 %
From 130 to 324	7.5%
> 324	5%

Table No. 5: Stability Sampling Withdrawal Schedule

S.NO.	STORAGE CONDITION	TEST PERIOD
1	40°C±2°C/75% ±5% RH	1st month
		2nd month
		3 months
		6 months
2	25°C±2°C/60% ±5% RH	3 months
		6 months
		9 months
		12 months

Table No. 6: Standard Graph of Zolmitriptan

Sl. No.	Concentration (mcg/ml)	Absorbance
1.	0	0
2.	5	0.030
3.	10	0.075
4.	15	0.105
5.	20	0.138
6.	25	0.170

Galley Proof

Table No. 7: Formulation Development of Zolmitriptan Oral Disinterating Tablets

S.no	Ingredients(mg)	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8	F-9
1	Zolmitriptan	5	5	5	5	5	5	5	5	5
2	Supertab 11 Sd	97	97	97	97	97	97	97	97	97
3	Avicel 102	19.6	18.3	17	19.6	18.3	17	19.6	18.3	17
4	Crospovidone	3.9	5.2	6.5	-	-	-	-	-	-
5	Ac-Di-Sol	-	-	-	3.9	5.2	6.5	-	-	-
6	Sodium Starch Glycolate	-	-	-	-	-	-	3.9	5.2	6.5
7	Aspartame	2	2	2	2	2	2	2	2	2
8	Peppermint	1	1	1	1	1	1	1	1	1
9	Mg Stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
	TOTAL wt per tablet (mg)	130	130	130	130	130	130	130	130	130

Table No. 8: Solubility studies of Zolmitriptan

S.no.	Media	Solubility for 5mg tablets (mg/ml)
1	purified water	0.03
2	pH 1.2 buffer	0.03
3	pH 4.5 acetate buffer	0.03
4	pH 6.8 phosphate buffer	0.03

Table No. 9: Drug release of Reference product

S.No	Time (min)	Drug Release (%)
1	0	0
2	5	96.9
3	10	97.8
4	15	98.9
5	20	100.2
6	30	100.2

Table No. 10: Solubility studies of Zolmitriptan

S.no.	Media	Solubility for 5mg tablets (mg/ml)
1	purified water	0.03
2	pH 1.2 buffer	0.03
3	pH 4.5 acetate buffer	0.03
4	pH 6.8 phosphate buffer	***0.03***

Table No. 11: Drug release of Reference product

S.No	Time (min)	Drug Release (%)
1	0	0
2	5	96.9
3	10	97.8
4	15	98.9
5	20	100.2
6	30	100.2

Galley Proof

Table No. 12: Pre compression Parameters

Formulation code	Bulk density(g/ml)	Tapped density(g/ml)	Carr'sIndex	HausnerRatio	Angle of repose(θ)	% LOD
F1	0.384±0.23	0.545±0.11	31.25±0.25	1.41±0.22	41.52±0.45	1.75±0.21
F2	0.362±0.29	0.485±0.25	25.36±0.12	1.33±0.52	40.61±0.25	1.80±0.23
F3	0.380±0.45	0.530±0.52	28.30±0.25	1.39±0.25	48.42±0.14	1.75±0.25
F4	0.371±0.56	0.493±0.35	24.74±0.55	1.32±0.21	37.41±0.25	1.50±0.52
F5	0.360±0.25	0.462±0.55	22.07±0.65	1.66±0.55	33.92±0.56	1.47±0.12
F6	0.419±0.69	0.477±0.25	12.26±0.41	1.14±0.58	24.28±0.58	1.37±0.25
F7	0.417±0.55	0.471±0.45	11.49±0.12	1.13±0.45	22.32±0.25	1.33±0.52
F8	0.416±0.89	0.475±0.12	12.44±0.22	1.13±0.54	25.54±0.56	***1.20±0.12***
F9	***0.428±0.21***	***0.456±0.22***	***18.22±0.12***	***1.25±0.21***	***24.56±0.32***	***1.19±0.32***

Table No. 13: Post compression Parameters

Formulation Code	Average weight (mg)	Thickness(mm)	Hardness(kp)	Percentage Friability (%)	Disintegration Time (sec)
F1	131.2±0.32	3.71±0.029	3.8±0.089	0.63±0.32	80±0.98
F2	130.6±0.23	3.65±0.025	4.2±0.054	1.22±0.23	71±0.88
F3	132.3±0.21	3.69±0.055	4.0±0.024	1.50±0.52	65±0.98
F4	131.8±0.24	3.68±0.054	4.3±0.065	0.78±0.23	59±0.87
F5	129.8±0.21	3.72±0.089	4.3±0.025	0.90±0.52	54±0.58
F6	129.6±0.52	3.66±0.086	4.4±0.025	1.75±0.54	50±0.88
F7	132.0±0.12	3.65±0.029	4.0±0.025	0.32±0.21	30±0.84
F8	130.5±0.25	3.72±0.048	4.2±0.052	0.45±0.12	25±0.88
F9	130.2±0.12	3.70±0.024	4.0±0.052	0.68±0.21	20±0.85

Table No. 14: % drug release of Zolmitriptan oral disintegrating tablets F1, F2 and F3

Time (min)	Formulations		
	F1	F2	F3
0	0	0	0
5	91.1±0.025	91.8±0.05	92.3±0.064
10	91.3±0.083	93.1±0.08	94.5±0.084
15	92.6±0.057	95±0.055	97.0±0.046
20	92.8±0.063	96.3±0.05	98.6±0.044
30	93.4±0.068	97.1±0.04	99.9±0.014

Table No. 15: % drug release of Zolmitriptan oral disintegrating tablets F4, F5 and F6

Time (min)	Formulations		
	F 3	F 4	F 5
0	0	0	0
5	92.8±0.075	93.2±0.087	96.6±0.056
10	94±0.054	95.1±0.056	97.0±0.087
15	95.2±0.058	96.8±0.056	97.8±0.078
20	97.1±0.085	98.9±0.054	98.2±0.078
30	99.2±0.052	99.8±0.085	100.5±0.045

Table No. 16: % drug release of Zolmitriptan oral disintegrating tablets F7, F8 and F9

Time (min)	Formulations		
	F 7	F 8	F 9
0	0	0	0
5	95.3±0.085	96.8±0.085	97.3±0.045
10	96.2±0.058	97.0±0.065	98.5±0.085
15	97.5±0.078	98.2±0.071	99.6±0.041
20	97.9±0.074	98.6±0.074	100.5±0.074
30	99.8±0.045	99.8±0.024	101.5±0.047

Galley Proof

Table No. 17: Moisture uptake observations at 29% RH

Parameter	Time(h)								
	Initial	1	2	4	6	8	24	48	72
Observed RH(%)	29±0.25	29±0.52	28±0.54	27±0.21	28±0.14	29±0.45	29±0.45	29±0.54	28±0.14
Observed temperature (0C)	30±0.15	30±0.23	31±0.65	30±0.45	30±0.75	30±0.02	29±0.65	30±0.42	29±0.23
Physical observation	Nc	Nc	Nc	Nc	Nc	Nc	Nc	Nc	Nc
Observed weight (g)	1.322 ± 0.31	1.322 ± 0.23	1.322 ± 0.41	1.322 ± 0.12	1.322 ± 0.14	1.322 ± 0.14	1.320 ± 0.23	1.321 ± 0.25	1.322 ± 0.52
Percentage moisture uptake (%)	0	0.032 ± 0.25	0.025 ± 0.54	0.021 ± 0.44	0.052 ± 0.84	0.062 ± 0.44	0.071 ± 0.41	0.077 ± 0.14	0.084 ± 0.11

Table No. 18: Moisture uptake observations at 75% RH

Parameter	Time (h)								
	Initial	1	2	4	6	8	24	48	72
Observed RH (%)	75 ± 0.23	75 ± 0.24	75 ± 0.27	75 ± 0.51	75 ± 0.56	75 ± 0.85	75 ± 0.24	75 ± 0.65	75 ± 0.32
Observed temperature(0C)	30 ± 0.23	30 ± 0.52	31 ± 0.54	30 ± 0.12	30 ± 0.54	30 ± 0.41	29 ± 0.22	30 ± 0.44	29 ± 0.14
Physical observation	NC	NC	NC	NC	NC	NC	NC	NC	NC
Observed weight(g)	1.316 ± 0.21	1.318 ± 0.55	1.320 ± 0.44	1.323 ± 0.54	1.329 ± 0.54	1.339 ± 0.44	1.340 ± 0.44	1.339 ± 0.54	1.321 ± 0.44
Percentage moisture uptake(%)	0	0.564 ± 0.14	0.676 ± 0.12	0.894 ± 0.14	1.034 ± 0.25	1.115 ± 0.41	1.148 ± 0.14	1.108 ± 0.87	0.817 ± 0.24

Table No. 19: Stability study data

Parameters Tested	Storage Conditions 400c±20c / 75% ±5% rh		
	Initial	1st month	2nd month
Description	White colored flat faced	No change	No change
Average weight (mg)	130.5	131.2	132.0
Thickness(mm)	3.79	3.80	3.81
Hardness (kp)	4.0	3.9	3.5
Friability (%)	0.51	0.61	0.56

Table No. 20: Dissolution data of stability sample

Time Interval(min)	400C±20C / 75% ±5% RH		
	Initial	1st month	2nd month
0	0	0	0
5	95.2	95.3	95.7
10	97.5	97.7	96.8
15	98.3	98.3	97.7
20	99.2	99.1	98.9
30	99.8	99.4	99.4

Galley Proof

List of Figures

Figure 1: Standard graph of Zolmitriptan

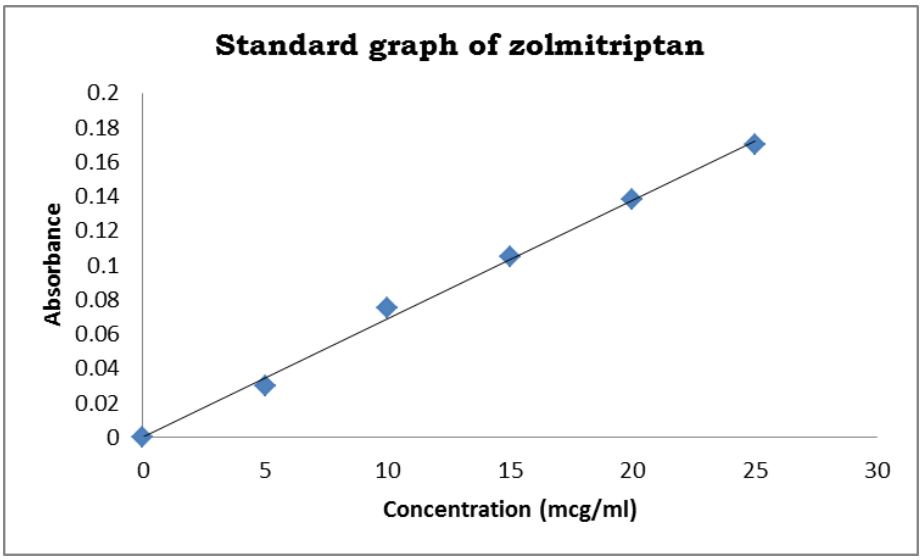

Figure 2: Cumulative percentage of drug release (ZOMIG-ZMT-5 mg)

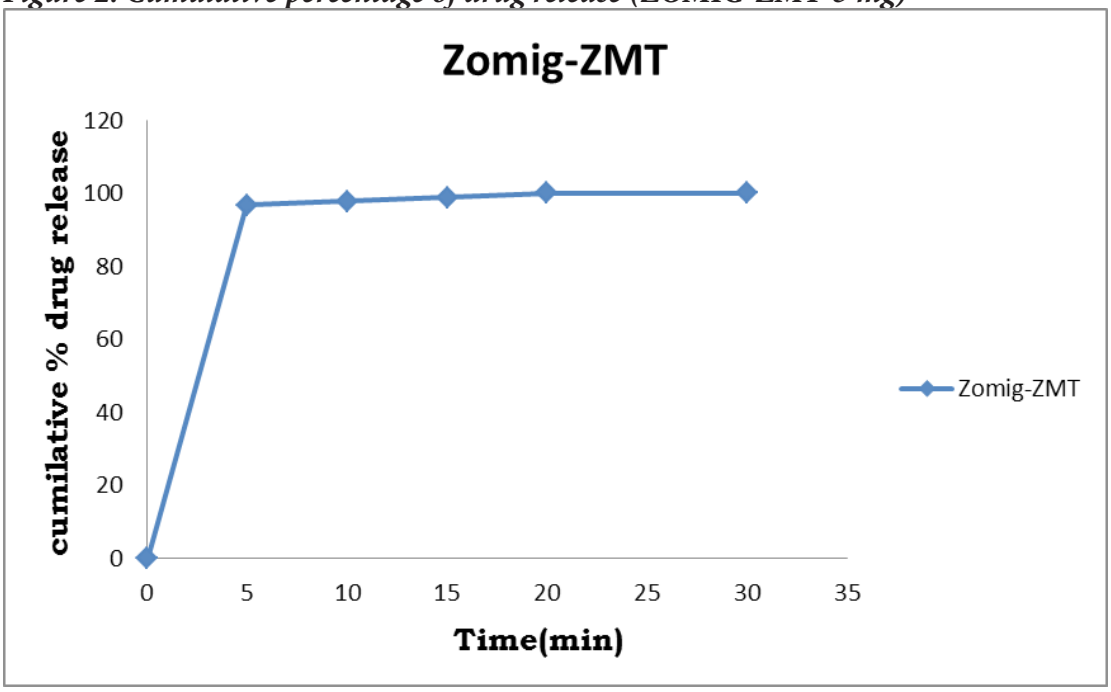

Figure 3: FTIR Spectra Of Zolmitriptan

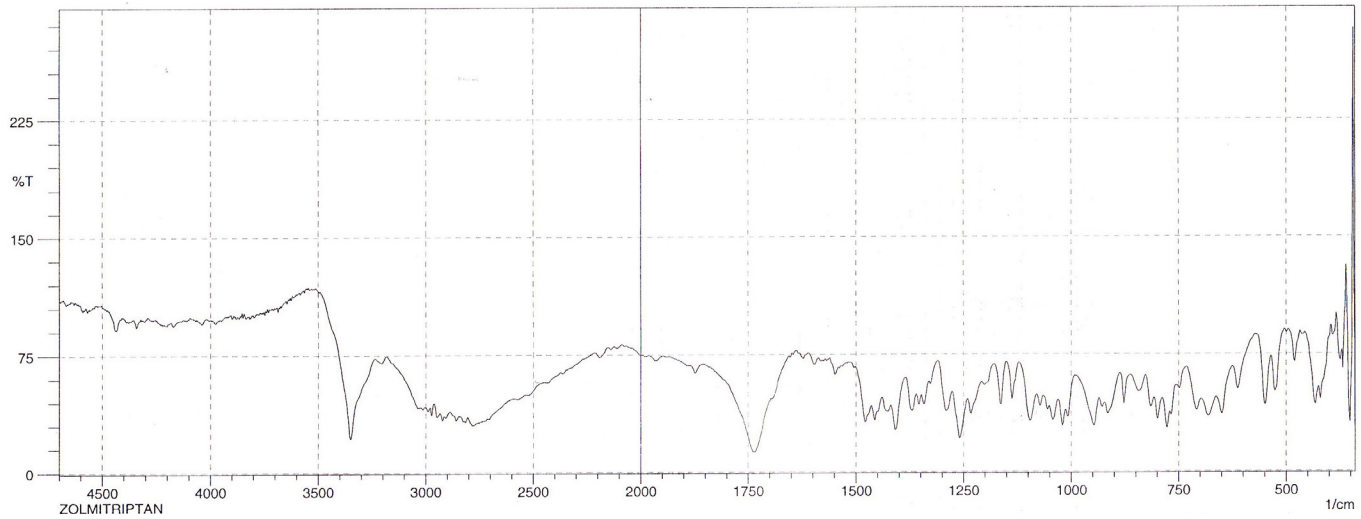

Figure 4: FTIR Spectra of Avicel PH 102

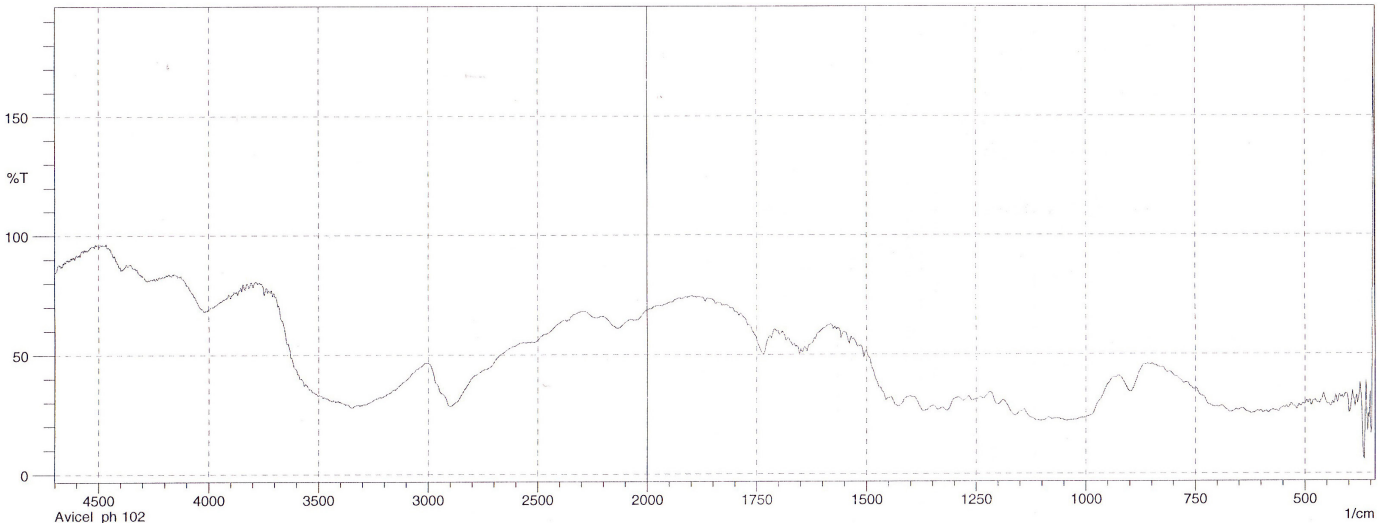

Figure 5: FTIR Spectra of Supertab 11SD

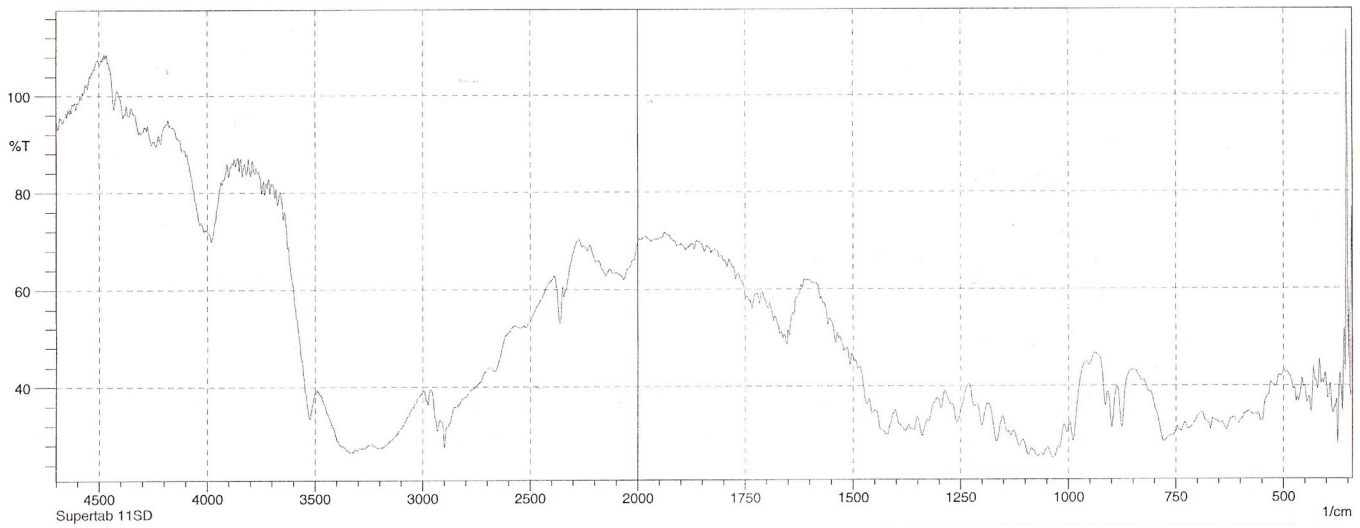

Figure 6: FTIR Spectra of Ssg

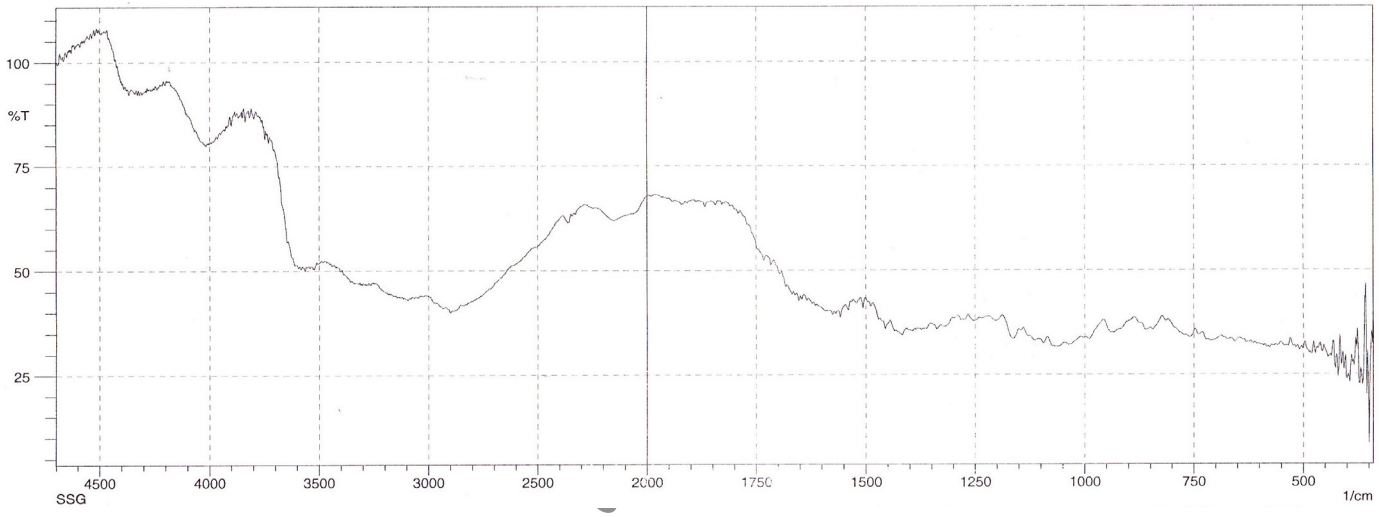

Figure 7: FTIR Spectra of Mg Stearate

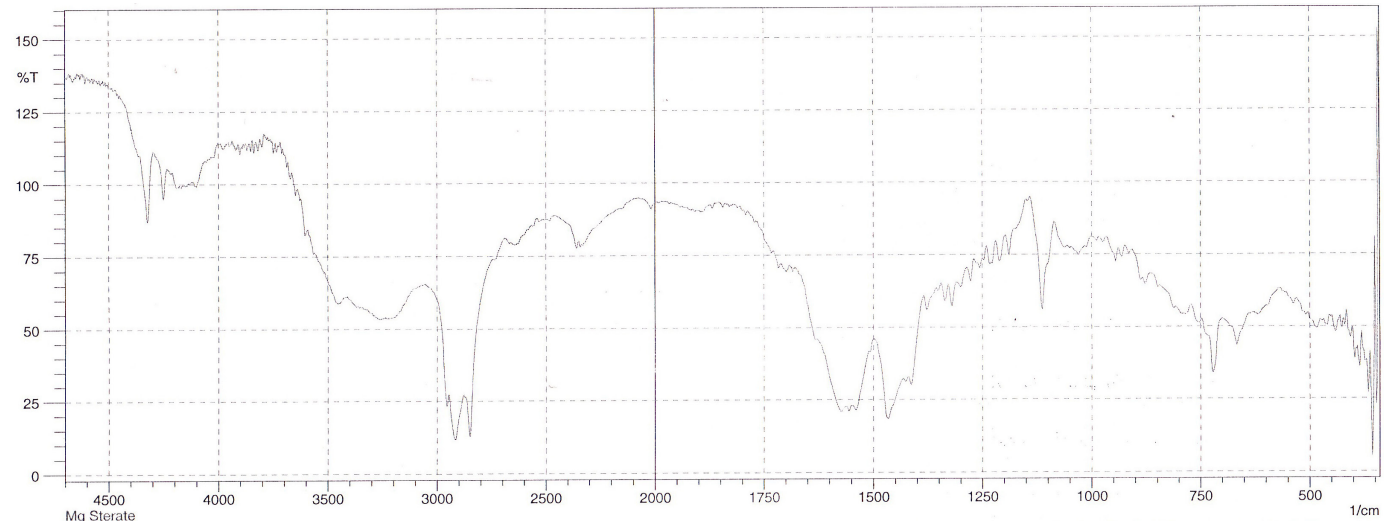

Figure 8: FTIR Spectra of Final Mixture

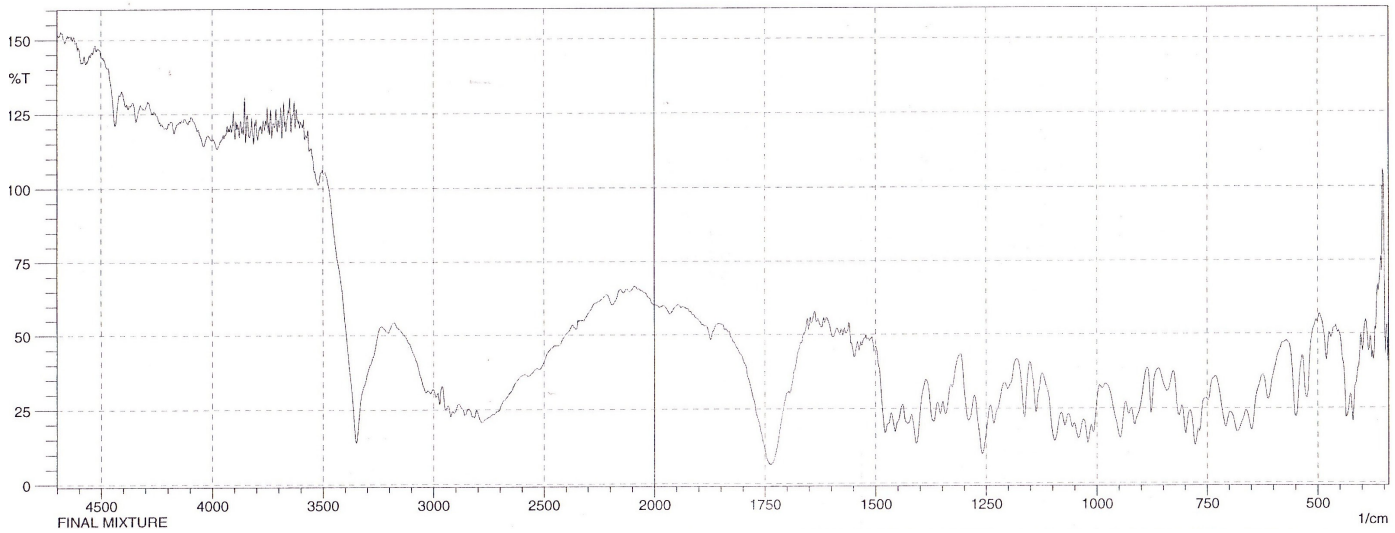

Figure 9: Purity Index of Zolmitriptan And Final Mixture

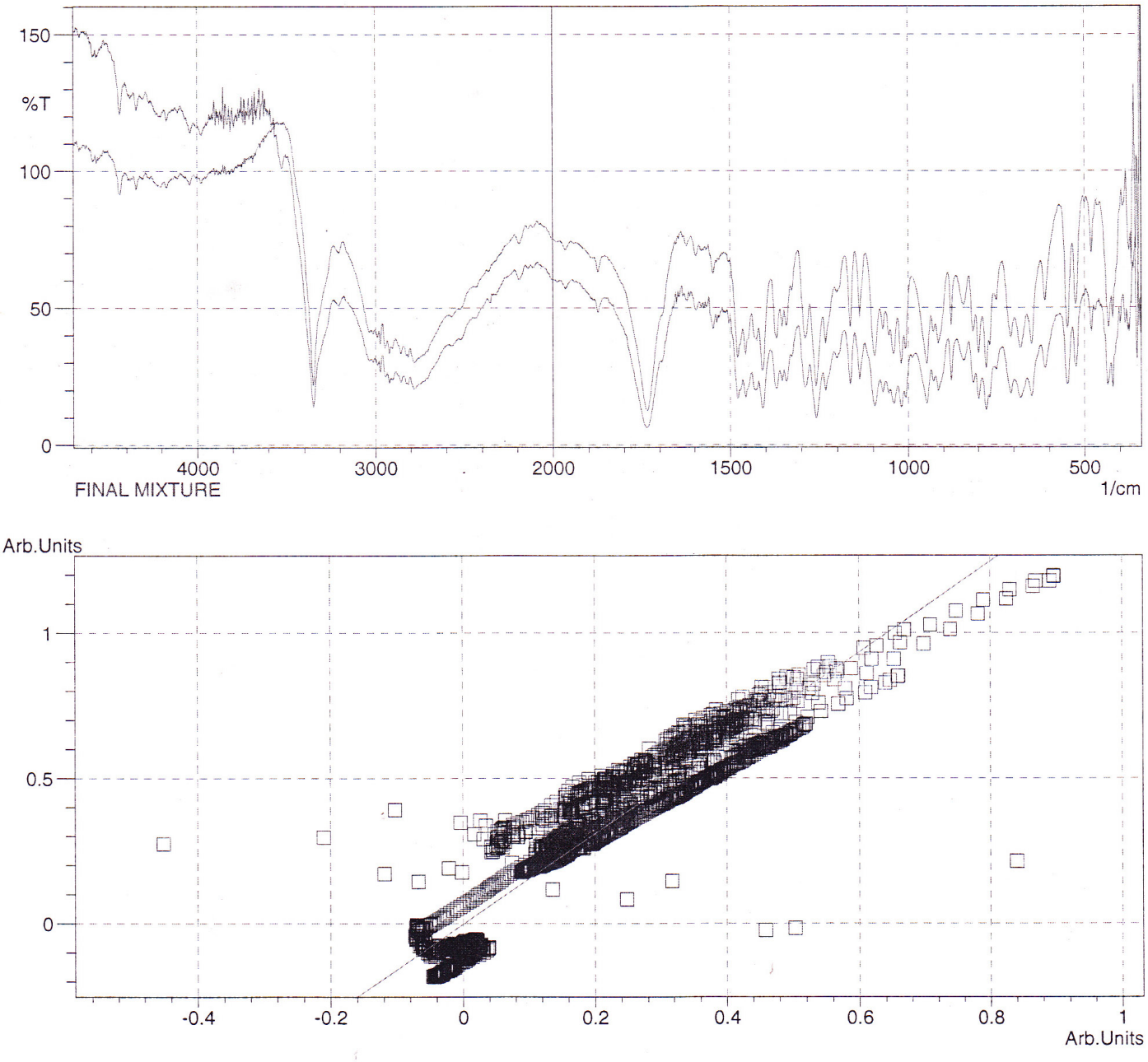

Figure 10: Comparison of reference product (ZOMIG-ZMT) with F1, F2 and F3

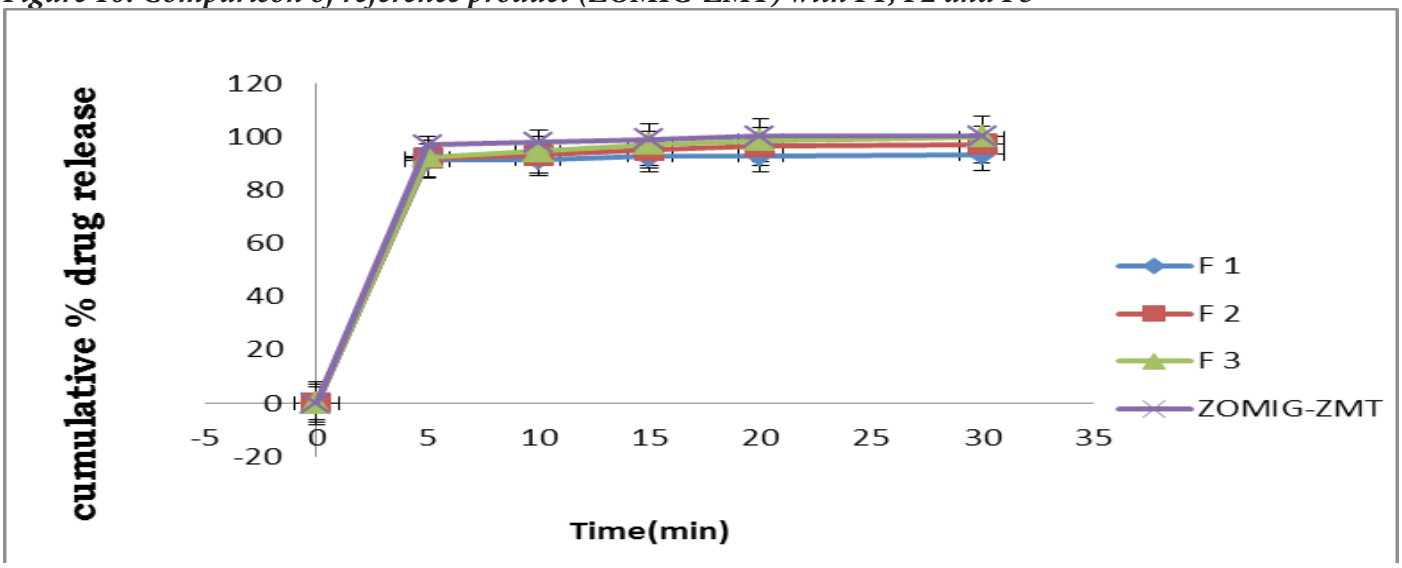

Figure 11: Comparison of reference product (ZOMIG-ZMT) with F4, F5 and F6

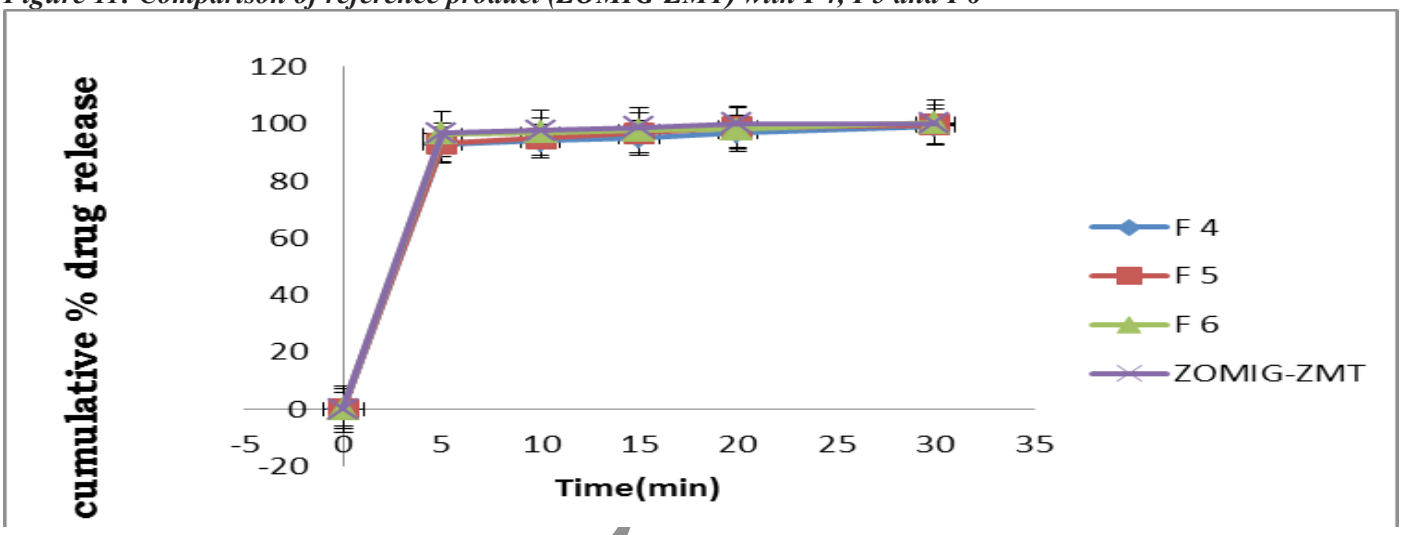

Figure 12: Comparison of reference product (ZOMIG-ZMT) with F7, F8 and F9