2. LITERATURE REVIEW

1. **Abu-Izza, Khawla A. et al, Patent No. 6733781, (2004)** have received patent on processes for the preparation of tablets which dissolve rapidly in the mouth and provide an excellent mouthfeel. The tablets of the invention comprise a compound which melts at about 37° C. or lower, have a low hardness, high stability and generally comprise few insoluble disintegrants which may cause a gritty or chalky sensation in the mouth. Preferably the tablet has a hardness of about 3 kP or less, more preferably about 2 kP or less, and still more preferably about 1 kP or less. Preferably, the minimum hardness of the tablet is about 0.1 kP, although lower values, including 0.05 kP, are possible.


3. **Augello. et al. U.S patent no 09/330445, (2000)** invented the use of croscarmellose sodium to coat bitter-tasting active agents in a manner that will mask the bitter taste of these materials, taste masked pharmaceutical compositions in which the particles of pharmaceutically active agent are coated with croscarmellose sodium, taste masked pharmaceutical tablets made therefore, in which the rapid disintegration of tablets that is imparted by croscarmellose sodium is preserved, and to a method for preparing such coated particles by preparing them in a fluidized bed coating process.

4. **Chien et al, U. S. patent no. 09/880420, (2001)** invented a method to modify the taste profile of consumables by adding esters of quinic acid and cinnamic acid derivatives. These esters, which belong to the family of chlorogenic acids, may be synthetic or may be extracted from a natural source such as a botanical. Chlorogenic acid is added to consumables to mask bitter off-tastes or other displeasing tastes imparted by one or more natural, synthetic or semi-synthetic components in the consumable.

5. **DAFRA PHARMA N.V., International application number: PCT/EP2005/009851, (2005)** invented a pharmaceutical composition comprising an antimalarial agent selected from the group consisting of artemether, arteether, artemisinin, dihydroartemisinin and artemunate; sulfamethoxypyrazine; and a dihydrofolate reductase inhibitor and further
comprising one or more pharmaceutical acceptable excipients, carriers and/or diluents suitable for providing treatment of malaria in a period of one day.

6. **Dinkar Sharma, et al, (2010)** prepared Taste-Masked orally disintegrating tablets of paracetamol by Flash Tab Technology. Taste masked granules of paracetamol were prepared by coating the granules of the drug using a pH-sensitive polymer Eudragit EPO in a fluidized bed coater. Disintegration time of the tablets was found to be 27 sec and almost 100% drug released in 30 minutes. The taste of the formulation was found to be acceptable by analyzing the responses of the healthy human volunteers.

7. **DP Venkatesh, et al, (2010)** formulated Oro-dispersible tablets of Ambroxol hydrochloride (HCL) by masking the taste with the help of complexation with ion exchange resins method, which also acts as super disintegrating agents. Cation exchange resins like Indion-204 and Indion-234 were utilized for the sorption of drug. Drug-resinates were prepared in drug to resin ratio of 1:5 and 1:6. The prepared tablets were evaluated for general appearance, content uniformity, hardness, friability, taste evaluation, mouth feel, wetting time, in vitro and in vivo disintegration time, and in vitro dissolution studies. Tablets with both the resins have shown quick disintegrating features, i.e., within 20 s, which is very characteristic of oro-dispersible tablets. Also, the dispersion not showing any bitter taste, indicate the capability of ion exchange resins used, both as taste masking and super disintegrating agents.

8. **Gedam Shweta, et al, (2010)** prepared microparticles of bitter taste - Diphenhydramine hydrochloride. Drug was masked by preparing microparticles of drug with certain hydrophilic polymers such as Hydroxypropyl methylcellulose (HPMC) and polyvinyl pyrrolidone (PVP) by using spray drying technique. Microparticles of Diphenhydramine hydrochloride and polymers were prepared in ratio of 1:3:3 (0.1gm drug, 0.3gm HPMC and 0.3gm PVP respectively) by spray drying technique.

9. **George K. E. Gregory, et al USA patent No. 4,305,502, 4,371,516, and 5,738,875 (1981)** has invented Zydis technology based on freeze-drying, which is used to manufacture rapidly dissolving tablets. The potential drug should have a particle size <50 µm and should not have a bitter taste. Although the process is quite popular in the pharmaceutical industry, it is expensive and time-consuming. The products produced by this technology are fragile and require special packaging and handling USP 5,178,878, 6,269,615 and 6,221,392, all assigned to R.P. Scherer to Cima Labs, Inc., teach the art of manufacturing friable orally disintegrating tablets by direct compression and packaging in specially
designed dome-shaped blister package using a robot-controlled integrated tableting-packaging system.

10. Gerard Cousin et al US Patent No. 5,464,632 and 6,106,861 (1995) disclosed methods of producing rapidly disintegrating multiparticulate tablets which disintegrate in the mouth within 60 seconds comprising an active in the form of microcrystals, coated microgranules or uncoated microgranules, 3 to 15% disintegrant, 40 to 90% of a soluble diluent which is a mixture of directly compressible polyols with an average particle size of 100 to 500 µ and powdered polyols with an average particle size of less than 100 µ.

11. Gupte et al U. S. patent no. 10/158715 (2002) have claimed, A taste-masked formulation comprising: a taste-masking layer surrounding said at least one active ingredient, said taste-masking layer including from about 2% to about 20% of a water-soluble polymer and from about 80% to about 98% of a water-insoluble polymer, said water-insoluble polymer being selected from the group consisting of ethyl cellulose, CAP, hydroxypropyl methyl cellulose phthalate, polyvinyl acetate phthalate, hydroxypropyl methyl cellulose succinate, and shellac, and wherein said taste-masking layer has a coating thickness from about 2% to about 100% by weight, based on the weight of said taste-masked particles, taste-masked formulation releases less than about 20% of the at least one active ingredient in an aqueous solution at a basic pH in about 3 minutes and releases at least about 65% of said at least one active ingredient at an acidic pH in about 30 min.

12. Kanani R, et al, (2010) Formulated oro-dispersible tablet of Azithromycin that was intended to disintegrate rapidly into the oral cavity and form a stabilized dispersion. A direct compression method was failed to formulate dispersible tablet of Azithromycin so wet granulation method was used. In preliminary study different superdisintegrant croscarmellose sodium (CCS), sodium starch glycolate (SSG) and crospovidone (CPVP) were evaluated for weight variation, content uniformity, hardness, disintegration time, and friability of tablets. Avicel was used as diluents. Aspartame was used as a sweetening agent. Magnesium stearate and Aerosil were used as lubricant and glidant respectively.

13. Kumar B.S., et al, (2010) prepared taste masked oral dispersible tablets by sublimation method and investigate the effects of super disintegrant (Kollidon CL) on the disintegration time as well as the percent release of a model drug from Kollidon 30, Ispaghula husk and Guar Gum based formulations. Kollidon CL was found to cause a rapid disintegration of ODTs within 24 to 39 seconds. The overall study indicate a proper balance between the rate retarding polymers and disintegrant having a drug release profile
of ODT under the presence of a volatilizing agent showed an acceptable disintegration time with a percent of drug release.

14. **Lagoviyer et al. U.S. Pat. No. 6,284,270, (2001)** prepared in making fast disintegrating tablets with the use of mannose. For instance, fast disintegrating tablets are proposed by sintering a preformation product (which is a mixture of active agent, binding agent, bulking agent and/or structural agent and/or solvent). Sintering is a process of melting a binding agent and then resolidifying it at temperatures of 50-100 degree., mannose is listed only as a bulking agent and is not indicated for making mechanically strong tablets.

15. **Lakshmi C.S.R, et al, (2010)** studied the effect of subliming agents on the oral dispersible property of cinnarizine tablets. The fundamental principle used in the development of the oral dispersible tablets by sublimation technique is to maximize pore structure of the tablets. Compressed tablets prepared using a water soluble material like mannitol, does not rapidly disperse in water since it is difficult for water to penetrate into the tablets due to their low porosity. To increase the porosity of the tablets which are prepared by direct compression using mannitol, subliming agents such as camphor, menthol, ammonium bicarbonate or thymol are to be used. These compressed tablets which have high porosity (approximately 30%) rapidly dissolved within 25 s in the mouth. We developed a direct compression method for the formulation of cinnarizine (an anti emetic drug) tablets with high porosity which dissolves rapidly using mannitol as diluent and camphor, menthol, ammonium bicarbonate or thymol as subliming agents.

16. **Mahaveer P. Khinchi, et al., (2010)** studied for Salbutamol Sulphate which is readily available in conventional tablet dosage form. These are not suitable for pediatric as well as geriatric patient because it is not easy to swallow during asthmatic attack. Hence it was decided to formulate orally disintegrating tablets of salbutamol sulphate by employing direct compression technique using directly compressible mannitol (pearlitol SD 200), micro crystalline cellulose (MCC), various concentration of super disintegrating agents like Ac-di-sol, Primojel, and Polyplasdone R- XL as 2%, 3%, 4%, and 5%. All the Formulations has showed satisfactory the result i.e. disintegration was less than one minute and in-vitro release was within three minute thus ensure the immediate effect. The formulation A-4 and A-8 prepared by Ac-di-sol 5% and Polyplasdone R- XL 5% showed 100% drug release within two minute and three minute respectively while 100% drug release of marketed conventional tablet was found to be within twenty five minute.

17. **Mukherji et al U. S. patent no. 09/587535, (2003)** invented a taste masked composition which comprises a bitter tasting drug, a combination of two enteric polymers comprising,
a methacrylic acid copolymer and a phthalate polymer is described. The composition of the present invention is prepared by dissolving the active ingredient, the methacrylic acid copolymer and the phthalate polymer in a solvent and recovering the composition from the solution.

18. *N. Damodharan et al, (2010)* prepared formulations containing croscarmellose sodium and sodium starch glycolate showed decrease in angle of repose with increase in concentration. Angle of repose increased with increase in concentration of crospovidone. Formulations prepared with direct compression method showed good release properties when compared with wet granulation method. The wetting time decreased with increase in the concentration of crospovidone, while the wetting time of the tablets containing croscarmellose sodium and sodium starch glycolate did not change with increase in concentration.

19. *Nitin B., et al., (2010)* prepared tablets which were prepared by dry granulation method using different concentrations of superdisintegrants such as modified gum Karya, modified natural agar, croscarmellose sodium and sodium starch glycollate. The formulations were evaluated for weight variation, hardness, friability, in-vitro disintegration time and in vitro dissolution study.

20. *Platteueuw et al., U.S. patent no. 20040265375, (2004)* received the patent on Silicifimicrocrystallincellulose which is used to provide a tablet with oral disintegration. The tablet contains at least 50% of the silificied microcrystalline cellulose and an effective amount of an active agent, especially a pharmaceutically active agent.

21. *Ranbaxy Laboratories Limited, international application number, PCT/IB2007/052436, (2007).* Invented high dose oral pharmaceutical compositions of artemether and lumefantrine, and process for preparation thereof. The compositions comprise of artemether and lumefantrine comprising artemether in an amount of from about 40 mg to about 80 mg, lumefantrine in an amount of from about 240 mg to about 480 mg. The compositions are useful for treatment of uncomplicated infections with Plasmodium falciparum, including strains from multi-drug-resistant areas.

22. *S.R. Shahi, et al, (2010)* has prepared oro-dispersible tablets of etoricoxib with enhanced dissolution rate. The another purpose of the present investigation was to evaluate effect of superdisintegrants like Crospovidone (Polyplasdone XL), Croscarmellose Sodium (Ac-Di-Sol) and Sodium starch glycolate (Primojel) on dissolution of poorly soluble, selective COX-2 inhibitor in oro-dispersible tablets. The effect of superdisintegrants specifically at
2 and 4% level in oro-dispersible tablet formulation on the in vitro dissolution was evaluated.

23. **Schwartz, et al U. S. patent no. 12/300,465, (2007)** invented a Oral dispersible tablets which containing from 20% to 50% by weight of racetadotril. Orally disintegrating dosage form has a in-vitro disintegration time of less than thirty seconds, orally disintegrating dosage form has a hardness of less than 5 kp/cm³.

24. **Shah PP, et al, (2008)** researched on taste masking of the intensely bitter taste of artemether (ARM) and formulated a rapid-disintegrating tablet (RDT) of that taste-masked drug. Taste masking was done by solid dispersion with mono amino glycyrrhizin pentahydrate (GLY) by solvent evaporation method. To characterize and formulate taste masked rapid disintegrating tablets (RDTs) of ARM, the 1:1M solid dispersion was selected based on bitterness score. Fourier transform infrared spectroscopy (FTIR), differential scanning calorimetry (DSC), and X-ray powder diffraction (XRPD) were performed to identify the physicochemical interaction between drug and carrier, hence its effect on dissolution. RDTs were evaluated for weight variation, disintegration time, hardness and friability. In vitro drug release studies were performed for RDTs at pH 1.2 and 6.8. Bitterness score was evaluated using mini-column method and compared with gustatory sensation test.

25. **Shimizu, Toshihiro Morimoto et al., (2008)** prepared Orally disintegrable tablets in which an orally disintegrable tablet which comprises (i) fine granules having an average particle diameter of 400 µm or less (ii) an additive, has superior disintegrability or dissolution in the oral cavity so that it as an orally disintegrable tablet capable of being administered to the aged or children and easily administered without water. This invention contains fine granules having the average particle diameter such that it will not impart roughness in mouth, it can be administered easily without discomfort at the administration.

26. **Simone Schiermeier, et al, (2002)** formulated the fast dissolving tablet of Ibuprofen, containing 26% galactomannan and 5% crospovidone, disintegrates before the galactomannan starts to swell. These tablets disperse in water within 40 s and show a crushing strength of 95 N. To develop an orodispersible tablet, a rotatable central composite design was applied to predict the effects of the quantitative factors mannitol and crospovidone as well as compression force on the characteristics of the tablet. An optimum tablet formulation, containing 34% mannitol and 13% crospovidone, provides a short wetting time of 17 s and a sufficient crushing strength of 40 N.
27. **T.Y. Puttewar, et al, (2010)** prepared tablets of Doxilamine orodispersible with considerable increase in drug release as compared to marketed formulations. To prevent bitter taste and unacceptable odour of the drug, the drug was taste masked with weak cation exchange resins like Indion 234, Indion 204 and Indion 414. The drug was characterized according to different compendial methods, on the basis of identification by UV spectroscopy, pH, organoleptic properties and other tests.

28. **Ulrich.et al U.S. Patent No. 10/083775, (2004)** have claimed in his invention that, a taste masked pharmaceutical composition comprising a microcapsule, wherein the microcapsule comprises a pharmaceutically active agent core coated with a taste masking effective amount of a water-insoluble enteric coating, wherein the coating comprises a weakly acidic methacrylic acid-ethyl acrylate copolymer.

29. **Venkata Ramana Reddy, et al, (2010)** prepared oral disintegrating tablets (ODT) by using low bitter hypertensive drugs like amlodipine besylate using taste enhancers as a taste masking agents. ODT of amlodipine besylate were prepared using different superdisintegrants by direct compression method. Mannitol was used as a diluent and sodium lauryl sulphate was used as a wetting (surfactant) agent. Aspartame and Acesulfame Potassium were used for unpleasant taste masked from the amlodipine besylate by cosifting and serial of blending with other excipients.

30. **Wang, Wen-Che et al., (2005)** formulated the fast dissolving tablet and method of preparing the same, which was comprised of a pharmaceutically active ingredient, a starch, a hydrophilic polymer, a surfactant, and excipients. A method of preparing the fast dissolving tablet is also disclosed. A method of preparing a fast dissolving tablet, comprising: providing a first solution comprising a hydrophilic polymer and a starch; providing a second solution comprising a pharmaceutically active ingredient and a surfactant; blending the first and second solutions to form a plurality of granule powders by a granulating; blending the granule powders and excipients; and performing a compression-molding process to form the tablet.