2.1 Fast Dissolving Tablet of Anti-Emetic Drugs

Gudas GK et al., (2010), prepared FDT of chlorpromazine. The tablets were prepared with sodium starch glycolate, crospovidone, croscarmellose, L-HPC, pre-gelatinised starch. The blends were examined for angle of repose, bulk density, tapped density, compressibility index and Hausner’s ratio. The tablets were evaluated for hardness, friability, disintegration time, dissolution rate and drug content.¹

Kumar DN et al., (2010), prepared fast dissolving tablets of granisetron HCl using novel coprocessed superdisintegrants consisting of crospovidone and sodium starchglycolate in the different ratios (1:1, 1:2 & 1:3). The developed superdisintegrants were evaluated for angle of repose, carr’s index and Hausner’s ratio in comparison with physical mixture of superdisintegrants. The angle of repose of the developed excipients was found to be < 25°, carr’s index in the range of 10-15% and Hausner’s ratio in the range of 1.11-1.14. Short-term stability studies on promising formulation indicated that there were no significant changes in drug content and in vitro dispersion time (p<0.05).²

Randale SA et al., (2010), masked the intensely bitter taste of metoclopramide and formulated a rapid disintegrating tablets of the taste masked drug. Taste masking was done by complexing metoclopramide with Eudragit in different ratio by the extrusion-precipitation method. Drug-polymer complexes (DPCs) were tested for drug content, in vitro taste in simulated salivary fluid, taste evaluation in oral cavity. The complex having drug-polymer ratio of 1 : 2 shows significant taste masking, confirmed by drug. Prepared tablets were evaluated for various parameters like tensile strength, wetting time, water absorption ratio, in vitro disintegration time and disintegration in oral cavity.³

Goel H et al., (2010), developed a disintegrating system that could be used for preparing fast disintegrating tablets of highly water soluble drug metoclopramide without compromising on the mechanical strength. For this purpose disintegrating system consisting of chitosan-alginate (CTN-ALG) complex (1:1): glycine and chitin was developed. The results revealed that when CTN-ALG and glycine were mixed in the ratio of 30:70, the granules exhibited a minimum water sorption time and maximum effective pore radius. The results suggested incorporation of chitin (5-10%
w/w) while preparing FDTs of metoclopramide to enhance the disintegration without compromising their mechanical strength.⁴

Shirshand SB et al., (2010), developed fast disintegrating tablets of proclorperazine maleate with a view to enhance patient compliance by direct compression method. In this method, crospovidone and croscarmellose sodium in combination were used as superdisintigrant.⁵

Dahima R and Sharma R, (2010), masked the intensely bitter taste of metoclopramide hydrochloride and to formulate orodispersible tablets of taste mask drug. Drug-resin complex were optimize by considering parameters such as optimization of resin concentration, optimization of swelling time, optimization of stirring time, optimization of pH and optimization of temperature on maximum drug loading. In vitro drug release study of taste masked tablets showed that more than 85% of the drug release within 10 min. Thus, results conclusively demonstrated successful masking of taste and rapid disintegration of the formulated tablets in the oral cavity.⁶

Mahamuni SB et al., (2009), prepared fast dissolving tablets, which can rapidly disintegrate in the saliva using taste-masked granules of drugs with a bitter taste, Promethazine HCl. The taste masked granules were prepared using gastro erodible Eudragit E-100 by extrusion method. Fast dissolving tablets were prepared using taste-masked granules and a mixture of excipients containing optimized level of microcrystalline cellulose and starch. The effect of various superdisintegrants crospovidone, sodium starch glycolate, croscarmellose sodium was also studied. The prepared tablets were evaluated for taste, crushing strength, disintegration time and dissolution.⁷

Singh SK et al., (2009), prepared fast disintegrating combination tablets of omeprazole and domperidone by using pertinent disintegrant. The tablets were prepared using mannitol as diluent and sodium saccharin as sweetening agent along with three different levels of disintegrant. The superdisintegrant used in this study were Kollidon CL, Ac-di-sol and SSG. The tablets were evaluated for weight variation, hardness, friability, wetting time, water absorption ratio, disintegration time and dissolution study. Using the same excipients, the tablets were prepared by direct compression and were evaluated in the similar way. Drug content was estimated by using HPLC. Tablet formulation prepared with 4.76% Ac-di-sol i.e. 10 mg showed
disintegration time 15 s. Also the hardness, friability, dissolution rate and assay of prepared tablets were found to be acceptable according to standard limits.\textsuperscript{8}

\textbf{Shirsand SB et al., (2009),} designed fast disintegrating tablets of prochlorperazine maleate by direct compression method. Mucilage of plantago ovata and crospovidone were used as superdisintegrants (2-8\% w/w) along with microcrystalline cellulose (20-60\% w/w) and directly compressible mannitol to enhance mouth feel. The prepared batches of tablets were evaluated for hardness, friability, drug content uniformity, wetting time, water absorption ratio and \textit{in vitro} dispersion time. Formulation prepared by using 8\% w/w of plantago ovata mucilage and 60\% w/w of microcrystalline cellulose emerged as the overall best formulation.\textsuperscript{9}

\textbf{Fars KA, (2007),} formulated metoclopramide FDT with sufficient mechanical strength and fast disintegration from bases prepared by both spray and freeze drying techniques. Different disintegration accelerators were utilized to prepare the proper FDT using various superdisintegrants (Ac-di-sol, kollidon and sodium starch glycolate), a volatilizing solvent (ethanol) and an amino acid (glycine).\textsuperscript{10}

\subsection*{2.2 Fast Dissolving Tablet of Other Drugs}

\textbf{Khemariya P et al., (2010),} developed mouth dissolving tablet of meloxicam by sublimation technology. The tablets were prepared by wet granulation procedure. The tablets were evaluated for friability, wetting and disintegration time. Sublimation of camphor from tablets resulted in better tablets as compared to the tablets prepared from granules that were exposing to vacuum.\textsuperscript{11}

\textbf{Bhardwaj S et al., (2010),} developed fast disintegrating tablets of accelofenac. Tablets were prepared by sodium starch glycolate following by direct compression technique. The tablets were evaluated for hardness, friability, weight variation, disintegration time, water absorption ratio and wetting time. All the formulation showed disintegration time in range of 12.2 to 27.5 s along with rapid \textit{in vitro} dissolution.\textsuperscript{12}

\textbf{Abed KK et al., (2010),} prepared orodispersible tablets of diazepam using different types of superdisintegrants (Ac-di-sol, sodium starch glycolate and crospovidone and different types of subliming agents camphor and ammonium bicarbonate at different concentrations and two methods of tablets preparations (wet granulation and direct compression methods). The formulations were evaluated for flow properties, wetting time, hardness, friability, content uniformity, \textit{in vivo} disintegration time, release
profiles and buccal absorption tests. All formulations showed satisfactory mechanical strength except formulation which contains camphor and formulation which was prepared by direct compression method. The results revealed that the tablets containing crospovidone as a superdisintegrant had good dissolution profile with shortest disintegration time.\textsuperscript{13}

Chandira RM \textit{et al.}, (2010), prepared FDT of etoricoxib using variety of superdisintegrants like primogel, kollidone, Ac-di-sol, L-HPMC, L-HPC. The prepared tablets were evaluated for weight variation, hardness, friability, \textit{in vitro} disintegration time, wetting time and \textit{in vitro} dissolution study. Formulation contain L-HPC 8\% shows the lowest disintegration time (44 s) and wetting time (52 s).\textsuperscript{14}

El-Massik MA \textit{et al.}, (2010), utilized a maltodextrin to prepare orally disintegrating tablets of meclizine. Tablets were prepared by both direct compression and wet granulation techniques. The effect of maltodextrin concentrations on ODT characteristics-manifested as hardness and disintegration time-was studied. The effect of conditioning as a post-compression treatment on ODT characteristics was also assessed. Maltodextrin-pronounced hardening effect was investigated using differential scanning calorimetry (DSC) and X-ray analysis.\textsuperscript{15}

Keny RV \textit{et al.}, (2010), developed mouth disintegrating tablets of rizatriptan benzoate to produce the intended benefit. Mouth dissolving tablets of rizatriptan benzoate were prepared using superdisintigrant crospovidone, carboxymethylcellulose calcium, indion 414 and indion 234 using direct compression method. The tablets prepared were evaluated for thickness, uniformity of weight, content uniformity, hardness, friability, wetting time, \textit{in vivo} and \textit{in vitro} disintegration time, mouth feel, \textit{in vitro} drug release and assay by high performance liquid chromatography.\textsuperscript{16}

Parikh BN \textit{et al.}, (2010), developed solid oral formulations of telmisartan which can be prepared using less complicated and expensive processes and fulfill all prerequisites for pharmaceutical use, i.e. long-lasting stability of the formulation under different climatic conditions and sufficient solubility of the active substance for sufficient gastrointestinal absorption in the slightly acidic and neutral pH region. Preferably, the formulations should have immediate release characteristics and a dissolution showing no essential pH dependency within the physiological relevant pH interval of the gastrointestinal tract. Tablets were evaluated for various parameters like, weight
variation, content uniformity, in-vitro dissolution studies were performed using United States Pharmacopeia (USP) apparatus type II.\textsuperscript{17}

**Shid SL et al., (2010)**, prepared orodispersible tablets of flurbiprofen using various superdisintegrants such as croscarmellose sodium, sodium starch glycolate, crospovidone and camphor (as subliming agent) in different ratio and subjected for evaluation. Results revealed that the tablets of all formulations have acceptable physical parameters.\textsuperscript{18}

**Rajalakshmi G et al., (2010)**, formulated pheniramine maleate a selective H\textsubscript{1} receptor antagonist into orodispersible tablets. The tablets were prepared by direct compression method using superdisintegrants like croscarmellose sodium, crospovidone, sodium starch glycolate, low hydroxypropyl cellulose and pre-gelatinized starch in different ratios. The blends examined for various pre compression parameters. Tablets were evaluated by measuring hardness, friability, content uniformity, weight variation and drug release pattern.\textsuperscript{19}

**Kalia A et al., (2009)**, prepared mouth dissolving tablets of oxcabazepine using two different technologies, direct compression method and solid dispersion technology. Tablets produced by direct compression method contain crospovidone as a superdisintegrant and aspartame as a sweetener. Solid dispersions of oxcabazepine with polyvinylpyrrolidone K-30 and polyethylene glycol 6000 in different weight ratios were prepared with a view to increase its water solubility. Oxcabazepine solid dispersions with polyvinylpyrrolidone K-30 in 1:2 ratios of drug: carrier showed maximum drug release and hence, compressed along with other excipients into mouth dissolving tablet. The results compared for both the technologies showed that the oxcabazepine tablets prepared using solid dispersion technology was found to have good technological properties and satisfying and reproducible drug dissolution profiles.\textsuperscript{20}

**Rao NG et al., (2009)**, developed rapidly disintegrating oral tablets by direct compression using cogrinding and solid dispersion methods by using chlorthalidone as a model drug. The tablet formulation containing polyvinyl pyrrolidone K-12 solid dispersion showed maximum drug release than the chlorthalidone polyvinyl pyrrolidone K-12 co-grinding method. The prepared tablets were evaluated for hardness, friability, wetting time, disintegration time and *in vitro* drug release. DSC
and FTIR studies revealed that no chemical interaction between the drug and the carrier. The stability studies were conducted as per the ICH guidelines and the formulations were found to be stable with insignificant change in the hardness, and disintegration time.\textsuperscript{21}

**Kumar DN \textit{et al.}, (2009),** prepared fast dissolving tablets of fexofenadine by effervescent method with a view to enhance patient compliance. Three superdisintegrants viz., crospovidone, croscarmellose sodium and sodium starch glycolate along with sodium bicarbonate and anhydrous citric acid in different ratios were used and directly compressible mannitol to enhance mouth feel property of tablets. The prepared batches of tablets were evaluated for hardness, friability, drug content uniformity and \textit{in vitro} dispersion time. Among the three promising formulations, the formulation containing 8\% w/w of crospovidone and mixture of 24\% w/w sodium bicarbonate, 18\% w/w of anhydrous citric acid emerged as the best based on the \textit{in vitro} drug release characteristics compared to conventional commercial tablet formulation. Short-term stability studies on the formulations indicated that there were no significant changes in drug content and \textit{in vitro} dispersion time (P<0.05).\textsuperscript{22}

**Swamy PV \textit{et al.}, (2009),** designed orodispersible tablets of pheniramine maleate by effervescent method. Mixture of sodium bicarbonate and tartaric acid were used along with superdisintegrants pregelatinized starch, sodium starch glycolate, croscarmellose sodium and crospovidone. The prepared batches of tablets were evaluated for hardness, friability, drug content uniformity and \textit{in vitro} dispersion time. Formulation containing 4\% w/w crospovidone and mixture of sodium bicarbonate and tartaric acid emerged as the overall best formulation.\textsuperscript{23}

**Devireddy SR \textit{et al.}, (2009),** formulated orally disintegrating tablets of levocetirizine dihydrochloride with different superdisintegrants (sodium starch glycollate, croscarmellose sodium, and crospovidone) using mannitol as a diluent. Tulsion-335, Indion-204 and poly kyron T-134 cation exchange resins were used as taste-masking agents. The drug and resin complex was prepared by the kneading method. Ten formulations were prepared with varying combinations of superdisintegrants and ion-exchange resins by the wet granulation technique, using polyvinylpyrrolidone K-30 as the binder. The prepared tablets were evaluated for degree of taste masking, weight variation, hardness, friability, \textit{in vitro} and \textit{in vivo} disintegration time, content uniformity and water absorption ratio.\textsuperscript{24}
Okuda Y et al., (2009), designed a new orally disintegrating tablet that has high tablet hardness and a fast oral disintegration rate using a new preparation method. To obtain rapid disintegration granules (RGD), a saccharide, such as trehalose, mannitol, or lactose, was spray-coated with a suspension of corn starch using a fluidized-bed granulator. As an additional disintegrant, crospovidone, light anhydrous silicic acid, or hydroxypropyl starch was also included in the suspension. The RDGs obtained possessed extremely large surface areas, narrow particle size distribution, and numerous micro-pores. When tabletting these RDGs, it was found that the RDGs increased tablet hardness by decreasing plastic deformation and increasing the contact frequency between granules. In all tablets, a linear relationship was observed between tablet hardness and oral disintegration time.25

Giri TK and Sa B, (2009), described the formulation of rapidly disintegrating, diazepam tablets. The tablets were prepared by the conventional wet granulation method using solid dispersion of the drug with PEG-4000 and/or PEG-6000. A $3^2$ factorial design was used to reduce the number of experimental runs and to obtain several formulations by which tablets disintegrated within 3 min and released 85% of the drug in less than 30 min. Several tablet formulations prepared with different amounts of PEGs in solid dispersion met the above two criteria. However, tablets which were prepared with PEG-4000 alone at the lowest concentration disintegrated in the shortest time (32.12 s) and released 85% of the drug most rapidly (11.03 min).26

Gupta A et al., (2009), investigated correlation between disintegration and dissolution for immediate release tablets containing a high solubility drug and to identify formulations where disintegration test, instead of the dissolution test, may be used as the acceptance criteria based on International Conference on Harmonization Q6A guidelines. A statistical design of experiments was used to study the effect of filler, binder, disintegrating agent and tablet hardness on the disintegration and dissolution of verapamil hydrochloride tablets. All formulation variables, i.e., filler, binder and disintegrating agent were found to influence tablet dissolution and disintegration, with the filler and disintegrating agent exerting the most significant influence.27

Jacob S et al., (2009), prepared fast dissolving effervescent tablets were prepared by the modification of nonreactive liquid based wet granulation technique. 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 and
thereby does not delay the reaction between the acid source and base.\(^{28}\)

**Singh J and Singh R, (2009),** formulated and optimized orodispersible tablets of
meloxicam using a \(2^2\) factorial design for enhanced bioavailability. The tablets were
made by non-aqueous wet granulation using crospovidone and mannitol. A \(2^2\) factorial
design was used to investigate the amount of crospovidone and taste masking,
soothening hydrophilic agent (mannitol), as independent variables and disintegration
time as dependent response.\(^{29}\)

**Madan J et al., (2009),** prepared fast dissolving tablets of the nutraceutical, freeze-
dried aloe vera gel by dry granulation method. The tablets were evaluated for crushing
strength, disintegration time, wetting time, friability, drug content and drug release. A
\(3^2\) full factorial design was applied to investigate the combined effect of two
formulation variables - amounts of microcrystalline cellulose and mannitol. The results
of multiple regression analysis revealed that in order to obtain fast dissolving tablets of
the aloe vera gel, an optimum concentration of mannitol and a higher content of
microcrystalline cellulose should be used.\(^{30}\)

**Late SG et al., (2009),** investigated effects of calcium silicate (disintegration-
promoting agent) and various lubricants on an optimized cyclodextrin-based fast
disintegrating tablets formulation. Effects of moisture treatment were also evaluated at
75, 85 and 95% relative humidities. A two factors at three levels (\(3^2\)) full factorial
design were used to optimize concentrations of calcium silicate and lubricant.
Magnesium stearate, being commonly used lubricant, was used to optimize lubricant
concentration in optimization study. Results of multiple linear regression analysis
revealed that concentration of calcium silicate had no effect; however concentration of
lubricant was found to be important for tablet disintegration and hardness.\(^{31}\)

**Fujii M et al., (2009),** investigated 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 tabletting
process analyzer. Results indicated that the bulk density of mixed excipient powder
used for tablet preparation affects both DTM and STP. As the value of bulk density increased, STP became longer and DTM shorter. The results of a combination of granules and powder with or without drug showed linear relation between apparent volume and DTM ($r^2 = 0.7332$). For a DTM less than 60 s, a formulation with a bulk density greater than 0.5 g/mL should be chosen with a compression force of 5 kN. The hardness of tablets could be greater than 3 kg if at least one high-compressibility excipient was used in the formulation.32

Madgulkar et al., (2009), developed novel taste masked mouth-dissolving tablets of tramadol that overcomes principle drawback of such formulation which was inadequate mechanical strength. In this work, the bitter taste of tramadol HCl was masked by forming a complex with an ion exchange resin Tulsion335. The novel combination of a superdisintegrant and a binder that melts near the body temperature was used to formulate mechanically strong tablets that showed fast disintegration. A $3^2$ full factorial design and statistical models were applied to optimize the effect of two factors, i.e., superdisintegrant (crospovidone) and a mouth-melting binder (gelucire 39/01). It was observed that the responses, i.e., disintegration time and percent friability were affected by both the factors. The statistical models were validated and can be successfully used to prepare optimized taste masked mouth-dissolving tablets of tramadol HCl with adequate mechanical strength and rapid disintegration.33

Zade PS et al., (2009), prepared bitterless fast dissolving tablet of tizanidine hydrochloride using Eudragit E 100 as a taste masking agent. Mass extrusion was the technique used for preparing taste masked granules. The tablets were prepared with three superdisintegrants e.g. sodium starch glycolate, crosscarmellose sodium and crospovidone.34

Chaulang G et al., (2009), prepared solid dispersion of furosemide in SSG in ratios of 1:1 and 1:2 by kneading method. The solid dispersion was characterized FTIR, DSC and XRD to ascertain if there were any physicochemical interactions between drug and carrier that could affect dissolution. Tablets containing the solid dispersion were formulated and their dissolution characteristics compared with commercial furosemide tablets.35

Furtado S et al., (2008), prepared orodispersible tablets of famotidine using camphor as subliming agent and sodium starch glycollate together with crosscarmellose sodium
as superdisintegrants. The formulations were evaluated for weight variation, hardness and friability, drug content, wetting time, *in vitro* and *in vivo* dispersion time, mouth feel and *in vitro* dissolution. The results revealed that the tablets containing subliming agent had a good dissolution profile.\(^{36}\)

**Mohapatra A et al., (2008),** prepared the tablets of metformin using starch RX1500 and microcrystalline cellulose by direct compression. The tablets showed erosion behavior rather than disintegration. Then lactose was incorporated which created pores to cause burst release of drug. But these tablets did not give good mouth feel. Thus, Pearlitol SD 200 (spray dried mannitol) was used to prepare tablets by wet granulation (10% polyvinylpyrrolidone in Isopropyl alcohol as binder). The optimized batches of tablets not only exhibited desired mouth feel but also disintegration time, *in vitro* dispersion time, water absorption ratio and *in vitro* drug release. All the batches contained 15% starch and 4% of croscarmellose sodium.\(^{37}\)

**Kuno Y et al., (2008),** 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. The effect of the type of lubricant on the tablet characteristics was evaluated using magnesium stearate, sodium stearyl fumarate (SSF) and talc as lubricants.\(^{38}\)

**Seong HJ and Kinam P, (2008),** investigated complex formation between drugs and ion-exchange resins and the effects of coating by various aqueous polymeric dispersions on the complexes were evaluated for developing new sustained-release fast-disintegrating tablets. Complexes of ion-exchange resin and dextromethorphan, a model drug, were prepared using different particle sizes of the resins. Based on drug loading, release profiles and scanning electron microscopy images, the coated particles were granulated with suitable tablet excipients and then compressed into the tablets. As the particle size of resins increased, the drug loading and release rate decreased due to the reduced effective diffusion coefficient and surface area.\(^{39}\)

**Patel IM and Patel MM, (2008),** developed fast dissolving tablets of etoricoxib. Granules containing etoricoxib, crospovidone, aspartame and menthol prepared by wet granulation technique. Menthol was sublimed from the granules by exposing the granules to vacuum. The porous granules were then compressed into tablets.
Alternatively, the tablets were prepared and later exposed to vacuum. The tablets were evaluated for percentage friability and disintegration time. A $3^2$ full factorial design was applied to investigate the combined effect of two formulation variables; amount of menthol and crospovidone. The result of multiple regression analysis indicated that for obtaining for fast dissolving tablet optimum amount of menthol and higher percentage of crospovidone should be used.\textsuperscript{40}

**Masareddy RS et al., (2008),** studied two different methods direct compression and sublimation in formulation of mouth dissolving tablets of clozapine. Total four formulations using various superdisintegrants and subliming agents were prepared. All prepared formulations were evaluated for physico-chemical parameters. The formulations exhibited good disintegration properties with total disintegration time in the range of 25 to 35 s. Comparative evaluation of two methods showed direct compression method was a better alternative to sublimation method as its formulations rapidly disintegrate in oral cavity. Kinetic studies indicated that all the formulations followed first order release with diffusion mechanism.\textsuperscript{41}

**Shen YC et al., (2007),** designed an orally disintegrating tablet formulation of olanzapine to dissolve rapidly upon contact with saliva also described a manic patient who has an esophageal stricture and chronic pharyngitis, two conditions that impede the swallowing of medications. She was successfully treated for her mania with this orally disintegrating formulation.\textsuperscript{42}

**Mohammad BJ et al., (2007),** prepared carbamazepine solid dispersions by the co-grinding technique using an insoluble but highly hydrophilic crospovidone and soluble hydroxypropylmethylcellulose (HPMC) as the carriers. The ratios of drug to carrier were 1:1, 1:5 and 1:10. Comparison of the dissolution of the drug from its cogrounds with that of the unground drug, its ground form and the corresponding physical mixtures revealed considerable differences. The percentage of drug dissolved during the first 30 min ($\%D_{30}$), for the ground and coground drug was 75-95, whereas the $\%D_{30}$ for ungrounded drug and its physical mixtures ranged from 41-62.\textsuperscript{43}

**Malke S et al., (2007),** prepared fast dissolving tablets of oxycarbazepine containing Avicel PH 102 as a diluent and Ac-di-sol as a superdisintegrant by wet granulation process. All the formulations were evaluated for characteristics such as hardness, friability, weight variation, wetting ability, disintegration time and dissolution rate.\textsuperscript{44}
Pandey PV and Amarnath R, (2007), investigated performance of three disintegrants, sodium starch glycolate, croscarmellose sodium and crospovidone using intragranular and extragranular methods, both in the same quantity of 2% w/w. Chloroquine phosphate was the drug of choice for the present study. Other excipients used in the formulation of tablets were lactose monohydrate, polyvinylpyrrolidone K-30 (PVP K-30), aerosil and magnesium stearate.

Modi A and Tayade P, (2006), investigated enhancement of the dissolution profile of valdecoxib using solid dispersion with polyvinylpyrrolidine. They also described the preparation of fast-dissolving tablets of valdecoxib by using a high amount of superdisintegrants. A phase solubility method was used to evaluate the effect of various water-soluble polymers on aqueous solubility of valdecoxib.

Ahmed IS et al., (2006), developed ketoprofen tablets which dissolve rapidly in the mouth. The solubility and dissolution rate of poorly water-soluble ketoprofen was improved by preparing a lyophilized tablet of ketoprofen using freeze-drying technique.

Cirri M et al., (2006), developed a tablet formulation based on an effective flurbiprofen-cyclodextrin system, able to allow a rapid and complete dissolution of this practically insoluble drug. Three different cyclodextrins were evaluated the parent beta-cyclodextrin (previously found to be the best partner for the drug among the natural cyclodextrins) and two amorphous, highly soluble beta-cyclodextrin derivatives, i.e., methyl-beta-cyclodextrin and hydroxyethyl-beta-cyclodextrin.

Shishu and Bhatti A, (2006), formulated compressed tablets of diazepam using microcrystalline cellulose as directly compressible filler and sodium starch glycolate as superdisintegrant. The taste masked microspheres were prepared using amino alkyl methacrylate copolymer (Eudragit E-100) by solvent evaporation technique. Taste evaluation of these microspheres was done by both spectrophotometric taste evaluation technique and panel testing.

Takagi H et al., (2005), established a pharmaceutical composition useful for rapid disintegration, which comprises of a sparingly soluble medicament held on a gel-forming water-soluble polymer as a solid dispersion.

Francesco C, (2005), studied the feasibility of preparing fast-dissolving mucoadhesive microparticulate delivery systems containing amorphous piroxicam to
Literature Review

improve drug residence time on sublingual mucosa and drug dissolution rate. The two new mucoadhesive carriers Eudragit L 100 and Eudragit S 100 sodium salts, both characterized by a fast intrinsic dissolution rate, have selected.\textsuperscript{51}

\textbf{Rasetti EC and Grange V, (2005),} developed new non-steroidal anti-inflammatory drugs (NSAID) formulations with faster onset of analgesic action like fast dissolving tablets. An open-label, randomized, single dose, crossover study with a 18 days washout period was conducted in 16 healthy volunteers to compare the pharmacokinetic profile of 20 mg piroxicam freeze-dried tablet (Proxalyoc, Cephalon) with that of 20 mg piroxicam capsule (Feldene, Pfizer).\textsuperscript{52}

\textbf{Abdelbary G et al., (2005),} assessed the \textit{in vitro} disintegration profile of rapidly disintegrating tablets (RDT) was very important in the evaluation and the development of new formulations of this type. So far neither the US Pharmacopoeia nor the European Pharmacopoeia has defined a specific disintegration test for RDT; currently, it was only possible to refer to the tests on dispersible or effervescent tablets for the evaluation of RDT's disintegration capacity. In the present study, they have evaluated the disintegration profile of RDT manufactured by main commercialized technologies, using the texture analyzer.\textsuperscript{53}

\textbf{Yoshio K et al., (2005),} studied the properties of rapidly disintegrating (RD) tablets manufactured by the phase transition method. RD tablets were produced by compressing powder containing erythritol (melting point: 122°) and xylitol (melting point: 93-95°) and then heating at about 93° for 15 min. The hardness and oral disintegration time of the heated tablets increased with an increase of the xylitol content.\textsuperscript{54}

\textbf{Kuchekar BS et al., (2004),} in the present work, an attempt was made to formulated and evaluated mouth dissolving tablets of salbutamol sulphate. Formulations were prepared by factorial design technique. Different disintegrates were used to formulate fast dissolving tablets.\textsuperscript{55}

\textbf{Abu-Izza et al., (2004),} formulated tablets which dissolve rapidly in the mouth and provide an excellent mouth feel. The tablets of the invention comprise a compound, which melts at about 37° or lower, have a low hardness, high stability and generally comprise few insoluble disintegrants which may cause a gritty or bulky sensation in
the mouth. Convenient and economically feasible processes by which the tablets of the invention may be produced were also provided.56

Mizumoto T et al., (2004), developed a quick disintegrating tablet in buccal cavity, comprising a mixture of drug, a sugar (A) and an amorphous sugar (B) and after forming a tablet, it was humidified and dried. The tablet in the present invention was to provide stability against moisture at preserved, because the amorphous sugar changed to the crystalline state in a non-reversible reaction after it was humidified and dried in a manufacturing process.57

Johnson ES and Lacy J, (2004), formulated a composition for oral administration comprising a carrier and as active ingredient, an opioid (μ-receptor) agonist, such as fentanyl or a salt thereof, characterized in that the composition was in the form of a fast-dispersing dosage form designed to release the active ingredient rapidly in the oral cavity.58

Luber J and Bunick FJ, (2004), studied an immediate release tablet capable of being chewed or disintegrated in the oral cavity, which comprises a pharmaceutically active ingredient and a matrix comprising polyethylene oxide having a weight average molecular weight of from about 500,000 to about 10,000,000. The tablets possesses exceptionally good mouth feel and stability.59

Hall M et al., (2004), developed a composition comprising a carrier and an active ingredient, wherein the carrier was fish gelatin and the composition was a fast-dispersing dosage form designed to release the active ingredient rapidly on contact with a fluid. In one embodiment, the composition was designed for oral administration and releases the active ingredient rapidly in the oral cavity on contact with saliva. The fish gelatin can be obtained from cold water fish sources and was preferably the non-gelling, non-hydrolyzed form. A process for preparing such a composition and a method of using fish gelatin in a fast dispersing dosage form were also provided.60

Lalla JK and Mamania HM, (2004), studied the inclusion complex of rofecoxib, an NSAID with β-cyclodextrin using ball milling technique has been prepared and evaluated using differential scanning calorimetry thermograph. The fast dissolving tablet composition with 25 mg equivalent rofecoxib showed complete release of
rofecoxib in 12 min as compared to 20% drug release from the conventional release marketed tablets during the same period.\textsuperscript{61}

Shirwaikar AA and Ramesh A, (2004), formulated atenolol as fast disintegrating tablets using three superdisintegrants, croscarmellose sodium (Ac-di-sol), crospovidone (Polyplasdone XL) and sodium starch glycolate (Explotab). All the superdisintegrants were used at different concentration levels to assess their efficiency and critical concentration level.\textsuperscript{62}

Valleri M et al., (2004), investigated the possibility of developing glyburide tablets, allowing fast, reproducible and complete drug dissolution, by using drug solid dispersion in polyethylene glycol. The glyburide dissolution profile from the newly developed tablets was clearly better than those from various commercial tablets at the same drug dosage.\textsuperscript{63}

Drooge DJ et al., (2004), studied anomalous dissolution behavior of tablets consisting of sugar glass dispersions was investigated. The poorly aqueous soluble diazepam was used as a lipophilic model drug. The release of diazepam and sugar carrier was determined to study the mechanisms governing dissolution behavior.\textsuperscript{64}

Gohel M et al., (2004), developed mouth dissolving tablets of nimesulide. Granules containing nimesulide, camphor, crospovidone and lactose were prepared by wet granulation technique. Camphor was sublimed from the dried granules by exposure to vacuum. The porous granules were then compressed. Alternatively, tablets were first prepared and later exposed to vacuum. The tablets were evaluated for percentage friability, wetting time, and disintegration time. In the investigation, a $3^2$ full factorial design was used to investigate the joint influence of 2 formulation variables: amount of camphor and crospovidone.\textsuperscript{65}

Schroeder M and Steffens K, (2003), prepared rapidly disintegrating preparations containing at least one active pharmaceutical ingredient and at least one excipient by a simple process in which the predominant part of the complete composition of the ingredients was granulated, the resulting granules and where appropriate, the remainder of the ingredients were shaped in the presence of liquid virtually without pressure, and the resulting shaped articles were dried.\textsuperscript{66}

Zakarian N et al., (2003), invented dispersible tablets containing macrolides as active ingredients either on their own or associated with other active ingredients, in addition
to a method for the production thereof. The dispersible tablets were characterized in that the macrolide was chosen from a group that was made up of pristinamycin, azithromycin, roxithromycin, clarithromycin and spiramycin.\textsuperscript{67}

**Murray OJ et al., (2003)**, studied fast dispersing solid dosage forms that preferably dissolve in the oral cavity within sixty, more preferably within thirty, most preferably within ten seconds. A novel feature of the solid dosage forms according to the invention resided in the fact that the composition was essentially free or absolutely free of mammalian gelatin.\textsuperscript{68}

**Laruelle C et al., (2003)**, established pharmaceutical dosage forms with rapid disintegration in the mouth and to their process of preparation. The pharmaceutical dosage forms comprised of at least one active principle dispersed in a mixture of excipients and were characterized in that the mixture of excipients comprised at least one weakly compressible diluting agent other than trehalose and a copolymer of 1-vinylpyrrolidin-2-one and of vinyl acetate.\textsuperscript{69}

**Murali M et al., (2002)**, designed nimodipine tablets with fast in vitro release rates using nimodipine-modified gum karaya co-grinding mixtures. Co-grinding mixtures of nimodipine and gum karaya were also prepared to highlight the efficiency of modified gum karaya.\textsuperscript{70}

**El-Arini SK and Clas SD, (2002)**, studied in vitro disintegration behavior of fast dissolving system, manufactured by the main commercialized technology, using the texture analyzer instrument.\textsuperscript{71}

**Simone S and Peter CS, (2002)**, prepared two types of tablets containing coated ibuprofen as a high dosed model drug. The properties of the water dispersible tablet, such as porosity, hardness, disintegration time and increase in viscosity after dispersion, were investigated. The selected tablet formulation, containing 26\% galactomannan and 5\% crospovidone, disintegrated before the galactomannan started to swell. These tablets dispersed in water within 40 s and showed a crushing strength of 95 N.\textsuperscript{72}

**Sunanda H and Bi Y, (2002)** developed rapidly disintegrating tablets using both direct compression and wet compression methods. Tablet properties such as porosity, tensile strength, wetting time and disintegration time were evaluated and the formulation and disintegration time of the tablets were elucidated. Formulation and
preparation conditions were optimized using polynomial regression or artificial neural network.\textsuperscript{73}

Khankari \textit{et al.}, (2001), formulated a rapidly dissolving robust dosage form. The invention was directed to a hard tablet that can be stored, packaged and processed in bulk. The tablet dissolved rapidly in the mouth of the patient with a minimum of grit. The tablet was created from an active ingredient mixed into a matrix of no direct compression filler and a relatively high lubricant content.\textsuperscript{74}

Gilis P and De Conde V, (2000), formulated a fast-dissolving tablets for oral administration comprising of an active ingredient, a therapeutically effective amount of galanthamine hydrobromide and a pharmaceutically acceptable carrier, characterized in that the said carrier comprised a spray-dried mixture of lactose monohydrate and microcrystalline cellulose as diluents, and a disintegrant; and direct compression process for preparing such fast dissolving tablets was used.\textsuperscript{75}

2.3 Formulations of Promethazine Theoclate

Argemi A \textit{et al.}, (2010), prepared and characterized of transdermal patches of promethazine. A mixture of ethylene vinyl acetate and Eudragit (E100) (80:20, w/w) was used as a polymeric matrix to obtain a thin membrane. Patches synthesized in this way were loaded with about 1% promethazine. The drug release and diffusion process through a membrane have been studied chromatographically using a Franz diffusion cell. Results have shown that a sustained delivery for more than 24 h was obtained.\textsuperscript{76}

Bhanja S \textit{et al.}, (2010), formulated and evaluated of mucoadhesive buccal tablets containing promethazine to circumvent the first pass effect and to improve its bioavailability with reduction in dosing frequency and dose related side effects. The tablets were prepared by direct compression method. Eight formulations were developed with varying concentrations of polymers like carbopol 934, polyethylene oxide and hydroxy propyl methyl cellulose. The tablets were tested for weight variation, hardness, surface pH, drug content uniformity, swelling index and bioadhesive strength and \textit{in-vitro} drug dissolution study. The \textit{in vitro} release kinetics studies reveal that all formulations fits well with zero order kinetics followed by korsmeyer-peppas, first order and then higuchi’s model and the mechanism of drug release was non-fickian diffusion.\textsuperscript{77}
Adhikari SN et al., (2010), developed buccal patches for the delivery of promethazine using sodium alginate with various hydrophilic polymers like carbopol 934 P, sodium carboxymethyl cellulose, and hydroxypropyl methylcellulose in various proportions and combinations were fabricated by solvent casting technique. Various physicomechanical parameters like weight variation, thickness, folding endurance, drug content, moisture content, moisture absorption, and various ex vivo mucoadhesion parameters like mucoadhesive strength, force of adhesion and bond strength were evaluated. An in vitro drug release study was designed and it was carried out using commercial semipermeable membrane. All these fabricated patches were sustained for 24 h and obeyed first-order release kinetics.\textsuperscript{78}

Patel RS and Poddar SS, (2009), prepared and evaluated of mucoadhesive buccal patches for the controlled systemic delivery of promethazine theoclate to avoid first pass hepatic metabolism. The developed patches were evaluated for the physicochemical, mechanical and drug release characteristics. The patches showed desired mechanical and physicochemical properties to withstand environment of oral cavity. The in vitro release study showed that patches could deliver drug to the oral mucosa for a period of 7 h. The patches exhibited adequate stability when tested under accelerated conditions.\textsuperscript{79}

Sekhar K et al., (2008), described buccal permeation of promethazine theoclate and its transbuccal delivery using mucoadhesive buccal patches. Permeation of drug was calculated in vitro using porcine buccal membrane and in vivo in healthy humans. Buccal formulations were developed with hydroxyethylcellulose and evaluated for in vitro release, moisture absorption, mechanical properties and bioadhesion. Optimized formulation was subjected for bioavailability studies in healthy human volunteers.\textsuperscript{80}

2.4 Formulations of Prochlorperazine Maleate

Obata Y et al., (2010), developed transdermal drug delivery system for prochlorperazine (PCPZ) and performed an in vitro skin permeation study with hairless mouse skin. When the concentration of L-menthol in the hydrogel was 0-0.5%, the PCPZ flux was small; on the other hand, the flux was increased remarkably when the L-menthol concentration was higher than 1%. The optimal formulation of hydrogel would be contained 20% isopropanol (IPA), 10% N-methyl-2-pyrrolidone (NMP), 2% L-menthol and 1% PCPZ. The strong inhibitory effects to
stereotyped behavior were observed at 4 h after administration of PCPZ hydrogel, and the efficacy was sustained for at least 8 h after the administration in mice \textit{in vivo}. Thus, it was considered that PCPZ was delivered to brain via systemic circulation by the administration of PCPZ hydrogel.\textsuperscript{81}

\textbf{Suresh S et al., (2010)}, designed fast disintegrating tablets of prochlorperazine maleate with crospovidone (upto 3\% w/w) and croscarmellose sodium (upto 5\% w/w) in combination were used as superdisintegrants. The prepared formulations were evaluated for hardness, friability, drug content uniformity, dispersion time, wetting time and water absorption ratio. Among the formulations tested, formulation containing 5\% w/w of croscarmellose sodium and 3\% w/w of crospovidone as superdisintegrant emerged as the overall best based on drug release characteristics in pH 6.8 phosphate buffer compared to commercial conventional tablet formulation.\textsuperscript{82}

\textbf{Misao N et al., (2009)}, developed oral disintegrating film containing prochlorperazine using microcrystalline cellulose, polyethylene glycol and hydroxypropylmethyl cellulose as the base materials. The uniformity of dosage units of the preparation was acceptable according to the criteria of JP15 or USP27. The film showed an excellent stability at least for 8 weeks when stored at 40\degree and 75\% in humidity. The dissolution test revealed a rapid disintegration property, in which most of prochlorperazine dissolved within 2 min after insertion into the medium.\textsuperscript{83}

\textbf{Finn A et al., (2005)}, developed buccal dosage form of prochlorperazine and also conducted two clinical studies to characterize the single-dose and multiple-dose pharmacokinetics of prochlorperazine and its metabolites after buccal administration. The results of these studies demonstrate that buccal administration of prochlorperazine produces plasma concentrations more than twice as high as an oral tablet, with less than half the variability. In addition to the metabolites, N-desmethyl prochlorperazine and prochlorperazine sulfoxide, 2 new metabolites, prochlorperazine 7-hydroxide and prochlorperazine sulfoxide 4-N-oxide, were identified and quantitated. Exposure to metabolites after the buccal prochlorperazine formulation was approximately half that observed after the oral tablet. Buccal administration of prochlorperazine, twice daily, should enhance the therapeutic role of prochlorperazine in preventing and treating nausea and vomiting.\textsuperscript{84}
Singh S et al., (1999), prepared and evaluated buccal prochlorperazine (Bukatel) for its efficacy and tolerability with commonly used metoclopramide. Bukatel was well tolerated and well rated by both patients and investigators with no adverse effects on buccal mucosa and causing less drowsiness and sedation. Results indicated that Bukatel was safe and effective for the treatment of nausea and/or vomiting in patients suffering from vertiginous disorders and could be safely and strongly recommended as an alternative to less bioavailable and indiscriminately used oral metoclopramide tablets.\(^{85}\)

Nagarsenker MS et al., (1998), prepared coevaporates of prochlorperazine maleate (PCPM) by using different polymers by solvent evaporation technique. Ethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose phthalate were used in preparation of coevaporates. The coevaporates were characterized by X-ray diffraction studies, IR spectrophotometry and Differential scanning calorimetry. Dissolution behavior of coevaporates was studied using buffer solution with pH 1.2 and 6.8 by half change method. A two level, two factor factorial design was used to quantitate effect of polymers on dissolution profile of PCPM. Dissolution of drug in pH 6.8 buffer improved with increasing content of hydroxypropyl methylcellulose phthalate in coevaporates.\(^{86}\)
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