2. REVIEW OF LITERATURE

From the available literature review, it can be noted that great deal of work has been carried out towards development of orally disintegrating tablets or rapidly disintegrating tablets of various drugs belonging to the NSAIDs, Antihistaminics, Antibacterial, Antiemetics, Antipsychotic drugs etc. using different polymers and disintegrating agents. Watanabe Y, et al., (1997) investigated a new method of preparing high porosity rapidly saliva soluble compressed tablets using mannitol with camphor, a subliming material. These compressed tablets which have high porosity, rapidly dissolved within 15 seconds in saliva in the mouth. A high porosity was achieved due to the formation of many pores where camphor particles previously existed in the compressed mannitol tablets prior to sublimation of the camphor. They also developed a direct compression method for the preparation of tablets using mannitol and camphor of meclizine with high porosity, which dissolves rapidly in saliva

- **Abdelbary G et al., (2005)** determined the in vitro disintegration profile of rapidly disintegrating tablets and correlation with oral disintegration with the use of the Texture analyzer. The have shown in their study that the obtained time-distance profile or disintegration profile and calculated values reflected the mechanism of disintegration of different RDT and gave a qualitative measure of their mouth feel.

- **Akihiko I, et al., (1996)** have developed rapidly disintegrating tablets for elderly patients with impaired swallowing using agar powder and treated agar powders. The rapid disintegration of the treated agar tablets was seemed due to the rapid water penetration into the tablet resulting from the large pore size and large overall pore volume. It was also found that rapidly disintegrating oral tablets with proper hardness could be prepared using treated agar powders.

- **Akinori, et al., (1998)** have invented rapidly releasing and taste masking pharmaceutical dosage form and a process for preparing such oral dosage form. In their invention, the oral dosage form comprises at three layers i.e. a core containing a pharmaceutically active ingredient, low substituted hydroxyl propyl cellulose and microcrystalline cellulose; an inner coating layer containing a water soluble polymer; and an outer coating layer containing a saliva insoluble polymer.

- **Alekha KD, et al., (2000)** formulated rapidly disintegrating calcium carbonate tablets using 3 different forms of calcium carbonate (CC) direct compressed granules. CC tablets were evaluated for disintegration, dissolution properties, surface topography of the granules and tablets, moisture uptake studies, etc. This study clearly demonstrated rapidly disintegrating or quick disintegrating calcium carbonate tablets could be formulated without expensive effervescence technology.
• **Bi YX, et al., (1999)** have designed, optimized and evaluated rapidly disintegrating tablets prepared by a direct compression method. These tablets have sufficient mechanical integrity as well as a pleasant taste. The prepared formulations contained MCC, tablettose, cross-linked CMC or erythritol. Tablet properties such as porosity, tensile strength and disintegration time were determined.

• **Chue P et al., (2004)** investigated the disintegration profile, acceptability and tolerability of orally disintegrating tablets in patients with schizophrenia or schizoaffective disorder. In their investigation ten patients stable for at least 10 days on monotherapy with oral risperidone 2mg to 4mg taken once daily were switched for 7 days to an equivalent dosage of orally disintegrating risperidone and were tolerated and rated as very acceptable by all patients.

• **Danckwerts MP, (2003)** given review on intraoral drug delivery; A comparative drug. This review compares on many different and novel drug delivery system developed for better absorption through oral cavity as well as those that undergo quick disintegration or dissolution in the oral cavity.

• **Francesco Cilurzo et al., (2008)** studied maltodextrins (MDX) with a low dextrose equivalent as film forming material and their application in the design of oral fast-dissolving films. The loading of a drug as a powder decreased the film ductility, but the formulation maintained satisfactory flexibility and resistance to elongation for production and packaging procedures. The films present a high loading capacity, up to 25 mg for a surface of 6 cm². The PRX dissolution rate significantly improved in Series C films independently of the PRX/MDX ratio.

• **Ishikawa T, et al., (2001)** prepared rapidly disintegrating tablet using new types of microcrystalline cellulose (PH-M series) and L-HPC and spherical sugar granules by direct compression method. Sensory evaluation by volunteers showed that PH-M-06 was superior to PH-102 in terms of the feeling of roughness in the mouth. Tablets were also prepared using acetaminophen and ascorbic acid as model drugs and were evaluated.

• **Kaushik D, et al., (2004)** prepared Olanzapine mouth dissolving tablets by effervescent formulation approach. Sodium carbonate and citric acid were used as effervescent agents and their ratio in the formulation was optimized. The study revealed that 10 : 8 ratios of sodium bicarbonate and citric acid in the tablets gave a better soothing fizz, excellent mouth feel, good palatability and quick dissolution profile.
• **Kuchekar BS, et al., (2004)** prepared sumatriptin succinate mouth dissolving tablets using disintegrants such as sodium starch glycolate, carboxy methylcellulose sodium and treated agar by direct compression method. The prepared tablets were evaluated for various parameters. The tablets disintegrate *in-vitro* and *in-vivo* within 10 to 16 S and 12 to 18 S, respectively. The formulations containing combination of sodium starch glycolate and carboxy methylcellulose found to give best result.

• **Kusum Devi V, et al., (2003)** formulated mouth-dissolving tablets of Domperidone by using a meltable binder - PEG-4000, a diluent – mannitol and subliming component – camphor/ ammonium bicarbonate. The amount of volatilizable substance was varied from 10% to 60% w/w to obtain various formulations. Tablets were analyzed and evaluated for different parameters. Formulation of 40% w/w of ammonium bicarbonate and 20% w/w of camphor respectively emerged most satisfactory exhibiting disintegration time 21.33±1.16 second and other parameters also found satisfactory.

• **Lalla JK, et al., (2004)** prepared fast dissolving Rofecoxib tablets by forming inclusion complexes between Rofecoxib and β-cyclodextrin using Ball mill technique, evaluated using DSC. Tablets disintegration times were in the range of 30-40s. The dissolution study indicates either wet or dry granulation showed complete release of drug. Rofecoxib tablets showed complete release in 12 min as compared to 12% drug release from conventional marketed tablets during same period.

• **Mitesh Nagar et al., (2009)** developed mouth dissolving tablets of cinnarzine, they utilized Chitosan Superdisintegrant property to develop a fast mouth dissolving tablet by utilizing a novel method of treatment which can replace any other superdisintegrant. The properties of the rapidly dispersible tablet, such as porosity, hardness, disintegration time, wetting time and dissolution time, were investigated. In conclusion, they succeeded in confirming that the preparation method designed in this research is scalable, industrially applicable and useful for the preparation of ODTs containing drugs with poor solubility and poor bioavailability.

• **Morita Y, et al., (2002)** developed a novel method for evaluating the disintegration time of rapidly disintegrating tablets utilizing a CCD camera. Many kinds of rapidly disintegrating tablets have been developed to improve the ease of tablet administration, especially for elderly and paediatric patients. The novel device consists of a disintegrating bath and CCD camera interfaced with a personal computer equipped with motion capture and image analysis software. In conclusion, this
method is useful for the evaluation of the disintegration of RDT during pharmaceutical development, and also for quality control during production.

- **Mukesh G, et al., (2004)** formulated, designed and optimized the mouth dissolve tablets of Nimesulide using vacuum drying technique. Granules were prepared by using camphor and crospovidone, and then exposed to vacuum for camphor sublimation and compressed. Alternatively next tablets were first prepared and then exposed to vacuum. In conclusion a $3^2$ full factorial design was used to investigate the joint influence of 2-formulation variable: Amount of camphor and crospovidone. From multiple linear regression and contour plot, sublimation of camphor from tablets resulted superior tablets.

- **Ozeki T, et al., (2003)** examined the ability of disintegrants mixed with granules consisting of 5% acid treated yeast cells wall. Various parameters were evaluated. Thus from the results indicate that AYC is a unique pharmaceutical additive possessing opposing function with respective to binding and disintegration. Carboxycarmellose showed good disintegrating agent with 5% AYC.

- **Padma VD, et al., (2000)** designed a novel drug delivery and proposed formulation of melt in mouth or mouth dissolve tablets. Paracetamol was selected as a model drug and the technology was named as D-Zolv technology. Two steps were involved; one is masking of the taste and second is formulation of masked Paracetamol granules into tablets. Palatable granules of Paracetamol were obtained by solvent evaporation technique. Tablets were evaluated for various parameters including *in-vitro* and *in-vivo* disintegration time.

- **Padma VD, et al., (2000)** designed two different methods for the in-vitro evaluation of mouth dissolve tablets. The two different methods were evaluated are static method and dynamic method. Samples for the study included in house D-Zolv tablets and marketed formulations.

- **Pandey S, et al., (2003)** formulated optimized fast dissolving dosage form of diclofenac sodium by rapidly disintegrating agents like cross-linked CMC, sodium starch glycolate and cross-linked povidone. All the formulations were evaluated for the influence of disintegrants and their concentrations on the characteristics of fast dissolving tablet mainly in terms of disintegration time and dissolution rate. Cross linked CMC was found to be better suited for the formulation of fast dissolving tablets of diclofenac sodium when compared to other super disintegrants used in the study.

- **Popa G, et al., (2003)** wrote review on oral disintegrating tablets. This includes some methods of preparation, which gain applicability in industry like molding, lyophilization, and direct
compression with highly soluble excipients, superdisinTEGRants and effervescent systems. This also focused on patient’s impact on pharmaceutical market and more improvement expectation in future years with new drug formulation.


- **Seager H (1998)** disclosed the formulation and process technology of the Zydis dosage form. The bioavailability characteristics of Zydis products are summarized, and in particular, the design of Zydis products for the enhancement of oral bioavailability and the improvement of clinical activity, through transmucosal delivery and pregastric absorption has been discussed.

- **Semiya K, et al., (2000)** prepared and clinically evaluated the orally disintegrating Clonidine hydrochloride tablets by drying on aqueous suspension. Powdered lactose and drug taken in the ratio of 2:1. Hardness and disintegration time were evaluated. Clinically used this tablets on patients proved that this orally disintegrating tablets were useful in clinical situation for the pre-anaesthetic medication.

- **Shicheng Yang, et al., (2004)** developed the FDT using poly (acrylic acid) superporous hydrogel microparticles. Compression behavior of SPH microparticles, effects of various SPH microparticle sizes and a 19-run factorial design were evaluated. Factorial design was based on consisting of Ketoprofen, SPH microparticle, filler, tableting pressure and each factor contained three levels on the disintegration time and tensile strength of the prepared FDTS. SPH microparticles FDT showed fastest disintegration time and higher tensile strength and thus concluded good superdisintegrant.

- **Shimizu T, et al., (2003)** formulated Lansoprazol fast disintegrating tablet which consists of enteric-coated microgranules and inactive agents, MCC, L-HPC, L-HPC 33(New type) and Crospovidone were used as binders and disintegrants. Rapid disintegration time, in vitro, in mouth (<30 secs) and dissolution behavior studied in acid stage and buffer stage were evaluated and compared with current capsules.

- **Sophie-Dorotheeclas, et al., (2002)** studied *in-vitro* disintegration behaviour of fast dissolving systems manufactured by main commercialized technologies using the texture analyzer instrument.
Quantitative parameters were employed to characterize the effect of major test variables of disintegration profiles. The products were compared using test conditions that minimized these effects and at the same time mimicked the in-vivo situation in patient’s mouth. The in vitro disintegration times obtained under the simulated in vivo conditions were correlated with reported in vivo disintegration times.

- Srikonda VS, et al., (2000) made a review on recent technological advances in solid oral drug delivery. This includes recent technological advances in solid oral dosage forms, formulated by freeze-drying technique, three-dimensional printing technology and floss formation technique. This paper also discussed about material selection, binder selection, advantages and disadvantages of these technologies.

- Sugimoto M, et al., (2001) have formulated rapidly disintegrating tablets comprising of D-mannitol and freeze-dried amorphous sucrose with and without Tipepidine hibezate as a model drug. Prepared tablets were evaluated for the properties such as porosity, disintegration time in oral cavity, thermal analysis etc. It was concluded that crystalline transition method is a very useful method to prepare a rapidly disintegrating tablet.

- Sunita Dahiya et al., (2011) formulated and evaluate orodispersible tablets of granisetron hydrochloride, a highly water soluble, tasteless, antiemetic drug employing superdisintegrants explotab, crospovidone, Ac-Di-Sol. The mix powder blends of varying compositions were prepared and evaluated for micromeritic properties and then subjected to tablet preparation by direct compression method. Tablets prepared with crospovidone at 5% level (F4) was found to be the best formulation as it exhibited satisfactory physical parameters, least disintegration and wetting time and highest percent drug release (99.45%) at 10 min. Furthermore, F4 showed good stability at accelerated conditions (40°C ±75% RH). The studies aid in the judicious selection of type and concentration of superdisintegrants in order to formulate a cost effective and patient friendly dosage form.

- Toshifusa S. et al., (2002) attempted for the development of rapid oral disintegration tablets by direct compression using co-ground mixture of D-mannitol and crospovidone. The co-ground mixture was prepared with a vibration rod mill. It was presumed that crospovidone acted as a grinding assistant for D-mannitol in the co-grinding process, enhancing the hardness of tablets by increasing the contact area among powder particles.
• **Valleri M et al., (2004)** developed and evaluated Glyburide fast dissolving tablets using solid dispersion technique in polyethylene glycol. They prepared tablets by direct compression and showed that the Glyburide dissolution profile from the developed tablet was better than those from various commercial tablets.

• **Wadhwani AR, et al., (2002)** formulated Roxithromycin mouth dissolving tablets by masking the bitter taste. Various strategies were adopted for masking bitter taste by granulating with Eudragit NE 300 and Eudragit E100, granulating with flavors and sweeteners and complexes ion exchange resin Indion 204 in various ratios. Tablets were evaluated for various parameters. Indion 204 found to improve the palatability.

• **Watanabe A, et al., (1994)** discussed the use of sodium sulfate decahydrate in dosage forms for the elderly who may have difficulty in swallowing tablets and capsules. A tablet of sodium sulfate decahydrate prepared by direct compression dissolved into its own water of crystallization at 37°C, so that it could be used for the rapid dissolution of a tablet in the mouth without the addition of water.

• **Watanabe Y, et al., (1997)** investigated a new method of preparing high porosity rapidly saliva soluble compressed tablets using mannitol with camphor, a subliming material. These compressed tablets which have high porosity, rapidly dissolved within 15 seconds in saliva in the mouth. A high porosity was achieved due to the formation of many pores where camphor particles previously existed in the compressed mannitol tablets prior to sublimation of the camphor. They also developed a direct compression method for the preparation of tablets using mannitol and camphor of meclizine with high porosity, which dissolves rapidly in saliva.

• **Yunxia B, et al., (1996)** prepared and evaluated compressed rapidly disintegrating tablet in the oral cavity. The mixture of microcrystalline cellulose and L-HPC were compressed at 100-500 kg in the absence of an active ingredient. The properties of these tablets, such as hardness, porosity, wetting time, disintegration time were investigated. The MCC/HPC ratio in the range of 8:2 to 9:1; the shortest disintegration time were observed. The disintegration of tablets containing ethenzamide and ascorbic acid were examined next. A good correlation between the disintegration behaviours *in-vitro* and in the oral cavity was recognized.