Review on Formulation And Evalution of Medicated Chewable Tablet of Triamterene

Dehade Pooja B[1], Satpute V M[2], Ghodke S R[3],Gaikwad Ashlesha[4]
[1, 2, 3, 4] Dept of Pharmaceutics
[1, 2, 3, 4] Loknete Shri Dadapatil Pharate College of Pharmacy
Mandavgn Pharata Tal-Shirur Dist -Pune, Maharashtra, India

Abstract- *Chewable tablets are required to broken & chewed in between teeth before ingestion.*

These are usually uncoated. These are intended to be chewed in the mouth before swallowing and not intended to be swallowed directly . Chewable tablets are designed for use by the children and those persons who may have difficulty in swallowing the tablets.

The objective is to develop efficient formulation of Triamterene chewable tablet. Triamterene is potassium-sparing diuretic used for the treatment of hypertension. Triamterene medicated chewable tablets are prepared by Wet Granulation method using two super-disintegrants i.e Crospovidone and Sodium Starch Glycolate. Total 6 formulations are prepared and the blend is evaluated for pre-compression parameters i.e angle of repose , bulk & tapped density, compressibility index & Hausner's ratio. These formulated tablets are evaluated for Thickness, Diameter ,Hardness, Weight Variation, Disintegration, Friability and Drug Content. The result showed that all the physical parameters are within acceptable limits. From 6 formulations, formulation F4 is selected as promising formulation on the basis of In-Vitro drug release & In-Vitro dispersion time which is found to be 24.54±1.202 sec and 95.26±2.57 % respectively.

The stability studies for the formulation F4 showed no significant change in disintegration time, drug content and percentage drug release after stored at 40±2 oC/75±5%RH for a period of 90 days. Hence the study concludes that formulation F4 showed better characteristics of chewable tablet.

Keywords- Triamiterene, Chewable tablets, Crospovidone and Sodium starch glycolate

I. INTRODUCTION

Oral Dosage Form: The oral route of drug administration is the most important method of administering drug for systemic effects. Except in certain case the parental route is not routinely used for self-administration, e.g. insulin. The topical route of administration has only recently been employed to deliver drugs to the body for systemic effect. The parental route of administration is important in treating medical emergencies in which the subject is comatose or cannot swallow. Nevertheless, it is probable that at least 90% of all drugs used to provide systemic effect are administered by oral route. When a new drug is discovered one of the first question a pharmaceutical company asks is whether or not the drug can be effectively administered for its intended effect by oral route. Drugs that are administered orally, solid oral dosage forms represent the preferred class of product. Tablet and capsules represent unit dosage forms in which usual dose of drug has been accurately placed. Tablets and capsules represent unit dosage forms in which one usual dose of drug has been accurately placed. By comparison liquid forms such as syrups, suspensions, emulsions, solutions and elixirs are usually designated to contain one medication in 5 -30ml, such dosage measurements are typically error by a factor ranging from 20 -50%, when the drug is self-administered by patient.

TABLETS: Tablets are defined as solid dosage forms each containing a single dose of one or more active ingredients, obtained by compressing uniform volumes of particles. They are intended for the oral administration, some are swallowed whole, some after being chewed. Some are dissolved or dispersed in aqueous phase before being administered and some are retained in the mouth, when the active ingredients are "liberated". Tablets are used mainly for systemic drug delivery but also for local drug action. For systemic use drug must be released from tablet that is dissolved in the fluids of mouth, stomach and intestine and then absorbed into systemic circulation by which it reaches its site of action. The tablet is composed of the Active Pharmaceutical Ingredient (active drug) together with various excipients. These are biologically inert ingredients which either enhance the therapeutic effect or are necessary to construct the tablet. The filler or diluents (e.g. Lactose or Sorbitol) are a bulking agent, providing a quantity of material which can accurately be formed into a tablet. Binders (e.g. methyl cellulose or gelatin) hold the ingredients together so that they can form a tablet. Lubricants (e.g. magnesium stearate or polyethylene glycol) are added to

reduce the friction between the tablet and the punches and dies so that the tablet compression and ejection processes are smooth. Disintegrants (e.g. starch or cellulose) are used to promote wetting and swelling of the tablet so that it breaks up in the gastrointestinal tract; this is necessary to ensure dissolution of the API. Superdisintegrants are sometimes used to greatly speed up the disintegration of the tablet. Additional ingredients may also be added such as coloring agents, flavoring agents and coating agents. Formulations are designed using small quantities in a laboratory machine called a Powder Compaction Simulator. This can prove the manufacturing process and provide information.

CHEWABLE TABLETS

Chewable tablets which are required to be broken and chewed in between the teeth before ingestion. These tablets are given to the children who have difficulty in swallowing and to the adults who dislike swallowing. These tablets are intended to disintegrate smoothly in mouth at a moderate rate either with or without actual chewing, characteristically chewable tablets have a smooth texture upon disintegration, are pleasant tasting and leave no bitter or unpleasant taste. Successful tablet formulation development involves the careful selection of ingredients in order to manufacture a robust solid dosage form. Choosing the appropriate excipient to perform a specific function in a tablet formulation such as disintegration or lubrication can be critical to achieving acceptable manufacturing performance. Sweeteners, both naturally occurring and synthetic are one type of functional excipient commonly used in chewable tablet formulations to mask the unpleasant tastes and facilitate pediatric dosing. Ideally upon chewing, they are broken down in the mouth and release their ingredients in the process and therefore, do not have much lag time as required for the disintegration of tablets before absorption from stomach. Chewable tablet are often employed when the active ingredient is intended to act in a localized manner rather than systemically. Chewable tablet is one that is palatable and may be chewed and ingested with little or no water.

Advantages of Chewable Tablets:

1) Better bioavailability through bypassing disintegration (that increase dissolution)
2) Improved patient acceptance (especially pediatric) through pleasant taste.
3) Patient convenience; need no water for swallowing
4) Possible to use as a substitute for liquid dosage forms where rapid onset of action is needed
5) Absorption of drug is faster
6) Product distinctiveness through marketing prospective
7) The large size of the dosage form is difficult to swallow. In such cases chewable tablet offers advantages over it .
8) Effectiveness of therapeutic agent is improved by the reduction in size that occurs during mastication of tablet before swallowing.

Disadvantages of Chewable Tablets:

1) It contains sorbitol which causes diarrhoea and flatulence.
2) Flavouring agents present in chewable tablet may causes ulcer in oral cavity.
3) Prolonged chewing of chewable tablet results in pain in facial muscles.
4) They are hygroscopic in nature, so must kept in dry place.
5) They show the fragile, effervescence granules property.
6) Since these tablets have insufficient mechanical strength, so careful handling is required.
7) They require proper packaging for safety and stabilization of stable drugs.

EXCIPIENTS USED IN THE FORMULATION OF CHEWABLE TABLETS:

Excipients	Functions	Examples
Diluents	Diluents are fillers used to make required bulk of tablet	Lactose, Microcrystalline cellulose, Mannitol etc.
Binders	Binders are used to impart cohesive qualities to powdered materials.	Gelatin, Glucose, Acacia, ethyl cellulose, hydroxypropyl methyl cellulose etc.
Superdisintegrants	They facilitate tablet breaking when it comes in contact with water in oral cavity/GIT	Croscarmellose sodium, Crospovidone, Sodium starch glycolate, Starch etc.
Lubricants	These are added to prevent adhesion of tablet material to surface of dies and punches reduces inter particulate friction.	Magnesium sterate, Talc, Paraffin, sodium lauryl sodium, etc.
Glidants	These are added to improve flow characteristics of powder mixture. Glidant minimize the friction between particles.	Colloidal Silicon dioxide (Aerosil), Corn starch, Talc etc.
Sweeteners	These are added to produce a palatable dosage form.	Sucrose, Saccharin, Aspartame, etc.
Flavours	These are added to improve taste of dosage form	Peppermint, Vanilla, Orange, Cinnamon, Mango, Cherry etc.
Colours	These are added for better appearance of dosage form	Sunset yellow (Supra),Ferric oxide.

EVALUATION PARAMETERS FOR CHEWABLE TABLET:

The variety of evaluation parameters must be kept in mind during the formulation of chewable tablets. These are given as follows:

A. **In-process Organoleptic evaluation:** This evaluation takes place at various stages in thedevelopment of a chewable tablet. These are as follows:

1. **Evaluation of drug itself:** It involves characterization and comparison of the substance in an absolute amount or against a known reference standard.
2. **Evaluation of coated drug:** It involves comparison against the pure drug as well as different coating treatment.
3. **Evaluation of unflavoured baseline formulation:** It involves comparison among different vehicles, proportion of vehicles or other formulation variables in presence of coated drug.
4. **Evaluation of flavoured baseline formulation:** It involves comparison among different flavoured formulations.
5. **Evaluation of final selection and product acceptance test:** It involves comparison between two formulations orcompetitive product.

B. **Chemical Evaluation:** It involves the following:

1. Assay of drug content
2. Dosage uniformity
3. *In vitro* and *In vivo* Evaluation

C. **Physical Evaluation:** It involves the following:

1. Tablet physical appearance
2. Hardness
3. Friability
4. Disintegration
5. Dissolution ETC

Materials Used

Sr. No.	**Materials**	**Source**
1.	Triamterene	Cadila Healthcare Ltd. Matoda, Ahmedabad
2.	Sodium starch glycolate	Sd Fine Chemicals, Mumbai.
3.	Crospovidone	Sd Fine Chemicals, Mumbai.
4.	Mannitol	Sd Fine Chemicals, Mumbai.
5.	Aspartame	Sd Fine Chemicals, Mumbai.
6.	PVP-K30	Sd Fine Chemicals, Mumbai.
7.	Microcrystalline cellulose(PH 102)	Sd Fine Chemicals, Mumbai.
8.	Mg. stearate	Sd Fine Chemicals, Mumbai.
9.	Talc	Sd Fine Chemicals, Mumbai.
10.	Orange flavor	Sd Fine Chemicals, Mumbai.
11.	Potassium dihydrogen orthophosphate	Sd Fine Chem Limited, Mumbai.
12.	Methanol	Sd Fine Chemicals, Mumbai.

Equipment's Used

Sr. No.	Model	Source
1.	UV-Spectrophotometer (UV-1800)	Shimadzu, Japan.
2.	Electronic weighing balance	Shimadzu, Japan.
3.	Disintegration test apparatus ED-2L	Electrolab, Mumbai.
4.	Dissolution test apparatus TDT-08L	Electrolab, Mumbai.
5.	Digital pH meter	Micropro labmate.
6.	Test sieve (No.60)	Sethi.
7.	Hot air oven	Sisca thana, east Maharashtra.
8.	Stability chamber	Lab Control Equipment Co. Mumbai.
9.	Friabilator USP EF-2	Electrolab, Mumbai.
10.	10 station rotary tablet punching machine	Clit, Ahmedabad.
11.	Digital hardness tester	Electrolab, Mumbai.

II. CONCLUSION

In the present work, Chewable tablets of Triamterene were prepared by direct compression methods using super-disintegrants such as crospovidone, and sodium starch glycolate.

All the tablets of Triamterene were subjected to weight variation, drug contentuniformity, hardness, and friability, *in vitro* dispersion time and dissolution studies.

Based on the above studies, following conclusions can be drawn:

1) Tablets prepared by direct compression method were found to be good without any chipping, capping and sticking.
2) The hardness of the prepared tablets to be in the range of 3.66±0.12 to 3.93 ±0.02 Kg/cm² for direct compression method.
3) The friability values of the prepared batches of tablets to be less than 1%.
4) The thickness of the prepared chewable tablets to be in the range of 3.19 to 3.23 mm. The average drug content of the tablets was found to be within the range of 97.48±1.29 to 100.90±1.2 %

REFERENCES

[1] Udaykumar M, Nageswarao ABN, Kumar VTVS, Giri VV. Fast Dissolving Tablets: New Fangled Drug Delivery System, A Comprehensive Review. International Journal of Research in Drug Delivery. 2012; 2(3):15-18.
[2] Patel Y, Shukla A, Saini V, Shrimal N, Sharma P. Chewing Gum as a drug delivery system. International Journal of Pharmaceutical Sciences and Research. 2011; 2:748- 57.
[3] Smith DV, Margolskee RF. Making sense of taste. Scientific America 2001; 284(3):36.
[4] Nanda AR, Garg KS. An update on taste masking technologies for Oral pharmaceuticals. Indian journal Pharma. sci. 2002; 64(1).
[5] Roche. Roto-granulations and taste masking coatings for preparation of chewable pharmaceutical tablets. US Patent 5 260 072 9 November, 1993.
[6] Khar RK, Sohi H. Taste masking technologies in oral pharmaceuticals: Recent development and approaches. Drug. Dev. Ind. Pharma 2004: 30:429,448.
[7] Patel H, Shah V, Upadhyay U. New pharmaceutical excipients in solid dosage forms. International Journal of pharmacy and life sciences. 2011, 2(8).
[8] Orally Disintegrating Tablet and film technologies. Second edition, 2004, 177.
[9] Solanki HK, Bosuri T, Thakkar JH, Patel CA. Recent Advances in granulation technology. International Journal of Pharmaceutical Sciences Review and Research. 2010; 5(3):48-49.
[10] Ray C, Arora V, Sharma V. Fast dissolving tablets-A Novel drug delivery system for pediatric and geriatric patient. International bulletin of drug research, 1(2), 55-70.
[11] Hiroyuki Suzuki , Hiraku Onishi , Seiji Hisamatsu, Kosuke Masuda,Yuri Takahashi, Masanori Iwata,

Yoshiharu Machida. Acetaminophen-containing chewable tablets with suppressed bitterness and improved oral feeling. International Journal of Pharmaceutics 2004;278: 51–61.

[12] Matthew P Mullarney, Bruno C Hancock, Glenn T Carlson, Dauda D Ladipo, Beth A Langdon. The powder flow and compact mechanical properties of sucrose and three high-intensity sweeteners used in chewable tablets. International Journal of Pharmaceutics 2003;257: 227–236.

[13] Patsalos PN, Russell-Jones D, Finnerty G, Sander JWAS, Shorvon SD. The efficacy and tolerability of chewable Carbamazepine compared to conventional Carbamazepine in patients with epilepsy. Epilepsy Research 1990;5: 235-239.

[14] Gary M Landsberg, Patrick Melese, Barbara L Sherman Jacqueline C Neilson, Alan Zimmerman, Terrence P Clarke. Effectiveness of Fluoxetine chewable tablets in the treatment of canine separation anxiety. Journal of Veterinary Behavior 2008;3: 12- 19.

[15] Thomas J Nolan, John M Hawdon, Susan L Longhofer, Carolyn P Daurio, Gerhard A Schad. Efficacy of an Ivermectin/Pyrantel Pamoate chewable formulation against the canine hookworms, Uncinaria stenocephala and Ancylostoma caninum. VeterinaryParasitology 1992;41: 121-125.

[16] Hiroyuki Suzuki, Hiraku Onishi, Yuri Takahashi, Masanori Iwata, Yoshiharu Machida, "Development of Oral Acetaminophen Chewable Tablets with inhibited bitter taste" International Journal of Pharmaceutics 251 (2003) 123-132.

[17] Wayne J Puglia, Kanit J. Patanasinth, Andrew T. Lombardo, Walter Vink, "Compressed Chewable Antacid Tablets and Method for Forming Same" US Patent (Apr 27, 1982), 4327,077.

[18] Sumit Madan, Vikas Batra, Vinod Kumar Aror, "Sodium Feredetate Chewable Tablets" ipcom 000146876D,Priorartdatabase, ip.com

[19] Surender, Vinay, Navneet: Developed and evaluated Montelukast sodium colon targeted matrix tablets for nocturnal asthma: IJPSRR Vol. 8(1)2011 Pg. No. 129-137.

[20] Ajay, Satish: Developed and evaluated fast dissolving film of Montelukast sodium: World journal of medical pharmaceutical and biological sciences,Vol.1(1) 2011 Pg No.2249-2887.

[21] N G Rao, Mohd Abdul Hadi: Development and evaluation of tablets-filled-capsule system for chronotherapeutic delivery of Montelukast sodium IJPT, Vol.3(1) 2011, Pg. No. 1702-1721.

[22] Ahmed B.Eldin: Developed and evaluated a simple, sensitive and accurate stability indicating analytical method for Montelukast. Validation was done for linearity, accuracy and precision and showed that method is useful for routine quality control analysis and stability testing.:Acta Pharmaceutical Sciencia 53, 2011, Pg .No. 45-56.

[23] Ajmal Ali Khan, Eddie Brunson: "Chewable Tablet and Method of Formulating" U.S Patent (Jun19, 2008) 0145423 A1.

[24] Shaik, Harun., P.Sandhya., Shilpa: Formulation and development of chewable tablets of mebendazole:International journal of pharma world research, Vol.2(3), 2011, Pg. No. 1-14.

[25] Raghavendra Rao and Suryakar: Formulation and evaluation of montelukast sodium mucoadhesive buccal patches for chronic asthma attacks: International Journal of Pharma and Bio Sciences Vol.4 (2), 2010, Pg. No.1-14.

[26] Swati Jagdale, Mahesh Gattani: Formulation and evaluation of chewable tablet of levamisole: Int. J. Res. Pharm. Sci. Vol-1(3), 2010, Pg. No. 282-289,

[27] K Kathiresan, Vijin P, C Moorthi: Formulation and evaluation of loratadine chewable tablets : RJPBCS 1(4), 2010, Pg. No. 763-774.

[28] Swati Jagdale, Mahesh Gattani, Dhaval Bhanudas KUchekar, Aniruddha Chabukswar. Formulation and evaluation of chewable tablet of levimasole. Int J.Res Pharm Sci 2010;1(3):282-289.

[29] Sukhbir lal khokra, Bharat parashar. Formulation decelopment and evaluation of albendazole by different techniques. Int J Pharm Pharm Sci 2011;1(3):461-464.

[30] Sumit Madan, Vikas Batra, Vinod Kumar Aror. Sodium Feredetate Chewable Tablets. Ipcom [serial online] 1999 Aug 16[cited 1999 AUG 21]. Available from: URL:http://www.Priorartdatabaseip.com.

[31] Ian J. Bolt, David R. Merrifield, Paul L. Carter. Pharmaceutical Formulation. U.S. Patent 1993 Jul 6;5:197,225.

[32] Ronni L Robinson, James R. Domon, James R. Mossop, Michael D. Palmer. Soft Chewable Tablets Having Convexed shaped Face Surfaces. U.S. Patent2002 Oct 29 6; B2:471,991.

[33] Ajmal Ali Khan, Eddie Brunson. Chewable Tablet and Method of Formulation. U.S Patent. 2008 Jun 19:A1:0145423.

[34] https://en.wikipedia.org/wiki/Triamterene#References.

[35] https://www.drugbank.ca/drugs/DB00384.

[36] FDAApproval History NDA 016042: Dyazide.Page accessed Sept 8 2016.

[37] Raymond CR, Paul JS, Sian CO. Handbook of pharmaceutical excipients. 5th ed.London, Chicago: Pharmaceutical Press, American Pharmacists Association; 2006: p. 211-214.

[38] Raymond CR, Paul JS, Sian CO. Handbook of Pharmaceutical exicipients. 5thed. London, Chicago: Pharmaceutical Press, American Pharmacists Association; 2006: p. 701-4.
[39] Rowe RC, Paul JS, Owens S. Handbook of Pharmaceutical Excipients, 5th edition, London Pharmaceutical Press 2006: p.449-53.
[40] https://en.wikipedia.org/wiki/Aspartame.
[41] Rowe RC, Paul JS, Owens S. Handbook of Pharmaceutical Excipients, 5th edition, London Pharmaceutical Press 2006: p.53-5.
[42] https://en.wikipedia.org/wiki/Talc.
[43] https://pubchem.ncbi.nlm.nih.gov/compound/magnesium_stearate
[44] https://en.wikipedia.org/wiki/Microcrystalline_cellulose.
[45] Cooper J, Gun C. Powder Flow and Compaction. Inc Carter SJ, Eds. Tutorial Pharmacy. 6th ed. New Delhi: CBS Publication; 1986. p. 211-33.
[46] Martin A, Micromeretics. In: Martin A, ed. PhysicalPharmacy. Baltimores, MD: Lippincott Williams and Wilkins; 2001. p. 423-54.
[47] Government of India Ministry of Health & Family Welfare. Indian Pharmacopoeia. Delhi: Controller of Publications; 2007. p. 1689-90.
[48] Kakade SM, Mannur VS, Ramani KB, Dhada AA, Naval CV, Bhagavat A. Formulation and evaluation of mouth dissolving tablets of losartan potassium by direct compression techniques. Int J Res Pharm Sci 2010;1(3):290-5.
[49] Subhramanyam CVS and Thimasetty J. Laboratory Manual of physical pharmaceutics. 5th edition; 2005. p. 321-325.
[50] Subhramanyam CVS, Thimasetty J, Shivanand KM and Vijayendraswamy SM.Laboratory manual of industrial pharmacy. 6th edition; 2006. p. 95-98.
[51] Lachman L, Lieberman HA and Kanig JL. The theory and practice of industrial pharmacy. 3rd edition; 1991. p. 293.
[52] Nandgude TD, Chatap VK, Bhise KS and Sharma DK. Indian Drugs 2007; 44: 271-272.
[53] Indian Pharmacopoeia, the controller of publication, Ministry of Health and Welfare. 1st edition; 1996. P. 1178.
[54] Sukhbir LK, Bharat P, Hitesh KD, Rahul P, Abhishek C. Formulation development and evaluation of chewable tablet of albendazole by different techniques. InPharma Pharm Sci 2012; 4(1): 46
[55] Patil J, Vishwajith V, Gopal V. Formulation Development and Evaluation ofChewable Tablets Containing Non-Sedating Antihistamine. Journal of Pharmaceutical and Scientific Innovation. 2012; 3:112
[56] Lachmann L, Liberman HA, Schwartz JB. Pharmaceutical Dosage Forms. New York:Marcel Dekker Inc, 1989, 2(1).
[57] Shaik Harun Rasheed, Sandhya Vani P, Silpa Rani Gajavalli, Shahul Hussain SK, Venugopal B, Ravikiran T et al. Formulation and evaluation of chewable tablets of Mebendazole. *International journal of Pharma world research.* [Online] 2011;2(3): Available from http://www. www.ijpwr.com [Accessed on 25th December 2011].
[58] Fiza F, Sudhir B. Formulation and Evaluation of Chewable Tablets of Mebendazole by Different Techniques. PharmaTutor; 2014; 2(6); 183-189.