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REVIEW ARTICLE

Oral Disintegrating Tablets – A Current Review

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ABSTRACT

The patient compliance lies in the ease with which the drug is delivered into the body without affecting its efficacy and without causing any inconvenience to the patient. For the patients who have a problem in swallowing, mainly the children and the old, oral disintegrating tablets (ODT) is a good choice. The products are designed to disintegrate or dissolve rapidly on contact with saliva, thus eliminating the need to chew the tablet, swallow an intact tablet, or take the tablet with liquids. Design of an ODT requires enough porosity inside the ***tablet*** for fast dissolving or fast melting while maintaining the mechanical strength of the tablet. Processing techniques such as freeze-drying, molding and sublimation, spray drying, direct compression followed by vacuum drying can be used to formulate ODTs. Formulation techniques such as incorporation of high levels of disintegrant, extragranular microparticulate active in conjunction with an effervescent agent, highly compressible excipients, aminoacid as a disintegrant, amorphous ingredient, hydrophilic waxy binder, combination of ion exchange resin and cyclodextrin, combination of the superdisintegrants and sublimation technique, specialized excipients such as effervescent couple and highly micronized agents. Various studies carried out by several scientists in the world are presented in this review article.

Key words: Oral disintegrating tablets, porosity, freeze-drying, molding, spray drying, direct compression

INTRODUCTION

Drug delivery system plays a vital role in mitigating an unwanted response. The patient compliance lies in the ease with which the drug is delivered into the body without affecting its efficacy and without causing any inconvenience to the patient. The Dosage form plays an equally important role in producing an effective treatment. Oral administration is one of the most used ways for drug administration. The drug can be taken in the form of tablets, capsules with optimum amount of water. For the patients who have a problem in swallowing, mainly the children and the old, oral disintegrating tablets is a good choice. These can be taken without water and have a great bioavailability. These can be useful for the patients who are nearly unconscious, uncooperative, suffering from Parkinson's disorder and for the people who don't have access to water when required. The main advantage is that they are very easy to administer and the patient doesn't have a feeling of taking in a tablet rather excited for the method of delivery (disintegrating).

The United States Food and Drug Administration defined these Oral Disintegrating Tablets as "A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue. Oral Disintegrating tablets can also be called as Fast melt, quick dissolve, mouth dissolving, or disperse, freeze dried wafers, porous tablets or rapid melt etc. United States Pharmacopoeia (USP) approved these dosage forms as ODT's. In an effort to develop drug products that are more convenient to use and to address potential issues of patient compliance for certain product indications and patient populations, pharmaceutical manufacturers have developed products that can be ingested simply by placing them on the tongue. The products are designed to disintegrate or dissolve rapidly on contact with saliva, thus eliminating the need to chew the tablet, swallow an intact tablet, or take

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the tablet with liquids. This mode of administration was initially expected to be beneficial to pediatric and geriatric patients, to people with conditions related to impaired swallowing, and for treatment of patients when compliance may be difficult (e.g., for psychiatric disorders).

Design of an orally ***disintegrating*** tablet requires a significant amount of research work in order to develop a process that maintains enough porosity inside the compressed ***tablets*** for fast dissolving or fast melting while maintaining the mechanical strength of the tablet. Orally ***disintegrating*** dosage forms are known in the art and some of the most commonly used techniques are complicated processing techniques such as freeze-drying, molding and sublimation or use of specialized excipients such as effervescent couple, highly micronized agents or the likes.

U.S. Pat. No. 5,298,261 discloses freeze-drying a slurry or paste comprising an active ingredient and excipients placed in blister packets. PCT application WO 97/36879 discloses vacuum drying, at room temperature or a slightly elevated temperature, of a suspension including the active drug, a sugar alcohol, PEG 6000, talc, sweeteners and flavors, in preformed blisters. However, the freeze-drying process suffers from several disadvantages. The primary disadvantage is that solutions employed for freeze-drying are aqueous and, therefore, not suited for water sensitive medicaments. Freeze-drying is also limited to low dose actives. The process itself is typically laborious, costly and time-consuming. Finally, the resultant dosage forms, in addition to being hygroscopic, tend to be very soft, and therefore require special moisture-resistant and impact-resistant packaging and careful handling.

U.S. Pat. No. 5,464,632 claims the use of high levels of disintegrants, such as 16% starch 1500 and 13.3% crospovidone, for a disintegration time of 35 seconds to 45 seconds. However, such ***tablets*** have a chalky or dry feel when placed in the mouth.

U.S. Pat. No. 5,178,878 discloses a rapidly dissolving ***oral*** formulation that requires an extragranular microparticulate active in conjunction with an effervescent agent incorporated into a tableted matrix in order to achieve rapid ***oral*** disintegration. Many fast-dissolving ***tablets*** are also formulated by the inclusion of effervescent compounds. U.S. Pat. No. 5,178,878 and WO 91/04757 disclose the addition of an effervescent couple (such as sodium bicarbonate and citric acid) to a tablet. Exposure of such tablet to moisture results in contact and chemical reaction between the effervescent couple which leads to gas production and tablet disintegration. However, ***tablets*** which include effervescent pairs are highly sensitive to moisture and require a specific, very costly plant including special handling equipment, controlled-humidity environments, as well as special moisture resistant packaging. Such preparations have an unpleasant mouth feel.

Another orally ***disintegrating*** technique is spray drying technology as explained in U.S. Pat. Nos. 5,958,471 and 6,165,511, which includes preparing an aqueous solution of more than 80% of one or more non-hygroscopic polyols, and spraying the resulting mixture into an air stream. The resulting composition of the spray-drying process contains a filamentous structure. Similarly PCT application WO 03/051338A1 relates to a method for producing a directly compressible and highly compactible composition by co-spray drying of mannitol and sorbitol solution resulting in nonfilamentous microstructure. Both these patents describe use of highly concentrated aqueous solutions, which are to be maintained and sprayed at high temperature, thus demanding special equipment.

Another approach to develop orally ***disintegrating*** dosage form involves optimal selection of excipients which would result in desired disintegration time. These are typically compressed dosage forms. EP 1145711 describes the preparation of flash-melt dosage forms that disintegrate in the mouth in less than 25 second. They consist of granules composed of a superdisintegrant (4-8%), a dispersing agent such as calcium silicate (20-70%), a distributing agent selected from amorphous silica, fumed silica, diatomaceous earth, talc, kaolin, magnesium aluminum trisilicate, and a binder (10 to 50% by weight). Although a larger amount of binder may produce stronger ***tablets,*** the disintegration times tend to increase. To counter this, a large amount of dispersing and distributing agent is included in the formulation which increases the weight of the tablet. This may increase the cost of the formulation.

U.S Patent No 8,545,890 describes a directly compressible composite excipient prepared by coating calcium silicate with a carbohydrate leads to a formulation that rapidly disintegrates or dissolves on in the mouth. More specifically, it has been discovered that a composite excipient

formed by substantially completely coating the calcium silicate in a carbohydrate, the calcium silicate is prevented from reacting with the API or processing equipment, and further exhibits greatly improved flow properties. ***Tablets*** made with this improved composite excipient exhibit low friability, low ejection forces and hardness sufficient to be processed in high speed tableting machines and shipped in low cost packages, while retaining rapid disintegration or dissolution properties. The ***tablets*** have a pleasant mouth feel and good mechanical strength such that they do not require special handling or packaging conditions.

This review article is a collection of recent advancements in ODT's.

Mahmoud developed Fast disintegrating sublingual zolmitriptan tablet (FDST) using freeze-drying technique. The FDSTs were prepared using different concentrations of gelatin as binder and mannitol or L-alanine as matrix supporting/disintegration enhancing agents. This sublingual formulation gave faster and higher zolmitriptan plasma concentration in rabbits compared to the oral zolmetriptan market product. [1]

Jung prepared sildenafil lactate-loaded orally disintegrating tablet tablets with various amounts of menthol and colloidal silica using the direct compression technique followed by vacuum drying. It gave higher AUC and C (max), and shorter T (max) values than did the commercial tablet, indicating that it improved the oral bioavailability of sildenafil in rabbits compared with the commercial tablet. [2]

Dinunzio investigated the use of Ceolus (™) microcrystalline cellulose, a highly compressible excipients, for the production of rapidly disintegrating tablets containing a hydrophilic solid dispersion of a poorly soluble drug, indomethacin.[3]

Roblegg investigated the suitability of Ludiflash (®), a direct compression aid for orally disintegrating tablets. Micropellets consisting of Ludiflash (®) and small amounts of microcrystalline cellulose were prepared via the wet extrusion/spheronization technique. Paracetamol and ibuprofen were applied as model drugs. It was concluded that Ludiflash (®) can be applied as main excipients for the preparation of individually dosable pellets combining fast drug release and a high mechanical stability.[4]

Laitinen prepared an orally fast-disintegrating tablet (FDT) by direct compression, containing a poorly soluble drug (Perphenazine, PPZ) formulated as a stable solid dispersion. FDTs containing 60% of mannitol, 15% of calcium silicate, 15% of crospovidone, and 10% of 1/5 PPZ/PEG solid dispersion exhibited fast disintegration times (37 +/- 3), sufficient hardness (1.28 +/- 0.06 MPa), and fast onset of drug dissolution (34% of PPZ dissolved in 4 minutes), and these properties were found to be retained with storage. [5]

Jacob prepared Fast-dissolving effervescent tablets by the modification of nonreactive liquid-based wet granulation technique. Fast-dissolving effervescent tablets (FETs) of glibenclamide based on highly plastic granules that can be compressed at low pressure to form fast-melting pharmaceutical tablets. Citric acid was coated with plastic materials such as polyethylene glycol (PEG), which provide a physical barrier to the reaction. The inherent hygroscopic nature of PEG could decrease the affinity for moisture of effervescent mixtures and can provide a stabilizing effect. Sodium bicarbonate was blended with sugar alcohol like mannitol, which would give a protective coating. PEG 1000 melts at body temperature (approximately 37 degrees C) and thereby does not delay the reaction between the acid source and base. Formulation using citric acid-sodium bicarbonate and citric acid-sodium glycine carbonate tablet with PEG and mannitol was found to have better reaction properties and reaction stability than does the standard citric acid-sodium bicarbonate tablet. [6]

Maeda determined the optimum composition for sustained-release of tamsulosin hydrochloride from microparticles intended for orally disintegrating tablets. Microparticles were prepared from aqueous ethylcellulose dispersion (Aquacoa®), and an aqueous copolymer based on ethylacrylate and methyl methacrylate dispersion (Eudragit®) NE30D), with microcrystalline cellulose as core particles with a fluidized bed coating process. The in vivo absorption properties from microparticles were comparable to Harnal® pellets, and there was a linear relationship between in vitro drug release and in vivo drug release. This development produces microparticles in single-step coating that provided a sustained-release of tamsulosin hydrochloride comparable to Harnal® pellets. [7]

Rahman assessed the utility of non-destructive techniques in the evaluation of risperidone solid dispersions (SD) with methyl-β-cyclodextrin (MBCD) and subsequent incorporation of the SD into orally disintegrating tablets (ODT) for a faster release of risperidone. SD-3 (risperidone: MBCD, 1:3) was incorporated into ODT tablets containing diluents (D-mannitol, FlowLac (®) 100 or galenIQ™-721) and super disintegrants (Kollidon (®) CL-SF, Ac-Di-Sol or sodium starch glycolate). Disintegration time, T (50) and T (90) were decreased in the formulations containing mannitol and Kollidon (®) CL-SF, but increased with galenIQ™-721 and sodium starch glycolate, respectively. NIR-CI images confirmed the homogeneity of SD and ODT formulations. [8]

Mady evaluated the potential influence of carboxymethyl-beta-cyclodextrin (CM-beta-CyD) on the aqueous solubility, chemical stability and oral bioavailability of famotidine (FMT) as well as on its bitter taste. They examined the effect of the CM-beta-CyD on the acidic degradation of FMT compared with that for sulfobutyl-ether-beta-cyclodextrin (SBE-beta-CyD). The potential use of CM-beta-CyD for orally disintegrating tablets (ODTs) was evaluated in vitro and in vivo. CM-beta-CyD complexation appears to be an acceptable strategy for enhancing the oral bioavailability of FMT owing to its dramatic effect on the aqueous solubility and chemical stability of the drug. In addition, it has a pronounced effect on masking the bitter taste of FMT. [9]

Kayitare E developed taste-masked quinine tablets suitable for children and offering dosing flexibility to adjust the quinine dose in function of body weight. Fast-dispersible and taste-masked quinine pamoate tablets improved dosing accuracy, allowed easy administration and resulted in a high efficacy during the treatment of children with uncomplicated malaria.[10]

Seminega B recommended oral dosage of scored Lamivudine and Zidovudine Tablets USP for pediatric patients who weigh greater than or equal to 30 kg and for whom a solid oral dosage form is appropriate is 1 tablet administered twice daily. Before prescribing Lamivudine and Zidovudine Tablets USP, children should be assessed for the ability to swallow tablets. If a child is unable to reliably swallow a lamivudine and zidovudine tablet USP, the liquid oral formulations should be prescribed: EPIVIR® (lamivudine) Oral Solution and RETROVIR® (zidovudine) Syrup. Because Lamivudine and Zidovudine Tablets USP is a fixed-dose combination tablet, they should not be prescribed for pediatric patients weighing less than 30 kg or patients requiring dosage adjustment, such as those with reduced renal function (creatinine clearance less than 50 mL/min), patients with hepatic impairment, or patients experiencing dose-limiting adverse reactions. Liquid and solid oral formulations of the individual components of Lamivudine and Zidovudine Tablets USP are available for this population. [11]

Armando *et al* evaluated bioequivalence of two commercial 8 mg tablet formulations of ondansetron available in the Brazilian market. Vonau flash, as test formulations and Zofran as reference formulation were evaluated following a single 8 mg dose to 23 healthy volunteers of both genders. The 90% confidence interval for the ratio of C(max) (87.5-103.8%), AUC(0-t) (89.3-107.2%) and AUC(0-infinity) (89.7-106.0%) values for the test and reference products is within the 80-125% interval, proposed by FDA, EMEA and ANVISA. It was concluded that two ondansetron formulations are bioequivalent in their rate and extent of absorption. [12]

Yamamoto *et al* described an investigation of the factors affecting disintegration time in the mouth (DTM) of rapidly disintegrating tablets. The relation between DTM and stationary time of upper punch displacement (STP) was examined using a tableting process analyzer (Tab All). [13]

Bovet LL evaluated the potential of microspheres for taste masking when incorporated into orally disintegrating tablets. The microspheres were produced by spray drying a mixture of the model compound (famotidine) with taste masking material. Results from an evaluation by a panel of six human volunteers demonstrated that the orally disintegrating tablets with taste masking microspheres improved the taste significantly. [14]

Sugimoto M investigated a tablet with high porosity is required for rapid disintegration, but such a tablet is generally fragile. To make a tablet having both high porosity and practical strength, amorphous sucrose, which has good compatibility, was used. Mannitol powder with freeze-dried amorphous sucrose was tableted at low compression and stored under certain conditions. The tablet disintegrated rapidly in the mouth, because of its high porosity. The tensile strength of the tablet increased remarkably during storage, while the porosity of the tablet seemed almost

unchanged.[15]

Fukami prepared a rapidly disintegration tablet in the oral cavity using a glycine as a disintegrant. Evaluation of rapidly disintegrating tablets containing glycine and carboxymethylcellulose was carried out. Wetting time prepared from carboxymethylcellulose (NS-300) having the hardness of 4 kg was 3 s. Tablet containing NS-300 showed fastest disintegration compared to other formulations. It was suggested that the tablet formulation containing NS-300 and glycine was highly applicable to water-insoluble drug, such as ethenzamide. [16]

Sugimoto investigated the factors affecting the characteristics of rapidly disintegrating tablets containing an amorphous ingredient prepared by crystalline transition method (CTM) under various storage conditions. It was concluded that the formulating ratio of 10-20% of the amorphous sucrose in the tablet is suitable for the rapidly disintegrating tablet in the mouth when prepared by CTM. [17]

Abdelbary determined the in vitro disintegration profile of rapidly disintegrating tablets and correlation with oral disintegration. Evaluated the disintegration profile of RDT manufactured by main commercialised technologies, using the texture analyser (TA). In order to simulate as much as possible the oral disintegration of these dosage forms, a new operating structure was developed. This structure mimics the situation in the patient's mouth and provides a gradual elimination of the detached particles during the disintegration process. The obtained time-distance profiles or disintegration profiles enabled the calculation of certain quantitative values as the disintegration onset (t1) and the total disintegration time (t2). Results obtained when artificial saliva at 37 degrees C was employed as disintegration medium were used to correlate the in vitro (t2) and oral disintegration times. [18]

Abdelbary prepared orally disintegrating tablets using a hydrophilic waxy binder. Superpolystate (PEG-6-stearate) is a waxy material with a melting point of 33-37 degrees C and an HLB value of 9. The incorporation of Superpolystate in the formulation of RDT was realised by means of two different granulation methods: wet granulation by using an emulsion of this waxy binder as granulating liquid and melt granulation where the molten form of the binder was used. An improvement in tablet hardness and friability was observed with both granulation methods where we were able to obtain RDT with a disintegration time of 40 +/- 2 s and a hardness of 47.9 +/- 2.5N. [19]

Kondo prepared a novel ODT containing taste-masked coated particles (TMP) in the centre of the tablets were prepared using one-step dry-coated tablets (OSDrC) technology. These findings suggest that OSDrC technology is a useful approach for preparing ODT containing functional coated particles. [20]

Sheshala formulated and optimized orally disintegrating tablets of sumatriptan succinate. Taste masking was performed by coating sumatriptan succinate with Eudragit EPO using spray drying technique. The tablets were formulated by mixing the taste masked microspheres with different types and concentrations of superdisintegrants and compressed using direct compression method followed by sublimation technique. In human volunteers, the optimized formulation was found to have a pleasant taste and mouth feel and disintegrated in the oral cavity within 41 s. The optimized formulation was found to be stable and bioequivalent with Suminat®. [21]

Harada *et al* demonstrated the usefulness and wide applicability of a taste sensor and a new disintegration testing apparatus in the development and/or evaluation of orally disintegrating tablets (ODTs). They were able to evaluate the taste of propiverine hydrochloride and the Effectiveness of various masking agents in ODTs. [22]

Kakutani developed a new disintegration test method (Kyoto-model disintegration method or KYO method), which is useful to predict the oral disintegrative properties of an ODT easily. In the KYO method, ODT samples were classified in terms of their water permeability, and a moderate water volume was decided. These results suggested that the KYO method reflected the disintegration nature of the ODTs in the oral cavity, and could easily be applied to development stages and the quality control field of ODT products. [23]

Randale did taste masking by complexing metoclopramide HCl with amino alkyl methacrylate copolymer (Eudragit EPO) in different ratio by the extrusion-precipitation method. Drug-polymer complexes (DPCs) were tested for drug content, in vitro taste in simulated salivary fluid (SSF) of pH 6.8, taste evaluation in

oral cavity and molecular property. Taste evaluation of DPCs in human volunteers revealed considerable taste masking with the degree of bitterness below threshold value (0.5) within 10 s, whereas, metoclopramide HCl was rated intensely bitter with a score of +3 for 10 s. [24]

Kawano Y, Investigated several methods of taste masking in the preparation of orally disintegrating tablets (ODTs), using furosemide (FU) as a model drug. Four types of FU preparations were prepared: granules with maltitol (MA), granules with yogurt powder (YO), a physical mixture of FU and MA, and a physical mixture of FU and YO. All taste-masking granules were prepared using the dry granulation method. We found that YO is more useful than MA in masking unpleasant tastes and confirmed that orally disintegrating tablets with taste-masking function can be prepared using granules of YO prepared using the dry granulation method as a new corrective. [25]

Sasatsu M investigated the masking of the taste of furosemide (FU) as a model drug with correctives and prepared orally disintegrating tablets. Using maltitol (MA) as a corrective, granules were prepared employing mixing, coating, and mixing/coating methods using a desktop granulator. The taste was masked well when granules were prepared by the mixing and mixing/coating methods. Tablets were prepared from these granules with mannitol and crystalline cellulose added as fillers. Tablets made from granules prepared by the mixing and mixing/coating methods showed appropriate strength and disintegrated rapidly. The results showed that orally disintegrating tablets of insoluble drugs with an unpleasant taste such as FU should be prepared with the taste masked employing the methods used in this study. [26]

Danileviciūte V acquires data on efficacy, safety, and preference of mirtazapine orally disintegrating tablets during a 17-week treatment of depression. This prospective, open-label, multicenter study in patients with mild to severe depression was conducted at 47 mental health centres of Lithuania by 78 psychiatrists. The vast majority of patients (80%) preferred the new formulation of mirtazapine - mirtazapine orally disintegrating tablet. In this study conducted in Lithuania with depressed patients, a significant improvement was shown in all efficacy measures. In addition, mirtazapine orally disintegrating tablet was a well-tolerated and preferable formulation for the treatment of depressed patients. [27]

Chen L developed an orally disintegrating tablet (ODT) 5-mg formulation of finasteride was recently developed. The aims of this study were to compare the bioavailability of finasteride ODTs and standard tablets in healthy adult male Han Chinese volunteers and to determine whether any observed differences exceeded Chinese regulatory guidelines for bioequivalence. In this single-dose study, based on the rate and extent of absorption, the ODT (i.e., test) and standard tablet (i.e., reference) formulations of finasteride met the regulatory criteria for bioequivalence in this fasting healthy adult male Han Chinese volunteers. [28]

Motoyama evaluated the potential use of beta-cyclodextrin (beta-CyD) and 2-hydroxypropyl-beta-cyclodextrin (HP-beta-CyD) as excipients for orally disintegrating tablets containing dl-alpha-tocopheryl acetate (VE), an oily drug. VE tablets containing lactose and 5% (w/w) of HP-beta-CyD, not beta-CyD, maintained the high hardness and rapid disintegration under the accelerated stability test using different conditions for 4 weeks. [29]

Sevilla C investigated Multicenter, cross-sectional study of patients with probably AD by DSM-IV or NINCDS-ADRDA criteria, on monotherapy with donepezil, ODT or film-coated tablets. Results show that caregivers of AD patients on donepezil treatment are more satisfied with ODT versus film-coated tablets, especially due to its better ease of use. [30]

Liu YM developed new orally disintegrating tablet (ODT) of flurbiprofen has recently been developed; this study was conducted to provide support for this drug to obtain marketing authorization in China. The aim of the study was to compare the pharmacokinetic properties and bioequivalence of flurbiprofen 50-mg ODT (test) with a conventional flurbiprofen 50-mg tablet (reference) under fasting conditions in healthy volunteers. This single-dose 150-mg (three 50-mg tablets) study of each formulation of flurbiprofen found that the test and reference products met the regulatory criteria for bioequivalence in these fasting healthy Chinese male volunteers. Both formulations were generally well tolerated. [31]

Hori H did an open-label study was performed to investigate the clinical efficacy and tolerability of olanzapine orally disintegrating tablets (Zyprexa Zydis) in ameliorating excitement symptoms in

the acute phase of schizophrenia. These results suggest that olanzapine orally disintegrating tablets are effective and well-tolerated for treatment excitement in the acute phase of schizophrenic patients. In addition, it is possible that adherence to medications is improved by using olanzapine orally disintegrating tablets. [32]

Maanen R proposed to make it easier for patients who are prescribed zonisamide to administer their medicine; a rapidly disintegrating oral tablet formulation has been developed. These 2 trials assessed the bioequivalence of a new orally dispersible tablet formulation of zonisamide (test) versus an immediate-release reference capsule. The test formulation of zonisamide met regulatory criteria for bioequivalence to the reference formulation in these healthy male volunteers. Both formulations were generally well tolerated at both dose levels. [33]

Aguilar-Díaz JE proposed new SeDeM Diagram expert system was used to analyze the suitability of 43 excipients for direct compression with disintegrant properties from eight chemical families. It provides the profile of a substance in powder form in terms of its suitability for direct compression. This study, which was based on the current concept of "Quality by Design ICH Q8", evaluated the pharmacotechnical properties of disintegrants in powder form and selected the candidates that were most suitable for direct compression and their use in formulation of orally disintegrating tablets (ODT). To achieve this, each disintegrant and its chemical families were individually analyzed. It was concluded that nine disintegrants had a SeDeM value with the index of good compression (IGC) over 5. Most of these disintegrants were from the micro cellulose family. Other disintegrants had indexes that were close to 5. It is assumed that these excipients can be used in direct compression, when they are added to other excipients. [34]

Karagianis J proposed primary objective of this study was to investigate the change in body mass index (BMI) in patients who had previously gained weight with SOT and continued with this therapy during the study period, compared with those patients who switched to ODO during the study period. In this study, patients treated with ODO experienced a similar mean change in BMI and weight from baseline, to those patients treated with SOT. [35]

Fass R developed oral tablet formulations of metoclopramide are effective therapies for gastroparesis and gastro-oesophageal reflux disease; however, difficulty swallowing tablets or nausea/vomiting may reduce patient adherence to therapy. Because of this, a metoclopramide orally-disintegrating tablet (ODT) has been developed. To evaluate the bioequivalence of a single administration of a 10-mg metoclopramide ODT and a conventional 10-mg oral metoclopramide tablet in healthy volunteers. In healthy volunteers, single administration of 10-mg metoclopramide ODT was well tolerated and bioequivalent to single administration of a conventional 10-mg metoclopramide tablet. [36]

Tokuyama E proposed development of a lyophilized orally disintegrating tablet (ODT) that enhanced the in vitro dissolution and in vivo absorption of Nimesulide (NM), a drug with poor solubility and poor bioavailability, is presented. The ODTs were prepared by freeze-drying an aqueous dispersion of NM containing a matrix former, a sugar alcohol, and a collapse protectant. In addition, different disintegration accelerators were tested. & compared the palatability of the original and eight generic versions of famotidine orally disintegrating tablets by means of human gustatory sensation tests, a comparison of the release profiles, and using an automated taste sensor, the alpha-Astree Electronic Tongue. There was a good Correlation between the taste predicted by principal component analysis and the Euclidean distance obtained by the taste sensor, and bitterness intensities obtained in the human gustatory tests. [37]

Shukla designed a simple, rapid, cost effective and highly efficient process to fabricate a tasteless complex of risperidone using ion exchange resin (IER), evaluate the molecular properties of the resinate and finally incorporate it into orally disintegrating tablets (ODT). The complex was compressed into orally disintegrating tablet. The drug release from the complex was about 2.5% in 120 s in 5 ml of pH 6.8 phosphate buffers which has been used to mimic the salivary fluid volume and pH. Resinate was tasteless while the fabricated ODTs were pleasantly tasting without any bitterness of drug as confirmed by the taste panel. [38]

Kozumplik O reported weight loss in patients with schizophrenia after switching from olanzapine standard oral tablet (SOT) to olanzapine orally disintegrating tablets (ODT). Switching patients from olanzapine SOT to olanzapine ODT treatment resulted in significant weight loss that

was maintained during 12 months in both case reports. [39]

Nadal-Sánchez A assessed compliance with oral lansoprazole disintegrating tablets (LODT) in patients treated by traumatology specialists. Compliance with lansoprazole orally disintegrating tablets was high. Patients reported that this formulation improved their compliance and that they

Preferred LODT to previous medication. Tolerability was excellent. [40]

Goel H formulated and evaluated orodispersible tablets (ODTs) of ondansetron HCl possessing sufficient mechanical strength by wet granulation or direct compression method. The results suggested that the chitosan-glycine system not only improved disintegration time but also made it possible to prepare ODTs with higher crushing strength as compared to tablets containing superdisintegrants. [41]

Rai P discussed the patents relating to orally disintegrating systems with respect to the use of different formulation ingredients and technologies. [42]

Chandrasekhar R optimized FDTs using a progressive three-stage approach. A series of hardness, fracturability and disintegration time tests were performed on the formulations at each stage. During Stage I, tablets were prepared in concentrations between 2% and 5% w/w, and were formulated at each concentration as single and combination bloom strength gelatin (BSG) using 75 and 225 BSGs. Analysis revealed that both hardness and disintegration time increased with an increase in gelatin concentration. A combination (5% gelatin) FDTcomprising a 50:50 ratio of 75:225 BSGs (hardness: 13.7+/-0.9 N and disintegration time: 24.1+/-0.6s) was judged the most ideal, and was carried forward to Stage II: the addition of the saccharides sorbitol, mannitol and sucrose in concentrations between 10% and 80% w/w. The best properties were exhibited by mannitol-containing formulations (50%-hardness: 30.9+/-2.8 N and disintegration time: 13.3+/-2.1s), which were carried forward to the next stage: the addition of viscosity-modifying polymers to improve mouth-feel and aid pre-gastric retention. Addition of carbopol 974P-NF resulted in the enhancement of viscosity with a compromise of the hardness of the tablet, whereas Pluronic F127 (6%) showed an increase in disintegration time and viscosity with retention of mechanical properties. [43]

Sakamoto S, investigated safety profile of voglibose oral disintegrating tablet (VODT), and whether treatment with VODT results in improvement of medication compliance and glycemic control. The survey suggested that the safety profile of VODT is comparable with that of CVT, and switching from CVT to VODT has positive impact on medication compliance which may lead to an improvement in glycemic control.Yoshida optimized salting-out taste-masking system for micro-beads containing drugs with high solubility. The salting-out taste-masking system is a multiparticulate system consisting of a drug core, a salting-out layer containing salts and water-soluble polymers, and a water-penetration control layer containing water-insoluble materials. The findings in this study will lead to the provision of numbness-masked oral disintegrating tablets to patients. [44]

Wang Z *et al* optimized the formulation of panax notoginsenoside orally fast disintegrating tablets.

The disintegration time and tensile strength of panax notoginsenoside oral disintegrating tablets were good, and the taste was satisfactory. Panax notoginsenoside oral disintegrating tablets achieve the goal of design and this method can be fairly used in formulation screening. [45]

Shah PP *et al* investigated the complete bitter-taste-masking of primaquine phosphate (PRM) using a solid dispersion with mono ammonium glycyrrhyzinate pentahydrate (GLY). This work also described the preparation of rapidly disintegrating tablets (RDTs) of PRM by a direct compression method using superdisintegrant, croscarmellose sodium. [46]

San L *et al* reviewed the properties, efficacy, and safety profile of olanzapine as an orally disintegrating tablet, and explores their association with medication compliance compared with standard oral formulation. [47]

Patel D formulated orally disintegrating tablets (ODTs) of etoricoxib. A combination of the superdisintegrants with a sublimation technique was used to prepare the tablets. Tablets were prepared using a direct compression method employing superdisintegrants such as low substituted hydroxypropyl methyl cellulose (L-HPMC), low substituted hydroxyl-propyl cellulose (L-HPC), crospovidone, croscarmellose sodium, and sodium starch glycolate. Tablets of

etoricoxib prepared using L-HPC exhibited the least friability and disintegration time (approximately 65 s). To decrease the disintegration time further, a sublimation technique was used along with the superdisintegrants for the preparation of ODTs. The use of sublimating agents including camphor, menthol, and thymol was explored. The addition of camphor lowered the disintegration time (approximately 30 s) further, but the percent friability was increased. [48]

Goel H said that the aim of this study was to optimize and formulate fast disintegrating tablets (FDTs) for nausea and vomiting using aminoacetic acid, carmellose and sodium alginate with enough mechanical strength. Ondansetron HCl (water soluble) or domperidone (water insoluble) drug were added to FDTs and their disintegration behaviour was evaluated. The data revealed that optimized domperidone FDTs were better than domperidone FDTs containing croscarmellose or crospovidone. Hence, this novel excipients combination can be used for delivery of water insoluble drugs in place of superdisintegrants. [49]

Sharma V developed a dosage form that was easy to administer and provides rapid release of the drug roxithromycin, using modified polysaccharides as rapidly disintegrating excipients. Modified polysaccharides co grinded treated agar (C-TAG) and co grinded treated guar gum (C-TGG) were prepared by subjecting pure polysaccharides namely agar and guar gum respectively to sequential processes of wetting, drying and co grinding with mannitol (1:1). Results indicated that lower levels of modified polysaccharides namely C-TAG in F (3) and C-TGG in F (7) and higher levels of microcrystalline cellulose, exhibited least disintegration times without friability concerns. In vitro release of optimized formulations F(3) and F(7,) both at salivary pH and physiological pH was found to be more than 90% within 30 min as compared to 27.82% at the same time point of conventional formulation. Stability studies carried out as per ICH Q1A guidelines suggested the formulations to be stable for a period of 6 months. Thus the approach of using modified polysaccharides as fast disintegrating excipients can be used to formulate a stable orodispersible formulation. [50]

Singh J optimized an orodispersible formulation of indomethacin using a combined approach of subliming agent and superdisintegrant. The tablets were made by non-aqueous wet granulation technique with superdisintegrant incorporated both intragranularly and extragranularly. Stability studies carried out as per ICH Q(1) A guidelines suggested the stable formulations for the tested time period of 6 months. The systematic approach of using subliming and disintegrating agents helped in achieving a stable, optimized orodispersible formulation, which could be industrially viable. [51]

Lee HJ investigated the acceptability and therapeutic efficacy of a preoperative single administration of long-acting 5-hydroxytryptamine type 3 (5-HT 3) receptor antagonists in an orally disintegrating tablet formulation, ramosetron, in breast cancer patients. [52]

Kuno Y evaluated the effect of lubricants on the characteristics of orally disintegrating (OD) tablets manufactured using the phase transition of sugar alcohol. OD tablets were produced by directly compressing a mixture containing lactose-xylitol granules, disintegrant, glidant and lubricant, and subsequent heating... Consequently, talc was demonstrated to be the most desirable lubricant for the preparation of OD tablets based on the principle of the phase transition of sugar alcohol. [53]

Mizumoto T proposed this study, the taste-masking of famotidine, which could apply to any fast-disintegrating tablet, was investigated using the spray-dry method. The target characteristics of taste-masked particles were set as follows: the dissolution rate is not to be more than 30% at 1 min and not less than 85% at 15 min, and the particle size is not to be more than 150 micron in diameter to avoid a gritty feeling in the mouth. The target dissolution profiles of spray-dried particles consisting of Aqua coat ECD30 and Eudragit NE30D or triacetin was accomplished by the screening of formulas and the appropriate lab-scale manufacturing conditions. Lab-scale testing produced taste-masked particles that met the formulation targets. This confirmed that the spray-dry method produced the most appropriate taste-masked particles for fast-disintegrating dosage forms. [54]

Golden G compared the bioequivalence of FazaClo (clozapine orally disintegrating tablets) 100 mg to Clozaril (clozapine standard oral tablets) 100 mg after multiple doses in patients with schizophrenia. FazaClo produced pharmacokinetic profiles almost identical to those

of Clozaril. This should provide clinicians with reassurance that patients who receive FazaClo will achieve plasma drug concentrations similar to those produced by the same daily dose of Clozaril, and that no cross-titration is necessary when switching from one of these clozapine formulations to the other. [55]

Chawla B investigated the long-term weight loss outcomes during usual clinical practice after switching from olanzapine standard oral tablet (SOT) to olanzapine orally disintegrating tablets (ODT). This study demonstrated that, in usual clinical practice, switching patients from olanzapine SOT to olanzapine ODT treatment resulted in significant weight loss that was maintained over 12 months. [56]

Bergamante V developed eight formulations were containing ibuprofen in the form of orally disintegrating tablets. To prevent bitter taste and side effects of the drug, the drug was associated with Phospholipon 80H, a saturated lecithin, by wet granulation. The granules were then coated using different film forming agents (Kollicoat SR 30, Amprac 01, Kollidon 90F, Eudragit RD 100) obtaining four lots 1-4. Coated granules were then formulated with a sweetener (Aspartame), mannitol-based diluents (Pearlitol SD 200) and Kollidon CL (1-4K) or Explotab (1-4E) were added as superdisintegrants and compacted under low compression force. By an appropriate combination of excipients it was thus possible to obtain orally disintegrating tablets and a delayed release of ibuprofen using simple and conventional techniques. [57]

Johnson CE, determined the stability of the powder for oral suspension over 45 days, evaluate the stability of a partial dose (<20 mg) following exposure to Simulated Gastric Fluid USP (SGF) over 2 hours, and determine the feasibility of administering the suspension through neonatal and pediatric nasogastric feeding tubes compared with lansoprazole. Omeprazole-sodium bicarbonate suspension 2 mg/ml prepared from 20 mg packets was stable for at least 45 days when stored at 3-5 degrees C. A partial dose of 12.7 mg was stable following exposure to SGF for 2 hours at 37 degrees C. This suspension can be easily administered through 5, 6, and 8 French neonatal/pediatric feeding tubes and, when taking time and ease of preparation into account, it is cost competitive with simple omeprazole suspension. [58]

Ponce J assessed the acceptability of lansoprazole orally disintegrating tablets (LODT) in patients with gastro-oesophageal reflux disease (GORD). LODT were well accepted by patients with GORD. Patients reported that this formulation improved compliance with therapy. Tolerability was excellent. [59]

Ondo WG conducted a 12-week, double-blind, placebo-controlled, parallel-design trial of selegiline ODT. The primary efficacy point was reduction in the percentage of average daily "off" time. Secondary measures included reductions in daily off hours and total daily off time, Clinical Global Impressions-Improvement (CGI-I), and Patient Global Impression-Improvement (PGI-I). Patients on LD received selegiline ODT (1.25 mg/d for 6 weeks, then 2.5 mg/d for 6 weeks) or placebo. Safety and tolerability were measured. This study showed no significant difference in improvement in percentage of off time with selegiline ODT versus placebo. Some clinical impressions (e.g., PGI-I, CGI-I) improved. This result contrasts with an identically designed study that showed a significant improvement in off time with selegiline ODT. A combined analysis of both studies suggested overall efficacy. [60]

Strickley RG proposed the intent of this review is to educate the reader on the various types of formulations administered orally to paediatrics, the rationale in deciding which type of formulation to develop, the excipients used, development challenges, the in-use handling of oral pediatric formulations, and the regulatory incentives. [61]

Barbanti P did a new sumatriptan fast disintegrating/rapid release tablet (FDT/RRT) using RT technology has been developed to enhance tablet disintegration and dispersion in the stomach with the intention of speeding absorption and onset of effect, hence mitigating the effects on the gastrointestinal dysmotility that typically accompanies the attack. Sumatriptan FDT/RRT is bioequivalent to conventional tablets, although it provides slightly faster absorption during early post-dose interval. Clinical trials indicate that sumatriptan FDT/RRT is rapidly effective in terms of freedom from pain and return to normal activities, both with early and late treatment. The drug is well tolerated. In an oral formulation, which is the patients' preferred dosing route, sumatriptan FDT/RRT may therefore constitute an advance in the management of acute migraine attacks. [62]

Erdman K evaluated the effect of a standardized meal on the bioavailability of alprazolam formulated as an immediate-release orally disintegrating tablet (ODT) in healthy volunteers. Co administration of food was shown to have no effect on extent of absorption of immediate-release alprazolam ODT 1.0 mg when compared with drug administration in the fasted condition; however, the rate of drug absorption was decreased. The clinical significance of the difference in rate of alprazolam absorption is unknown but thought to be minimal. [63]

Development of a fast-disintegrating lyophilized dry emulsion (LDE) tablet that enhanced the in vitro dissolution and in vivo absorption of griseofulvin (GF) is presented. The LDE tablets were prepared by freeze-drying o/w emulsions of GF, a drug for which bioavailability is known to be enhanced by fat co-administration. Oil-in-water emulsions were prepared using a gelatin solution (2%, w/v) as the water phase and medium chain triglycerides (Miglyol) or sesame oil as the oil phase. Results obtained from dissolution studies showed that LDE tablets of GF improved the dissolution rate of the drug compared to the plain drug. [64]

Khan S evaluated taste masking was done by complexing ondansetron HCl with amino alkyl methacrylate copolymer (Eudragit EPO) in different ratios by the precipitation method. Drug-polymer complexes (DPCs) were tested for drug content, in vitro taste in simulated salivary fluid (SSF) of pH 6.2, and molecular property. Taste evaluation of RDT in human volunteers revealed considerable taste masking with the degree of bitterness below threshold value (0.5) ultimately reaching to 0 within 15 minutes, whereas ondansetron HCl was rated intensely bitter with a score of 3 for 10 minutes. Tablets of batch F4 also revealed rapid drug release (t(90), 60 seconds) in SGF compared with marketed formulation (t(90), 240 seconds; $P < .01$). Thus, results conclusively demonstrated successful masking of taste and rapid disintegration of the formulated tablets in the oral cavity. [65]

Chue P evaluated safety and maintenance of effect in symptomatically stable patients transitioned from compressed risperidone tablets to orally disintegrating risperidone tablets. Patients stabilized on compressed risperidone tablets transitioned to the equivalent dose of orally disintegrating risperidone tablets with continued maintenance of effect, no decompensation and with minimal side effects.[66]

Thyssen A described the results from clinical studies that have assessed the taste, time to disintegration, and tolerability of RD risperidone tablets, and bioequivalence of RD risperidone tablets (2 x 0.5 mg, 2 mg, and reduced-size 4 mg) versus conventional (CV) risperidone tablets. In the 10 studies analyzed, the taste of RD risperidone tablets was found to be acceptable in the majority of healthy subjects and patients with schizophrenia or schizoaffective disorder. In addition, RD risperidone tablets were found to be bioequivalent to CV risperidone tablets. [67]

Lew MF evaluated long-term safety, efficacy, and tolerability of adjunctive selegiline ODT 2.5 mg in patients who completed either of two large phase 3 double-blind studies. The study was to end after 12 months but was amended to be open-ended. Long-term selegiline ODT 2.5 mg/day was effective, safe, and well tolerated in patients with Parkinson's disease experiencing off episodes during levodopa therapy. [68]

Varia I conducted a 10-week, open trial of mirtazapine orally disintegrating tablets in 16 elderly subjects with major depressive disorder and one or more serious medical illnesses. Quality of life was measured by the Medical Outcomes Study Short Form-36 Health Status Survey (SF-36). Mirtazapine orally disintegrating tablets may improve depression, insomnia, anxiety, somatic symptoms, and certain quality-of-life measures in elderly depressed subjects with medical disorders. A randomized, placebo-controlled study is warranted to confirm these promising findings. [69]

Danileviciūte V ascertained the opinion of depressed patients towards a new formulation of antidepressant drug, mirtazapine - orally disintegrating tablet Remeron Sol Tab. Most of the patients (n=189, 41.81%) had a positive opinion about the taste of medication ("very pleasant Statistically significantly more patients (81.86%) noted that they would choose Remeron Sol Tab compared to the patients who would prefer conventional form of the medication (2.21%). [70]

Normann C said 191 schizophrenic patients were treated upon admission to hospital with fast orally disintegrating risperidone tablets for up to seven days. Co-medication was per usual clinical practice and at physician's discretion. Psychopathology was rated at baseline, 2, 24 and

48 hours and 4 and 7 days after initiation of therapy. Oral treatment of acutely exacerbated schizophrenic patients with fast orally disintegrating risperidone tablets, alone or in combination with benzodiazepines, was associated with a rapid onset of action and a significant and clinically relevant improvement of acute symptoms. [71]

Shapero G the 'Zomig Appropriate for Primary care' programme was developed to address the needs of primary care physicians (PCPs) to improve migraine management. As part of the programme, an international, open-label, 6-month clinical study was performed. The study included new and tangible outcome variables relevant to PCPs and recruited patients presenting in primary care with an established migraine diagnosis. Patients treated up to three migraine attacks per month with zolmitriptan orally disintegrating tablet (ODT) 2.5 mg. The results of the study indicate that patient-orientated end-points are more motivational and meaningful to physicians than traditional end-points used in controlled clinical trials, allowing them to make informed decisions regarding migraine management. [72]

Nelson JC did treatment studies of depression in the very oldest patients are infrequent. For these reasons, this study of mirtazapine orally disintegrating tablets was carried out in nursing home residents>or=85 years old with physician-diagnosed depression. Although lacking a placebo control, this naturalistic study suggests that mirtazapine orally disintegrating tablets were effective and well tolerated in this sample of depressed nursing home residents>or=85 years of age. [73]

Sugimoto M determined the optimal ingredients for the rapidly disintegrating oral tablets prepared by the crystalline transition method (CT method). The oral disintegration time of the tablet significantly depended on diluents, due to differences in the penetration of a small amount of water in the mouth and the viscous area formed inside the tablet. The oral disintegration time was 10-30 s for tablets with a tensile strength of approximately 1 MPa, when erythritol, mannitol or xylitol was used as the diluents. [74]

Benkert O developed study designed to compare specifically the onset of antidepressant action of mirtazapine orally disintegrating tablets (ODT) with venlafaxine extended-release (XR) formulation in outpatients with major depression. Significant differences in favour of mirtazapine ODT were evident in the CGI of change on days 8 ($P = 0.019$), 11 ($P = 0.004$), and 15 ($P = 0.031$), and the CGI of severity on days 8 ($P = 0.014$) and 11 ($P = 0.033$). Both treatments were well tolerated. These results indicate that mirtazapine ODT has a faster onset of antidepressant efficacy than venlafaxine XR in patients with major depressive disorder, and that this effect is independent of its sleep-improving properties. [75]

Fukami J developed fast disintegrating compressed tablets using amino acid as disintegration accelerator: evaluation of wetting and disintegration of tablet on the basis of surface free energy. The wetting time of the tablets increased in the order of L-lysine HCl, L-alanine, glycine and L-tyrosine, whereas the disintegration time in the oral cavity of the tablets increased in the order of L-alanine, glycine, L-lysine HCl and L-tyrosine. When the dispersion component of amino acid was large value or the dispersion component was small value, faster disintegration of tablet was observed, expect of L-tyrosine tablet. [76]

Carnaby-Mann G evaluated differences in swallowing physiology and safety in patients with dysphagia between conventional tablets and a new method of tablet transportation, orally disintegrating technology (ODT) (RapiTab; Schwarz Pharma Inc, Milwaukee, Wis). Patients with dysphagia frequently complain of trouble swallowing medication. In this study, an ODT formulation provided a method of delivery that required less effort to swallow, did not result in increased levels of airway compromise, and was preferred by dysphagic patients. The ODT medication delivery technology may provide benefit to adults with dysphagia in convenience, compliance, and accuracy of dosing. [77]

Henchcliffe C selegiline is currently the most widely used monoamine oxidase-B inhibitor for Parkinson's disease, but has a low and variable bioavailability, and is metabolized to L-methamphetamine and L-amphetamine that carry a risk for potential neurotoxicity. Selegiline orally disintegrating tablets prove to be clinically effective and safe in patients with moderately advanced Parkinson's disease. [78]

Lew MF selegiline orally disintegrating tablet dissolves in the mouth within seconds and is rapidly absorbed directly into the systemic circulation, increasing parent drug bioavailability and lowering plasma metabolites compared with conventional oral formulations. Adding selegiline

orally disintegrating tablet to levodopa in patients experiencing 'wearing-off' episodes significantly decreases off time and increases dyskinesia-free 'on' time. Adding selegiline orally disintegrating tablet to levodopa also significantly improves Unified Parkinson's Disease Rating Scale motor scores and patients' and physicians' ratings of disease severity. Selegiline orally disintegrating tablet has been demonstrated to be safe and well tolerated in placebo-controlled clinical trials. [79]

Ciper M, developed Fast disintegrating capsules for administration in the oral cavity were prepared either by perforation or by vacuum-drying of conventional hard capsules. When compared to other fast disintegrating dosage forms (e.g. lyophilized sponges or tablets), these capsules have various advantages, in particular, a high drug loading capacity and no compression steps. The disintegration time of conventional hard gelatin capsules (HGC) was reduced from 91 to 39 s by introducing 6-10 small holes (diameter =25-50 micron) into the capsule shell. Vacuum-drying of conventional hard gelatin capsules resulted in brittle capsules, which broke rapidly in the oral cavity. The brittleness of the hard gelatine capsules correlated well with their moisture content. The critical moisture value for sufficient brittleness of hard gelatin capsules was <4% w/w. [80]

Diener HC zolmitriptan has been developed in an orally disintegrating tablet (ODT) formulation that rapidly dissolves on the tongue and can be taken quickly, conveniently and discreetly without fluid intake. Zolmitriptan ODT has demonstrated high efficacy and excellent tolerability. In addition, patients found zolmitriptan ODT to be convenient and easy to use, and were willing to continue using the product. Following placebo-controlled studies, these PMS results provide insight into the use of zolmitriptan ODT in a setting more representative of real life than randomised clinical trials, further demonstrating that it provides a reliable and convenient alternative to conventional tablets. [81]

Dowson AJ proposed a bioequivalent, orally disintegrating tablet (ODT) of zolmitriptan, which dissolves on the tongue without the need for additional fluid intake, has been developed. In a study designed to compare patient preference for zolmitriptan ODT and conventional oral sumatriptan tablets, > 60% of the 186 patients questioned had an overall preference for zolmitriptan ODT, with > 80% of patients reporting that this was the more convenient and less disruptive therapy to take. Not only is zolmitriptan ODT a convenient tablets, such as the sumatriptan oral tablet, but patients generally consider it to be a more attractive option for the acute treatment of migraine than the orally disintegrating version of rizatriptan. [82]

Gendolla A migraine is characterised by recurrent episodes of head pain, often accompanied by other symptoms, such as nausea and vomiting. In addition to migraine impairing a patient's ability to function normally during an attack, fear of the next attack can detract from quality of life between attacks. Of those migraineurs who consult a physician for headache, the minority are prescribed migraine-specific triptans and many are dissatisfied with current therapy. Clinical trials have shown that triptans are capable of providing rapid and effective relief of headache pain, which is what patients primarily desire from acute migraine therapies. Patients generally prefer to administer acute migraine therapies orally, but conventional tablets do not suit all patients and situations. Some patients dislike swallowing tablets, nausea can make swallowing difficult and can be exacerbated by fluid intake, and attacks can easily strike when fluids are not readily available, especially as many young migraineurs lead busy, active lives. Patients need a treatment that enables any migraine attack to be treated promptly and effectively in any given situation. Tablets that dissolve rapidly on the tongue without a requirement for extra fluid intake are a popular alternative to conventional tablets, allowing discreet, convenient and early treatment of migraine anywhere and anytime it strikes. Several triptans are currently on the market in conventional tablet form, but some are available in other formulations, such as orally disintegrating tablets or nasal sprays, making it possible to prescribe rapidly effective migraine treatments in formulations that suit individual patient preferences, lifestyles and attack characteristics. [83]

Cohen IT evaluated postoperative nausea and vomiting (PONV), a major complication in children, is responsive to IV and oral ondansetron. Because these routes are not always available, we studied the acceptability and efficacy of ondansetron oral disintegrating tablets (ODT). In this double-blind, randomized, placebo-controlled study, 62 patients undergoing adenotonsillectomy, aged 5 to 11 years, preoperatively received ODT (4 mg) or placebo. Patients assessed the

medication for taste and sensation. Anaesthesia was induced with sevoflurane, maintained with desflurane, and supplemented with fentanyl 2.5 microg/kg and dexamethasone 0.5 mg/kg (maximum dose, 12 mg). An observer blinded to treatment evaluated patients for pain, agitation, and PONV. Postoperative treatment consisted of fentanyl 1 microg/kg for pain and agitation and metoclopramide 0.15 mg/kg (maximum dose, 10 mg) for PONV. There were no significant differences between study groups with regard to age, weight, recovery time, agitation, or pain. Approximately 90% of the subjects found the ODT to taste good. No subject rejected the study medication, but the ondansetron-containing tablets were found to be less palatable than the placebo. The incidence of vomiting was significantly less in the ondansetron-medicated group. [84]

Jeong SH said this review describes various formulations and technologies developed to achieve fast dissolution/dispersion of tablets in the oral cavity. In particular, this review describes in detail FDT technologies based on lyophilization, molding, sublimation, and compaction, as well as approaches to enhancing the FDT properties, such as spray-drying, moisture treatment, sintering, and use of sugar-based disintegrants. In addition, taste-masking technologies, experimental measurements of disintegration times, and clinical studies are also discussed. [85]

Chue P investigated the disintegration profile, acceptability, and tolerability of orally disintegrating risperidone tablets in patients with schizophrenia or schizoaffective disorder. The orally disintegrating risperidone tablets were well tolerated and rated as very acceptable by all patients. [86]

Shibata Y used tableting process analyzer (Tab All) to predict disintegration time in the mouth of rapidly disintegrating tablet. Analyzer profiles recorded upper punch displacement and die wall force encountered during tablet processing. Analysis of the compaction process revealed a strong association between disintegration time in the mouth and stationary time, relaxation time of upper punch displacement, and relaxation time of die wall force; disintegration time in the mouth decreased as the three parameters increased. [87]

Howden CW evaluated dysphagia affects a large and growing number of individuals in the United States, particularly the elderly and those who are neurologically impaired. Swallowing difficulties may be due to age-related changes in oropharyngeal and oesophageal functioning as well as central nervous system diseases such as stroke, Parkinson disease, and dementia. Among institutionalized individuals, dysphagia is associated with increased morbidity and mortality. An appreciation of the physiology of swallowing and the pathophysiology of dysphagia is necessary for proper patient management. Careful history, physical examination, and evaluation of radiologic and endoscopic studies should differentiate oropharyngeal and oesophageal etiologies of dysphagia and distinguish mechanical (anatomic) disorders from functional (motor) disorders. A significant percentage of patients with dysphagia have concomitant acid-related disorders that are managed best with proton pump inhibitor (PPI) therapy. Three of the currently available PPIs are manufactured as capsules containing enteric-coated granules that may be mixed with soft foods or fruit juices before oral administration to those with swallowing difficulties. In addition, omeprazole and lansoprazole may be administered via gastrostomy or nasogastric feeding tubes as suspensions in sodium bicarbonate. Novel dosage formulations of lansoprazole that may be appropriate for patients with dysphagia include the commercially manufactured lansoprazole strawberry-flavored enteric-coated granules for suspension and lansoprazole orally disintegrating tablets. [88]

Freston JW upon this study assessed the pharmacokinetic profile of lansoprazole orally disintegrating tablet dispersed in a small volume of water and administered through a small-bore nasogastric tube. Dispersion of the lansoprazole orally disintegrating tablet in a small volume of water and administering via nasogastric tube does not reduce the pharmacokinetic profile of the intact lansoprazole orally disintegrating tablet. This alternative dosing method may be useful in patients with nasogastric or gastric tubes. [89]

Narazaki R developed a simple and suitable disintegration method specific for rapid disintegrating tablets (RDTs). Manufactured several placebo RDTs and exposed them to severe storage conditions (60 degrees C/75%RH for 1 week) in order to obtain RDTs with a wide range of disintegration times. These placebo RDTs were utilized to compare the disintegration times obtained by several methods, including the proposed method. As expected, the disintegration time of the placebo RDTs in human sensory test varied widely. This new method might provide a valuable approach for the establishment of the

official disintegration test for RDTs in the future. [90]

1. Reeves RR the orally disintegrating formulation of olanzapine dissolves rapidly on contact with saliva. 2. In certain cases, orally disintegrating olanzapine may be administered, instead of injection of an antipsychotic agent. 3. Orally disintegrating olanzapine is intended to deliver a dose analogous to regular olanzapine tablets. [91]

Gremse DA assessed the effect that dispersing the lansoprazole orally disintegrating tablet in water would have on lansoprazole pharmacokinetics. Dispersing the 15 mg lansoprazole orally disintegrating tablet in water and administering the dose orally via syringe is bioequivalent to the 15 mg intact lansoprazole orally disintegrating tablet with respect to lansoprazole area under the plasma concentration and C (max). This dosing route provides an additional, convenient dosing option for lansoprazole. [92]

Popa G the pharmaceutical market shows lately an increasing interest in orally disintegrating tablets, due to their good acceptability among certain age categories (ex. elderly, children), and other patients with difficulties in swallowing classic solid dosage forms. Some of the methods of preparing such tablets have gained industrial applicability: molding, lyophilization, direct compression with highly soluble excipients, super disintegrants and/or effervescent systems. Some of the patients have had a good impact on the pharmaceutical market and more improvements are expected in the next few years, with new drugs to be formulated as fast dissolving dosage formulations. [93]

Roose SP evaluated the efficacy and tolerability of mirtazapine orally disintegrating tablets in depressed, elderly nursing home residents, under naturalistic study conditions. The results suggest that mirtazapine orally disintegrating tablets provide antidepressant efficacy and are a relatively well-tolerated treatment for depression in this patient population of elderly nursing home residents with medical and cognitive comorbidities. [94]

Samprasit W *et al* developed taste-masked oral disintegrating tablets (ODTs) using the combination of ion exchange resin and cyclodextrin, to mask the bitter taste and enhance drug dissolution. Meloxicam (MX) was selected as a model drug with poor water solubility and a bitter taste. The results from this study suggest that the appropriate combination of ion exchange resin and cyclodextrin could be used in ODTs to mask the bitter taste of drug and enhance the dissolution of drugs that are weakly soluble in water . [95]

Zeng F *et al* studied to improve the solubility and oral bioavailability of clozapine (CLZ), a poorly water-soluble drug subjected to substantial first-pass metabolism, employing cyclodextrin complexation technique. The ODTs showed a higher in vitro dissolution rate and bioavailability compared with the commercial tablets. [96]

Stirnimann T *et al* investigated the properties and usefulness of functionalized calcium carbonate (FCC) as a new pharmaceutical excipient for the production of ODTs. Oral dosage forms--based on the new pharmaceutical excipient. Oral dosage forms--based on the new pharmaceutical excipient. It was concluded that FCC--can be designed to have a short disintegration time combined with good mechanical strength. Due to these properties, FCC can be used for the preparation of ODTs. [97]

Tábi T *et al* A introduced a new formulation, an orally disintegrating tablet (ODT), to overcome pharmacokinetic problems by avoiding its presystemic metabolism. [98]

Nakano Y *et al* evaluated the taste and mouth feel of newly designed orally disintegrating tablets (ODTs) of pioglitazone, which is a typical type 2 diabetes medicine with an unpleasant taste, using a visual analog scale (VAS) analysis. It was concluded that VAS is a useful tool to evaluate the taste of ODTs and that gustatory masking can effectively mask the unpleasant

taste of pioglitazone ODT. [99]

Uchida S *et al* determined the amount of water required for ingesting an orally disintegrating tablet (ODT) of solifenacin (Vesicare(®), VES) and VES conventional tablets (VES-CT). Study showed that the amount of water required for ingesting VES-ODT is lower than that for ingesting VES-CT. [100]

CONCLUSIONS

Direct compression with highly soluble excipients, super disintegrants and/or effervescent systems and processing techniques such as freeze-drying, molding and sublimation, spray drying, direct compression followed by vacuum drying for preparing ODT tablets have gained industrial applicability. The main advantage is that they are

very easy to administer and the patient doesn't have a feeling of taking in a tablet rather excited for the method of delivery (disintegrating). Combinations of process techniques and choice of formulation ingredients are very much useful for improving critical product characteristics of pharmaceutical and Nutraceutical products and hence the administration of various therapeutic and preventive actives molecules for enhancing patient compliance.

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