REVIEW OF ORAL DISPERSIBLE TABLETS

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1. Mehul Dekivadia, Avinash Gudigennavar, Chandrashekar Patil, Bhaskar Umarji Development & optimization OF Levocetirizine (as Levocetrizine hydrochloride) is a third-generation non-sedative antihistamine, developed from the second-generation antihistamine Cetirizine. Levocetirizine Hcl works by blocking histamine receptors. It does not prevent the actual release of histamine from mast cells, but prevents it binding to its receptors. Fast dissolving tablets of Levocitirizine HCl were prepared using sodium starch glycolate, Croscarmellose sodium and Crosspovidone as superdisintegrants by direct compression method. The tablets prepared were evaluated for various parameters like weight variations, hardness, friability, in vitro dispersion time, drug content, wetting time, in vitro drug release, FTIR and XRD. The tablets prepared by direct compression method possess a weight variation below ±7.5%, hardness of 3 to 4.0 Kg/cm², percentage friability of 0.51 to 0.85, in vitro dispersion time of 17 to 58 seconds, Wetting time of 13 to 48 seconds, and in vitro drug release showed 94% to 99.00% within 20 min. The formulation (MD6) contains Crosspovidone and Sodium Starch Glycolate shows better Disintegration time and 99% drug release within 20 min.

2. Priyanka Nagar, Kusum Singh, Iti Chauhan, Madhu Verma, Mohd Yasir, Azad Khan, Rajat Sharma and Nandini Gupta was formulated Orally disintegrating tablets Oral delivery is currently the gold standard in the pharmaceutical industry where it is regarded as the safest, most convenient and most economical method of drug delivery having the highest patient compliance. Formulation of a convenient dosage form for oral administration, by considering swallowing difficulty especially in case of geriatric and pediatric patient leads to poor patient compliance. To troubleshoot such problems a new dosage form known as orally disintegrating tablet (ODT), has been developed which rapidly disintegrate & dissolve in saliva and then easily swallowed without need of water
which is a major benefit over conventional dosage form. In addition, patients suffering from dysphasia, motion sickness, repeated emesis and mental disorders prefer such preparation because they cannot swallow large quantity of water. Further, drugs exhibiting satisfactory absorption from the oral mucosa or intended for immediate pharmacological action can be advantageously formulated in such type of dosage form. The popularity and usefulness of the formulation resulted in development of several ODT technologies for preparation. The current article is focused on ideal characteristics, advantages and disadvantages, formulation aspects, formulation technologies, evaluation of products and future potential. Various marketed preparations along with numerous scientific advancements made so far in this avenue have also been discussed.

3. **Laskhmana Rao et al** A simple, accurate, rapid and precise isocratic reversed-phase high-performance liquid chromatographic method has been developed and validated for simultaneous determination of levocetirizine and montelukast sodium in tablets. The chromatographic separation was carried out on Atlantis C-18 analytical column (4.6×150 mm; 5μm) with a mixture of 10Mm acetonitrile:ammonium acetate (65:35 % v/v and pH 4.2 was adjusted with orthophosphoric acid) as a mobile phase; at a flow rate of 1.0 mL/min. UV detection was performed at 230 nm. The retention times were 3.03 and 6.28 min for levocetirizine and montelukast sodium respectively. Calibration plots were linear ($r^2=0.999$) over the concentration range of 25-75 μg/mL for levocetirizine and 50-150 μg/mL for montelukast sodium. The method was validated for accuracy, precision, specificity, linearity, and sensitivity. The proposed method was successfully used for quantitative analysis of tablets. No interference from any component of pharmaceutical dosage form was observed. Validation studies revealed that method is specific, rapid, reliable, and reproducible. The high recovery and low relative standard deviation confirm the suitability of the method for routine determination of levocetirizine and montelukast sodium in bulk and tablet dosage form.

4. **Moiz Md, Prathima Srinivas M, Sadanandam M** The objective of present work was to formulate and evaluate bilayered tablets of Levocetrzine and Montelukast for treating allergic rhinitis effectively. Anti-allergic medicines (eg, some antihistamines) can cause adverse events such as somnolence and sedation. The Combining Montelukast with Levocetirizine gives additional benefits in comparison with either drug alone and could be considered for patients whose quality of life is impaired by persistent allergic rhinitis.
Montelukast sodium is alkaline stable (bioavailability 64%), most of drug being absorbed from the intestine while Levocetirizine Dihydrochloride is acid stable. When tablets of the combination of these are prepared, they tend to become unstable during the shelf life of the formulation. Hence it is recommended to prepare a bilayer tablet, by formulating Montelukast in sustained release layer and Levocetirizine as immediate release layer as it improves and increases the stability by reducing the acid base interactions of both the drugs in combination there by increasing the bioavailability. Taking this into account different formulations were prepared by wet granulation method using natural Tamarind Seed Polysaccharide and synthetic HPMCK100,K15M and K4M release rate controlling hydrophilic polymers. The formulations were evaluated for hardness, weight variation, friability, swelling index and drug content uniformity. The in vitro release of drug from the formulations was studied in pH 1.2 acidic buffer and pH 7.4 phosphate buffer, and it was found that the prepared tablets were able to sustain the release of the drug upto 12hours. The release of Montelukast and Levocetirizine of both layers from the tablets was found to be diffusion controlled and the release mechanism was non-Fickian based on the n value of Korsmeyer-peppas plot. The FTIR studies were performed on three optimized formulations (F4, F12, F16) and the plain drug controls(Levocetirizine,Montelukast).From the observed peaks it is evident that the polymers used and the drugs were found to be mutually compatible chemically. The Pharmacokinetic Studies were performed in two groups of male wistar rats. One group was administered with the optimized formulation containing tamarind Seed Polysaccharide(F12) while Plain Montelukast oral suspension acted as control in the second group. The results indicate that the formulation optimised with 1:4(drug:TSP) was able to sustain the release of montelukast upto 12hours.Insrease in Tmax and AUC(0-á) also were also observed in the studies indicating efficient sustained action and improved bioavailability of the drug. The formulated bilayered tablets using natural polymers provided immediate release of Levocetirizine and sustained release of Montelukast and therefore hold promise as an alternative dosage form in the treatment of allergic rhinitis and bronchial asthma.

5. Dr. M.M. Gupta, Lokesh Singla, P.K. Soni, Oral dispersible tablet is solid unit dosage form. The objective of present investigation was to prepared oral dispersible tablet of Levocetirizine Dihydrochloride, Paracetamol and Montelukast Sodium because it’s active working patients who are busy or travelling, especially those who have no access t water.
Such problems can be resolved by means of the oral dispersible tablet form which does not require water to aid swallowing. Oral dispersible tablet are put into the mouth, tablet disintegrates instantaneously releasing the drug which dissolves or disperses in the saliva. The saliva containing the dissolved or dispersed medicament is then swallowed and the drug is absorbed in the normal way. Prepared tablets were evaluated for different properties like hardness, friability, disintegration time, Wetting time, time of dispersion and In-vitro dissolution study.

6. B. V.V. Sandeep Kumar., et al A reverse phase HPLC method is developed for the determination of Levocetirizine Hydrochloride and Montelukast Sodium in pharmaceutical dosage forms. Chromatography was carried out on a C8 column [4.6 x 150mm, 3.5μm, Make: XTerra] using a mixture of potassium di hydrogen ortho phosphate buffer and acetonitrile (60:40 v/v) as the mobile phase at a flow rate of 0.8 ml/min. Detection was carried out at 230 nm .The retention time of Levocetirizine Hydrochloride and Montelukast Sodium was 2.432 min and 6.218 min. The method produced linear responses in the concentration range of 30 to 70μg/ml of Levocetirizine Hydrochloride and Montelukast Sodium. The LOD values for HPLC method for Levocetirizine Hydrochloride and Montelukast Sodium were found to be 3.36 and 3.20 ng/ml. The LOQ for Levocetirizine Hydrochloride and Montelukast Sodium were found to be 9.90 and 9.86 ng/ml respectively. The method was found to be applicable for determination of the drug in tablets.

7. Kanungo et al Purpose of undertaken project was to formulate crosslink polyacrilic resin based, technologically optimised, melt-in-mouth tablet (MIMT) containing 5 mg of Levocetirizine Dihydrochloride that was intended to disintegrate rapidly in the oral cavity so as to form a stabilised dispersion and possessing adequate physicochemical stability. Different grades of crosslink polyacrilic resin were utilised to prepare MIMTs; employing complexation technique; and using additives like Mannitol DC, Ac-di-sol, Avicep-pH 112, Tusil pineapple, Saccharine sodium, Aerosil and Magnesium stearate. MIMTs were evaluated for compliance to pharmacopoeial specifications. From in-vitro dissolution profile plot, values for the kinetic constant and the regression coefficient of model-dependent approaches were determined to find the best fit release kinetic model while from in-vitro dissolution profile data the difference factor, the similarity factor and the indices of rescigno of model-independent approaches were determined for comparing pair
of in-vitro dissolution profiles. MIMTs of levocetirizine was successfully developed complying pharmacopoeial specifications, with adequate stability at room temperature.

8. **Sree Giri Prasad B. et al** The purpose of the present research was to optimize the formulation of Orodispersible tablets of Levocetizine. Orodispersible tablets of Levocetizine were prepared by Melt Granulation Technology. The formulations were evaluated for Tablet weight variation, content uniformity, hardness, friability, wetting time, dispersion time, drug content and in vitro release also have been studied. All formulations showed satisfactory mechanical strength and tablets containing Crospovidone (10%) showed excellent in vitro dispersion time and drug release as compared to other formulations. The results revealed that the tablets containing 10% Crospovidone (F8) showed short dispersion time (12 sec) with maximum drug release (100%) in 20 min. FTIR & DSC results showed no evidence of interaction between the drug and polymers. This study helps in revealing the effect of formulation processing variables on tablet properties. It can be concluded that the Orodispersible tablets of Levocetizine tablets could be prepared by Melt Granulation Technology using Crospovidone as superdisintegrant.

9. **Mudgal Vinod Kumar et al** Orally disintegrating tablets (ODTs) are gaining prominence as new drug delivery systems and emerged as one of the popular and widely accepted dosage forms, especially for the pediatric and geriatric patients. To obviate the problem of dysphagia and to improve patient compliance, ODTs have gained considerable attention as preferred alternatives to conventional tablet and capsule formulations. Various scientific techniques including freeze drying, moulding, spray drying, sublimation, direct compression, cotton candy process, mass extrusion, melt granulation etc. have been employed for the development of ODTs. These techniques render the disintegration of tablet rapidly and dissolve in mouth without chewing or additional water intake. The current article is focused on ideal characteristics, significant features, patented technologies, formulation aspects including the use of superdisintegrants. Various marketed preparations along with numerous scientific advancements made so far in this avenue have also been discussed.

10. **Malay Kumar B Chotaliya et al** The need for delivering drugs to patients efficiently with minimum side effects has prompted pharmaceutical industries to be engaged in development of new drug delivery systems. Pediatric and geriatric patients find it difficult
to swallow solid dosage forms like tablets. Mouth dissolving tablet that dissolve or disintegrate rapidly in oral cavity result in solution, is an ultimate remedy for this problem. In addition they give pleasing mouth feeling. ODT has advantages such as patient compliance, quick onset of action, improved bioavailability, etc. Therefore, mouth dissolving tablets are attractive alternative to liquid and conventional tablet dosage forms. In recent past, several manufacturing technologies such as sublimation technique, spray drying technique… etc. are employed to overcome the limitations of conventional tablet dosage forms. Once the mouth dissolving tablets are prepared they are required to be evaluated for various parameters so as to have long term stability and better therapeutic efficacy.

11. Abhay Asthana*, Swati Aggarwal, Gayti Asthana The review relates to advancements in development of orodispersible tablet formulation to present an impact on drug candidate’s characteristics for improvement in bioavailability. The purpose of the article is to review potential advancements of ODT technology in drug delivery applications. Various techniques employed to prepare ODTs include direct compression method, freeze drying, spray drying, tablet moulding, sublimation and mass extrusion. ODTs could be preferred choice especially with those drugs sensitive to GI and for patients under category of paediatrics, geriatrics, bedridden, postoperative and who may have difficulty in swallowing the conventional tablets and capsules. Orally disintegrating tablet (ODTs) are solid dosage form that involves the rapid disintegration and dissolution of dosage form presenting as solution or suspension state when placed in the mouth. ODTs render enhanced acceptability due to its patient compliance as well as improved bioavailability and stability. This article reviews recent trends undertaken to develop ODTs, new ODTs technologies, suitability of drug candidate and characterisation of ODTs.

12. Rewar S. et Al Now-a-days, orodispersible drug delivery systems are extensively used to improve bioavailability and patient compliance. Over the past three decades, orodispersible tablets (ODTs) have gained considerable attention as a preferred alternative to conventional tablets and capsules due to better patient compliance, improved solubility and stability profiles. The purpose of the article is to review potential advancements of ODT technology in drug delivery applications. Various techniques employed to prepare ODTs include direct compression method, freeze drying, spray drying, tablet moulding, sublimation and mass extrusion. ODTs could be preferred choice
especially with those drugs sensitive to GI and for patients under category of pediatrics, geriatrics, bedridden, postoperative and who may have difficulty in swallowing the conventional tablets and capsules. ODTs are solid dosage forms containing medicinal substances which disintegrate rapidly, usually in a matter of seconds, when placed on the tongue. ODTs render enhanced acceptability due to its patient compliance as well as improved bioavailability and stability. This article reviews recent trends undertaken to develop ODTs, new ODTs technologies, suitability of drug candidate and characterization of ODTs.

13. M Ciebiada, M Gorska Ciebiada, T Kmiecik, LM DuBuske, P Gorski1

Background: Persistent allergic rhinitis often impairs quality of life. Objective: We assessed the extent to which treating persistent allergic rhinitis with montelukast, desloratadine, and levocetirizine alone or in combination improved quality of life. Methods: A 32-week randomized, double-blind, placebo-controlled, crossover study was performed in 2 arms: 20 patients received montelukast 10 mg/d and/or desloratadine 5 mg/d or placebo; 20 patients received montelukast 10 mg/d and/or levocetirizine 5 mg/d or placebo. The treatment periods were separated by 2-week washout periods. Quality of life was assessed on the day before starting treatment and on the last day of each treatment period using the Rhinoconjunctivitis Quality of Life Questionnaire. Sleep problems were also assessed. Results: In the desloratadine plus montelukast arm, the mean (SEM) quality of life score before treatment was 3.1 (0.41). After placebo, this score was 2.16 (0.43), after desloratadine it was 1.79 (0.38), after montelukast it was 1.48 (0.37), and after montelukast plus desloratadine it was 1.59 (0.37). In the montelukast plus levocetirizine arm, the mean quality of life score before treatment was 2.58 (0.49). After placebo it was 1.78 (0.46), after levocetirizine it was 1.38 (0.42), after montelukast it was 1.36 (0.37), and after montelukast plus levocetirizine it was 1.26 (0.39).

14. Velmurugan S and Sundar Vinushitha

Oral drug delivery remains the most preferred route for administration of various therapeutic agents. Recent advances in technology prompted researchers and scientists to develop oral disintegrating tablets (ODTs) with improved patient convenience and compliance. ODTs are solid unit dosage form which dissolve or disintegrate rapidly in the mouth without water or chewing. Novel ODT technologies address many patient and pharmaceutical needs such as enhanced life cycle management to convenient dosing particularly for pediatric, geriatric and psychiatric
patients who have difficulty in swallowing (Dysphagia) conventional tablet and capsules. Technologies used for manufacturing of ODTs are either conventional technologies or patented technologies. This review depicts the various aspects of ODT formulation, superdisintegrants and technologies developed for ODT, along with various drugs explored, evaluation tests and marketed formulations in this field.

15. Lavakumar et al The oral route of administration still continue to be the most preferred route due to its manifold advantages including ease of ingestion, pain avoidance, versatility and most importantly patient compliance. Recent advances in novel drug delivery systems aim to enhance safety and efficacy of drug molecule by formulation and to achieve better patient compliance. One such approach is ‘mouth dissolving tablets’. Their growing importance was underlined recently when European Pharmacopoeia adopted the term “Orodispersible Tablets” as a tablet that to be placed in the mouth where it disperses rapidly before swallowing. It is one of the fastest growing segments in the pharmaceutical market. The model drug used in the present study is an antidepressant drug used for the handling of unipolar mental depression. The present study was aimed to investigate on the best superdisintegrants which is more reliable for the preparation of oral dispersible tablets of Fluoxetine hydrochloride and it was concluded that the combination of the superdisintegrants (CCS: CP) shows the drug release profile in less time and hence it was concluded that the combination of superdisintegrants was best when compared individually.

16. Patel PG, Vaghela VM1, Rathi SG, Rajgor NB, Bhaskar VH This study describes the development and validation for the simultaneous estimation of rupatadine and montelukast by the 1st-order derivative UV spectroscopy method. The quantification was achieved by the 1st-order derivative spectroscopy method at 273.46 nm and 297.27 nm over the concentration range of 5-25 µg/ml for estimation of rupatadine and montelukast in a combined tablet formulation. Procedure does not require prior separation of components from the sample. Rupatadine and montelukast were determined at 15 µg/ml with a mean recovery of 99.59 + 0.225 and 99.21 + 0.76, respectively. Calibration curves were linear with a correlation coefficient of 0.9994 and 0.9992 for rupatadine and montelukast, respectively. The relative standard deviation was found to be <2.0%. The present result shows that the proposed method can be successfully used for simultaneous determination of the drug content in marketed formulations.
17. Chandrasekhar P. et al  Oral dispersible tablets has number of advantages viz., faster onset of action, ease of administration, ease of manufacturing, ease of storage and transport. A novel attempt has been made to develop oral dispersible tablets of atenolol by including different ratios of crospovidone, croscarmellose sodium and sodium starch glycolate as super disintegrants. The tablets were prepared by direct compression method. The formulated tablets were evaluated for Pre-formulation and post formulation parameters and they were found to be satisfactory. The formulated oral dispersible tablets possess good drug releasing property, good mouth feel and improved drug bioavailability with better patient compliance.

18. M. Saeed Arayne, Najma Sultana and Fida Hussain A simple ultraviolet spectrophotometric method for the estimation of montelukast in methanol has been devised and been compared with the existing pharmacopoeial RP-HPLC method for estimation of the drug. The limit of detection of montelukast at 283 nm was 75.2 ng/mL. The calibration was linear in the range of 3–45 μg/mL. Analytical parameters such as stability, selectivity, accuracy and precision have been established for the method in MONAKA tablets and in human serum and evaluated statistically to assess the application of the method. The method was validated under the ICH and USP guidelines and found to comprise the advantages for simplicity, stability, sensitivity, reproducibility and accuracy for using as an alternate to the existing non-spectrophotometric methods for the routine analysis of the drug in pharmaceutical formulations and in pharmaceutical investigations involving montelukast.

19. Errolla Mahesh, G.B. Kiran Kumar, Mohammed G Ahmed, Kiran kumar. P In the present work fast dissolving tablets of Montelukast sodium were prepared using novel co-processed superdisintegrants consisting of crospovidone and sodium starch glycolate in the different ratios (1:1, 1:2 & 1:3) in vice versa. Montelukast sodium is a drug of choice in treatment of asthma and allergic rhinitis. Drug compatibility with excipients was checked by FTIR studies. After examining the flow properties of the powder blends the results were found to be within prescribed limits and indicated good flowing property and it was subjected to tablet compression. All the formulations were subjected to post compression parameters like hardness and friability (≤1%), indicated that tablets had a good mechanical strength and resistance. Drug content was found to be in the range of 93.51 to 98.79 %. The wetting time is an important criteria for understanding the capacity
of disintegrants to swell in presence of little amount of water were found to be in the range of 20 to 55 sec. Among all the designed formulations, formulation F9 was found to be promising and showed an \textit{in-vitro} disintegration time of 25 sec, which facilitates faster disintegration in the mouth. When compared to marketed product, the formulation F9 containing co-processed superdisintegrant (1:3 mixture of sodium starch glycolate and crospovidone) emerged as the overall best formulation based on drug release characteristics with 0.5% SLS in distilled water as dissolution medium. Short-term stability studies on promising formulation F9 indicated that there were no significant changes in hardness, drug content and \textit{in-vitro} drug release. From this study, it can be concluded that dissolution rate of Montelukast sodium FDTs could be enhanced by tablets containing co-processed superdisintegrant.

REFERENCES


