2. Literature Review

One of the vital prominent elements at the beginning of a research work is the literature review. Systemic literature overview is the chief premise in the designing of some systematic work, and due to the alike rationales here the evaluation of literature has been done.

2.1 Review of work done on mouth dissolving tablet (MDT)

Zhang et al (2013) developed mouth disintegrating tablet Jiawei Qing’e, a kind of prescription of Chinese herbal medicine. The bitterness of Jiawei Qing’e was masked using Eudragit E-100 by solvent evaporation technique. The independent variables were Eudragit E-100/drug ratio (X1), amount of disintegrants (X2), and the amount of diluents (X3). The disintegration time (Y1), hardness (Y2), and weight differences of the formulated MDT were characterized. The models predicted levels of X1 = 4.63%, X2 = 5.25%, and X3 = 34.33%, for the optimal formulation having a hardness of 3.0 kg with the disintegration time of 30 s within the experimental region. Response surface methodology showed the good predictability and reliability in optimizing the formulation.

Sharma D (2013) prepared salbutamol sulphate as fast disintegrating tablet for pediatrics patients by direct compression technique which is used in the eradication of respiratory disorders. The fast disintegration tablets were fabricated by applying sodium starch glycolate as a superdisintegrants substance. The various physicochemical characters of the formulated tablets were assessed. The drug release profile of formulated tablets, drug-excipient interaction, and accelerated stability study was estimated to optimized formulation. From results, it was deduced that formulated rapidly dissolving tablets of salbutamol sulphate have all features and properties required for fast disintegrating tablets. The formulated tablets disintegrate quickly, provided fast onset of action, and improved the patient usefulness and compliance.
Reddy et al (2013) formulated fast dissolving tablets of Flurbiprofen employing various super disintegrant of enhanced dissolution and bioavailability. The results of optimized formulation of in vitro dissolution studies, indicates drug release in 15 min (Q15) was observed to be 91.46±1.42%. While the prevalent tablets formulated by the same manner displayed 22.92±0.47% in 15 min. Further, at starting dissolution rate and dissolution productivity for optimized formulation was 6.10%/min and 53.44. But the conventional tablets produce 1.53%/min and 10.96 dissolution rate and dissolution productivity respectively. They increased by 4.0 folds when compared to traditional doses. The pharmacokinetic evaluation displayed the optimized fast dissolving tablets produced peak plasma concentration\textsuperscript{55}.

Iyer et al (2013) formulated and evaluated Risperidone fast dissolving tablets employing solid dispersion method using Beta-cyclodextrin, crospovidone and croscarmellose as the carrier of improved solubility and dissolution. The solid dispersions were formulated as fast dissolving tablets by using Doshion P544 resin (C). The taste masking agent along with different super disintegrant such as Croscarmellose and crospovidone were used in formulation. The taste masking agent was used in various pre formulation and post formulations studies. Each formulation displayed considerable enhancement in the solubility behavior and bettered drug release. The results showed enhanced dissolution of Risperidone, may lead to improved bioavailability\textsuperscript{56}.

Elbary et al (2012) formulated and evaluated Meloxicam orodispersible tablets by two methods, including sublimation technique where different subliming agents like camphor, menthol and thymol were used with Ac-Di-Sol as a superdisintegrant. Author also prepared Meloxicam orodispersible tablets by freeze-drying method. In this method aqueous dispersion of Meloxicam comprising a matrix former, a sugar alcohol, and a collapse protectant were employed. It was concluded that tablet formulated by freeze drying method has given the best in vitro disintegration and dissolution results\textsuperscript{57}.

Roy et al (2012) formulated and evaluated amlodipine besylate fast dissolving tablets. The direct compression technique is used to prepare fast dissolving
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tables by employing utilizing varied quantity of super disintegrants like croscarmellose sodium, polyplasdone R-XL and sodium starch glycolate. Results of fast dissolving tablets of amlodipine besylate indicate that formulation including Ac-Di-Sol was mainly satisfactory which display less disintegration time and wetting time\(^5\).

**Thakre et al (2012)** investigated and developed Etoricoxib oral fast dissolving tablets. The dissolution of Etorioxib tablets were controlled by using solid dispersion technique. In this technique carrier Urea solid dispersion were manufactured through the physical blend, kneading and by fusion method. During preparation of tablets mannitol used to provide for rapid disintegration and Urea supplemented that imparts hydrophilic carrier and superdisintegrants. The bitter taste of Etoricoxib tablets was suppressed by applying Aspartame. The *in vitro* and *in vivo* taste valuation of tablets was concluded. The similarity study between drug and excipient were investigated by FTIR\(^5\).

**Kaurav et al (2012)** formulated Levocetrizine HCl fast dissolving tablets by direct compression method. During formulation author used Croscarmellose sodium and crospovidone in various quantity as super disintegrants. The bulk density, compressibility, angle of repose, etc precompression parameters were checked for blends. The physicochemical profile of formulated Levocetrizine HCl fast dissolving tablets was estimated. The results of all these parameters were satisfactory. From result it was concluded the formulation F6 was found best formulation. This formulation releases active ingredients up to 98.89% in 5 min\(^6\).

**Sharma et al (2012)** formulated the orally disintegrating tablets and bitter taste of Paracetamol tablets was masked by Flash Tab Technology. Author utilized a pH-sensitive polymer Eudragit EPO in a fluidized bed coater to mask the bitter taste. The physical characteristics of coated granules were investigated. The wet granulation technique was applied for the preparations of the orally disintegrating tablets. The disintegrant materials namely crospovidone and hydroxypropyl cellulose were employed to enhance the disintegration of the formulated tablets. The thickness, friability, weight
variation and other physicochemical parameters were studied for disintegrating tablets. Results inferred that formulated tablets takes 27 sec to complete disintegrates and 100% drug release in 30 minutes. The flavor of the tablets was acceptable.

Rane et al (2012) designed Albendazole fast dissolving tablet, which enhanced dissolution rate, and also tried to improved bioavailability of tablets. The direct compression method used to fabricate the fast dissolving tablets. The different types of disintegrate were used to improve the disintegration of fast dissolving tablets. The physicochemical parameters were investigated for disintegrating tablets. From outcomes it has been concluded that the formulation F3 considered best formulation among the other formulations of fast dissolving tablets. The F3 comprising 5%w/w super disintegrant Crospovidone and 20%w/w microcrystalline cellulose, and it release 99.09% drug in 99.097% in 40 min.

Patel et al (2012) prepared the MDTs of Telmisartan, belong to anti-hypertensive drug. The MDTs were prepared by applying skimmed milk powder and poloxamer-188 along with crospovidone to intensify the disintegration of formulated tablets. The diverse physicochemical parameters were determined. The results of drug compatibility indicate that drug and carriers were free from interaction. During process drug was changed into amorphous form it was confirmed from the results of XRD. The drugs consistently dispersed throughout the carriers. The formulation displayed, disintegrates below 31 sec.

Sharma et al (2011) formulated fast-disintegrating tablets of Cefixime. The superdisintegrants namely sodium starch glycolate, crospovidone, Kyron T 314 was used in tablets, to improve the disintegration of tablets. The physical characteristics of compound were performed. The physicochemical properties were evaluated for prepared fast disintegration tablets. The results exhibited that the fast-disintegrating tablets displayed good physical characteristics. The tablet formulated inferred disintegration time of 30 ± 2.4 s in vitro.
Ganure et al (2011) prepared Tramadol hydrochloride mouth dissolving tablets. The tablets were prepared by direct compression method. The Physicochemical parameters were scrutinized for the tablets. The result indicates that all the tablets were found to be under certified frontiers. The MDTs of tramadol hydrochloride can be prepared by utilizing simple and conventional techniques.

Solanki et al (2011) formulated and evaluated aceclofenac fast-disintegrating tablets. The wet granulation and direct compression method were utilized to fabricate the fast dissolving tablets. The fast-disintegrating tablets were manufactured by incorporating diverse concentration of excipients and diluents. The physical and chemical properties of tablets were evaluated. The dissolution of drug was performed in buffer Phosphate buffered Saline (PBS) pH 7.4. From outcomes of study, it has been concluded that direct compression of formulation C3 produces better dissolution than the wet granulation of formulation F2. The formulation F3 and C3 released 89.69% and 75.37% drug in 90 minutes respectively.

Masareddy et al (2011) developed Tizanidine HCl mouth dissolving tablets. The hardness, friability, in vitro disintegration time and in vitro drug release were evaluated for formulated tablets. Formulation F-3 prepared by addition of co-processed excipient base in the ratio of 1:3 showed minimum disintegration time of 9.15±0.04 s and the higher amounts of drug release of 93.75% at the end of 15 min. Granules obtained by spray drying technique were found to be more spherical, which improved its flow property and was supported by scanning electron microscope studies.

Kumar et al (2011) designed and prepared Felodipine fast disintegrating tablets. The direct compression method was utilized to manufacture the tablets. The fast disintegrating tablets were fabricated by using crospovidone as super-disintegrant and microcrystalline cellulose. Additionally mannitol was added to mask the bitter taste. The physicochemical studies were performed for formulated tablets. The results of physicochemical indicate satisfactorily value. Moreover the formulation does not produce any drug excipient
interaction. The formulation incorporating 2% w/w crospovidone and 15% w/w microcrystalline cellulose was pondered as foremost formulation.

**Sharma et al (2010)** developed Levocetirizine mouth dissolving tablet by employing wet granulation method. The PVP as binder was used to prepare the MDTS. Moreover the sodium starch glycolate and Crospovidone as super disintegrants tablets were used to improve disintegration of tablets. The value of disintegration time, wetting time and friability of formulation containing 7.5% crospovidone produces comparatively lower than the other formulation. The formulation containing crospovidone as superdisintegrate produced suitable drug-resin complex to obtain the low disintegration time, wetting time and friability of tablets.

**Keny et al (2010)** formulated mouth disintegrating tablets of Rizatriptan benzoate by employing direct compression method. The super disintegrant were used in formulation of tablets. The physicochemical studies were performed for tablets. The assay of tablets was done by high performance liquid chromatography. From the outcomes of study, it has been concluded that the formulation containing crospovidone and Indion 234 displayed best result compared to other formulations.

**Sawarikar et al (2010)** developed and evaluated mouth dissolving tablets inclusion complex of isoxsuprine hydrochloride with β-cyclodextrin by direct compression method. The complex contains super disintegrant, sodium starch glycolate, ac-di-sol and crospovidone. The physicochemical parameters of prepared tablets were evaluated. The results indicate that F6 considered best formulation among other formulations.

**Gnanaprakash et al (2009)** prepared fast dissolving tablets of Valdecoxib by employing some carriers and super disintegrants such as Polyvinyl Pyrrolidone (PVP), Sodium Carboxy Methyl Cellulose (SCMC), Crospovidone NF and β – Cyclodextrin, in varying proportions of 5, 10, and 15%. The fast dissolving tablets were manufacture by direct compression technique. The physical characteristics were determined for blend. An impressive delightful testing formulation released 99.88% drug within 10 minutes.
Parikh et al (2009) formulated and evaluated orodispersible tablets of Atenolol by employing direct compression technique. The Croscarmellose sodium, crospovidone and sodium starch glycolate were used to facilitate the dispersibility of formulated tablets. Among all the super disintegrates the Croscarmellose sodium was found to be foremost in formulations. The formulation comprising 8% w/w concentration level, exhibited lowest disintegrating time of 31 ± 2 seconds and highest release, i.e. more than 98% of drug in 10 minutes. Stability studies carried at room temperature for 30 days showed no significant change in tablets.

Zade et al (2009) formulated bitter less Tizanidine Hydrochloride mouth dissolving tablets by utilizing Eudragit E100 as a taste masking agent. The superdisintegrants were used to improve the disintegration of tablets. The physicochemical characters of formulated MDT were investigated. It has been concluded from the results that formulation prepared by inclusion of superdisintegrants exhibited less disintegration time.

Patel et al (2009) prepared and evaluated Glipizide fast dissolving tablets. The crospovidone and croscarmellose sodium (4%, 5%, 6%) were used to enhance the disintegration of tablets. Meanwhile distinctive binders PVP K-30 and pregelatinized starch (3%) were used in formulation to check the friability problem. The physicochemical characters were investigated for all formulations. Results of physicochemical indicates that formulation containing 5% croscarmellose sodium with 3% PVP K30 produces best results, and was selected as the optimized formulation.

Parmar et al (2009) formulated and evaluated Domperidone mouth dissolving tablets to conceal the acrid flavor and for better patients compliance. The mouth dissolving tablets were formulated by direct compression method using Avicel PH 102 and sodium starch glycolate. The hardness, friability, disintegration time and dissolution rate were checked for formulated MDTs. The formulated MDTs produces decent hardness of 3 kg/cm², disintegration time of 27 seconds and in vitro drug release of not less than 95% within 30 minutes, along with pleasant taste.
Jain et al (2009) prepared valsartan mouth dissolving tablets of by direct compression method. The MDTs were formulated by mixing with different super disintegrant. The physicochemical properties and in vitro dissolution were investigated for formulated tablets. Additionally the disintegration of formulated tablets was evaluated in artificial saliva, (pH 5.8). The results of wetting time and disintegration of mouth dissolving tablets incorporating of Crospovidone produces least value resembled to other formulations. From the results of drug release it considered that on increasing the concentration of super disintegrant, it increases the drug release, and was found to be stiffest with formulations containing Crospovidone.

Setty et al (2008) developed Aceclofenac fast dispersible tablets by using direct compression method. The fast dispersible tablets were manufacture by mixing superdisintegrants such as croscarmellose sodium, crospovidone and sodium starch glycolate, to improve the disintegrants of tablets. The physicochemical parameters were evaluated for formulated mouth dissolving tablets. The findings of wetting time, disintegration time and drug content exhibited satisfactorily.

Dinesh et al (2007) formulated and evaluated an orodispersible tablets containing Valdecoxib β-CD complexes employing direct compression technique. The results showed that the disintegration time was reduced, and dissolution profile was enhanced by using superdisintegrants. It was concluded that crospovidone was found the best superdisintegrant, which exhibit quick disintegration time and wetting time.

Swamy et al (2007) reported improved efficacy of orodispersible tablets using a combination of superdisintegrants namely sodium starch glycolate-crospovidone, croscarmellose sodium or sodium starch glycolate.

Malke et al (2007) formulated and evaluated oxacarbazepine mouth dissolving tablets. The mouth dissolving tablets were fabricated by wet granulation method. The Avicel PH 102 as diluent and Ac-Di–Sol as superdisintegrant used to improve the physicochemical characteristics of tablets. The physicochemical parameters were evaluated for formulated
mouth dissolving tablets. The results indicates that the formulation comprising of 12% Ac-Di-Sol, 25% Avicel PH 102 and 8.5% starch produces satisfactorily value hardness, disintegration time and drug release.

**Shishu et al (2006)** prepared compressed tablets of Diazepam. The microcrystalline cellulose and sodium starch glycolate were mixed before compressing the blend to formulate mouth dissolving tablets of Diazepam. The bitter taste of formulations was masked by utilizing microspheres of amino alkyl methacrylate copolymers (Eudragit E-100). The microspheres were prepared by solvent evaporation technique. From results it was considered that the formulations produce satisfactorily value.

**Kuno et al (2005)** formulated the orodispersible tablets by phase transition process. The excipients erythritol, xylitol, trehalose and mannitol were used during formulation of tablets. The physicochemical parameters were evaluated for orodispersible tablets. From results it has been concluded that the hardness of tablets enhanced after heating. The increase in hardness may be due to increment of inter particle bonds.

**Larry et al (2005)** formulated and evaluated Asprin matrix tablets. The Ac-Di-Sol, Primojel and Polyplasdone XL-10 were added to formulation in different concentration to improve the disintegration of formulated tablets. The Ac-Di-Sol has fiber like nature this can improve rapid disintegration with apparently fine particles and promotes faster drug dissolution.

Inclusion complex of Rofecoxib, an NSAID with cyclodextrin using ball mill technique has been prepared and evaluated using DSC by **Lalla et al (2004)**. The fast dissolving tablet composition with 25mg equivalent Rofecoxib showed complete release of drug in 12 min as compared to 20% drug release from the conventional release marketed tablets during the same period. The results of stability test indicate that insignificant loss in drug content at the end of the 6th month.

**Abdelbary et al (2004)** prepared mouth dissolving tablets by including a hydrophilic waxy binder PEG -6-stearate. In this formulation hydrophilic lipophilic balance of 9 were used to control immiscibility of the PEG -6-
stearate. The PEG -6-stearate was a waxy material with melting point of 33 - 37˚C. The results of studies exhibited that the PEG -6-stearate not only considered as a binder, but it also improves the physical resistance of formulations. Additional it also supports in disintegration of prepared tablets and solubilizes fastly leaving no residue26.

**Mahajan et al (2004)** formulated and evaluated Sumatriptan succinate MDTs by direct compression method. The formulations were fabricated by adding superdisintegrant (Sodium starch glycolate, Carboxy methyl cellulose sodium treated agar). The physicochemical properties were evaluated for formulated tablets. The results of physicochemical indicate that the formulation was disintegrating in- vitro and in- vivo within 10-16 sec and 12-18sec, respectively. Almost 10 min required to release 90% of drug from tablets. Tablets minimum required to release drug containing combination of SSG and CMC sodium showed best results86.

**Mahaejan et al (2004)** designed salbutamol sulphate mouth dissolving tablets by utilizing factorial design technique. In this formulation sodium starch glycolate, Croscarmellose sodium and managed agar were employed as the super disintegrant. The micro crystalline cellulose was used as the diluent in the formulation. The MDTs were manufacture by direct compression technique. The results indicates that the formulation comprising of sodium starch glycolate along with other super disintegrant, displayed fast in-vitro and in- vivo dispersion time87

**Kaushik et al (2004)** worked on the promotion of deliquesce of tablets in mouth by sublimation technique. This was indicative of the fact that the volatile salt was completely removed from the tablets resulting in the creation of pores in the tablets that were accountable for the fast disintegration of tablets88.

**Induwade et al (2002)** used several techniques to achieve these fundamentals in formulation of mouth dissolving tablet; like tablet moulding, freeze drying, spray drying, sublimation and addition of disintegrating agents89.
Allen et al (1996) prepared mouth dissolving tablets by using particulates support matrix. The bulking agent and sodium starch glycolate or croscarmellose sodium were added in formulations. It has been concluded that addition of citric acid and sodium bicarbonate in formulations it improves the disintegration and dissolution of formulated tablets\(^90\).

### 2.2 Review of work done on celecoxib

Madoria et al (2012) used solid dispersion method to improve the dissolution of celecoxib tablets. The solid dispersion components are water soluble carriers (PVP-K30 and Pearlitol-200 SD). It has concluded that the tablets were prepared by solid dispersion produces fast dissolving tablet\(^91\).

Pehlivan et al (2011) evaluated interactions on day 0 and day 7 (40°C) between celecoxib and some excipients (colloidal silicon dioxide (AerosilA), microcrystalline cellulose (AvicelA PH 102), lactose anhydrous, magnesium stearate by FT-IR and HPLC. The formulated tablet does not showed any interaction. After that drug dissolution and permeability were studied and results showed satisfactorily findings\(^92\).

Gangawat et al (2011) designed and developed Celecoxib fast dissolving tablet. The formulation were prepared by solid dispersion and camphor sublimation method using \(3^2\) full factorial design with carrier (PVP-K30) and different proportion of super disintegrant (Ac-Di-Sol) by direct compression method. Hardness, thickness, friability, disintegration time and wetting time were also evaluated. The results displayed that the optimized batch H7 shows the better release (88.51%) than marketed formulation (80.71586%). From the different batches F8 shows 92.10% release in one hour. To check the interaction The FTIR spectrum of optimized formulation (F8) was done. Result revealed that incorporation of camphor in tablet provide beneficial role in improving dissolution of drug\(^93\).

Kumar (2010) formulated and evaluated mouth disintegrating tablet of celecoxib using croscarmellose, sodium starch glycolate and crospovidone to improve the disintegration of tablets. The bitter taste of celecoxib tablets were masked by using ion exchange resin (Kyron T-114). The taste masked
complexes were compressed into tablets these were subsequently investigated for different physicochemical parameters. Resinate formulation showed the maximum release of drug i.e. 43.68%. F5, F10 and F15 which contains 5% of croscarmellose, sodium starch glycoylate and crospovidone showed the drug release at 81.1083%, 86.680% and 96.264% at 5 minutes respectively. Super disintegrant crospovidone in 5% W/W concentration (F15) formulation is the most promising dosage form for rapid release of celecoxib.

Tiwari et al (2010) formulated and assessed Celecoxib mouth dissolving tablets. The celecoxib tablets were prepared by using solid dispersion and hot melt extrusion methods. The formulation comprising of sodium starch glycolate as superdisintegrants, polyvinylpyrrolidone as binder and saccharine sodium used as sweetner. The physicochemical properties were studied for prepared tablets. The results of physicochemical parameters displayed the satisfactory value. The formulations including maximum concentration of sorbitol polymer and superdisintegrant displayed best drug release.

Dade et al (2010) formulated Celecoxib tablets, by solid dispersion technology. This method was utilized to facilitate the solubility and dissolution rate of formulation. The Celecoxib solid dispersions were prepared with Croscarmellosesodium, Crospovidone and βcd at varying ratios of drug and carrier. The drug content uniformity, dissolution rate and efficiency were evaluated for Celecoxib formulations. The solid dispersion celecoxib produces greater dissolution. The dissolution profile of formulation were obtained in following orders CCS>CP>βcd polymer. The results indicates that the formulation prepared by solid dispersion (co-evaporates) exhibited improve in the dissolution rate of Celecoxib.

Kadian et al (2010) developed a floating matrix tablet of celecoxib by using direct compression technique. They were used Hydroxypropyl Methyl Cellulose (HPMC), Ethyl Cellulose (EC) alone and in combination and effervescent sodium bicarbonate (NaHCO₃) to formulate the floating tablet matrix. The formulated tablets released nearly 92.5% drug in 24 h in vitro, while the floating lag time was not more than 0.35 min and the tablet remained floatable throughout all studies.
Pandya *et al* (2009) applied solid dispersion method to ameliorate the solubility and dissolution rate of celecoxib tablets. The PVP-K30 and croscarmellose sodium were used during formulation of tablets by using 1:2 solid dispersion technique. From the results it has been concluded that the drug completely dispersed in polymer and also improved the dissolution rate.

Chandran *et al* (2006) developed controlled release matrix embedded formulations of celecoxib (CCX). The formulations were prepared by using either alone or in combination of hydroxy propyl methyl cellulose (HPMC) and ethyl cellulose (EC). The wet granulation method was employed to formulate controlled release matrix tablets of CCX. The formulation containing only HPMC decreased release rate as the polymer proportion in the matrix base was enhanced. The results indicate that there was very less difference in the release rate upon increasing the polymer proportion in formulations of EC alone. But the formulation comprising combination of HPMC and EC showed drug release relied on the relative proportions of HPMC and EC used in the tablet matrix. The release of the active ingredients from these formulations was extended up to 21 h indicating they can serve as once daily controlled release formulations for CCX.

2.3 Review of work done on tolperisone

Jani *et al* (2012) developed floating tolperisone hydrochloride controlled release (CR). The microspheres (300 to 500 µm) were prepared by using solvent evaporation technique. Porous calcium silicate (Florite or FLR) used as porous carrier, tolperisone hydrochloride (API), Ethyl cellulose (EC), and HPMC 15 cps as rate controlling polymers. The morphology, micrometric properties, *in vitro* floating behavior, entrapment efficiency, and *in vitro* drug release were studied for formulations. The result exhibited greater than 80% entrapment efficiency for all formulations. The percentage buoyancy varied from 85% to 98% at the end of 12 h. The simulated gastric fluids were used to determine the release rate of drugs. All formulations followed Higuchi model, which indicates the diffusion control release of water soluble drug from polymer matrix.
Soni et al (2012) formulated and developed floating matrix tablet for Tolperisone HCl by employing direct compression technique. The prepared tablets were investigated for in vitro buoyancy study. The formulations were also evaluated for drug release in 0.1 N HCl as dissolution medium. It was found that polymer content and polymer ratio affect percentage drug release at 6 hours$^{101}$. 