3.1 Preamble of review of literatures

Currently, 90% of the NCEs filling belong to the poorly water soluble BCS Class II and IV compounds. Recent combinatorial chemistry and high throughput screening techniques commonly used in drug discovery have increased the number of drug molecules with high molecular weight, higher lipophilicity and poor water solubility (Lipinski et al., 2001, Benet et al., 2006). And it has been observed that delivery of poorly water soluble drugs by the oral route has been difficult due to the insufficient amount of a drug dissolved for absorption from the GIT (Teofilo et al., 2007). Although, there are number of formulation strategies that have been employed to enhance the dissolution rate of poorly soluble drugs such as particle size reduction, modification of crystal habits, salts formation, complex formation with cyclodextrin, use of surfactants, solid dispersions (SDP), fast dissolving oral films (FDF), lipid based formulations and pro-drug approaches (Shah et al., 2008, Siddiqui et al., 2011). However, fast dissolving oral films have great potential over other dosage forms for delivery of poorly soluble drugs since they provide distinct advantages over other oral formulations including rapid disintegration and dissolution in the oral cavity thus increased bioavailability with faster onset of action and avoidance of first pass effect (Figueroa et al., 2012). Nowadays, fast dissolving drug delivery systems have earned popularity and acceptance as new drug delivery systems to achieve better patient compliance by preparation of convenient dosage form with improved safety and efficacy of a drug. Fast dissolving dosage forms were initially prepared for providing substitute to conventional dosage forms such as tablets, capsules and liquids to achieve better patient compliance (Naziya et al., 2013). Whereas, to overcome the difficulties associated with poor water solubility solid dispersion formulations can be prepared by mixing drug with a carrier polymer through melting or dissolution in solvents (Park, 2014).

Extensive research works carried out in recent past by many researchers on poorly water soluble drugs with the objectives of improvement in delivery of antihypertensive drugs, preparation of solid dispersions, preparation fast dissolving orals films are summarized below.

3.2 Past work carried out on selected antihypertensive drugs

Hariprasanna et al., 2010 had prepared fast dissolving tablets of SDP of Felodipine by using croscarmellose sodium (superdisintegrants) and PVA as a
hydrophilic carrier. Post compressional analysis such as hardness, friability, *in-vitro* disintegration time, wetting time, *in-vitro* release studies and stability studies were performed. Similarly, **Rao et al., 2010** had studied comparative effect of different techniques used in the formulation of fast dissolving tablets of Felodipine. Tablets prepared by SDP with mannitol showed higher hardness than with PVP and PEG. Based on the studies it was revealed that dissolution rate of Felodipine can be enhanced by preparing tablets containing SDP.

Similarly, **Venkateswarlu et al., 2010** had formulated fast dissolving tablets of Carvedilol to enhance its solubility by using β-cyclodextrin as a complexing agent. FTIR and DSC studies were performed to investigate any interaction and stability of formulation. Results of the studies revealed that complexing of Carvedilol with β-cyclodextrin may enhance its dissolution profile. Whereas, **Verma et al., 2011** prepared mucoadhesive buccal patches of Carvedilol using chitosan as cationic polymer and solvent casting method. *In-vitro* drug release was found to be 10.96%, 15.42% and 12.32% within 1 hour and 37.77%, 50.23% and 42.87% after 8 hours.

Further, **Kumar et al., 2011** formulated mouth dissolving tablet of Felodipine by direct compression method with a view to enhance patient compliance. Superdisintegrants like crospovidone, disintegrant like MCC and mannitol was used to prepare the tablet formulation. Whereas, **Bukka et al., 2012** had prepared Felodipine containing buccal films using polyethylene oxide by solvent casting method with HPC or ethyl cellulose by the application of $2^3$ factorial designs. They reported that buccal mucosa has a rich blood supply and thus it facilitates rapid absorption of drugs and thus increase its bioavailability.

Furthermore, **Prasanna et al., 2012** developed tablets of solid dispersion of Tadalafil with poloxamer-188 and SSG. The dissolution rate of poloxamer-188 based SDP was found significantly higher than the SSG based preparations which reached closer to the dissolution profile of marketed product. Similarly, **Lokesh et al., 2012** had formulated orodispersible tablets of Telmisartan using response surface methodology with the objective to determine the influence of the certain excipients on physical properties of the tablets. The multiple linear regression analysis was used to find the effect of these variables on physical properties of final formulation. In addition, **Dhiman et al., 2012** formulated fast dissolving tablets of Telmisartan by using superdisintegrants
like croscarmellose sodium, MCC, SSG and their different level of addition to increase the rate of drug release from dosage form to increase the dissolution rate and hence its bioavailability. The disintegration time of fast dissolving tablets were found to be decreased by the addition of superdisintegrants.

Moreover, Ratnakar et al., 2013 prepared fast dissolving tablet of Telmisartan by direct compression method. The concentration of croscarmellose sodium, SSG and crospovidone was varied to formulate the tablet. However, Mantry et al., 2014 formulated tablets of SDPs of Felodipine. SDPs of Felodipine were prepared by solvent evaporation method using PVP-K30, PEG-4000 and PEG-6000 as hydrophilic carriers. The dissolution rate of formulations was markedly increased as compared to the pure drug. Whereas, Mahajan and Kokate, 2015 had developed pregelatinized hydroxyl propyl pea starch based oral dissolving films of Tadalafil to improve its oral bioavailability. Films were prepared by solvent casting technique based on Box-Behnken statistical design with concentrations of Lycot RS720® and glycerin (plasticizer) as independent variables. Tensile strength and drug release was considered as two dependent variables. Similarly, Mekonnen, 2016 had prepared fast dissolving film formulation of Tadalafil using low viscosity grade HPMC-E5 and HPMC-E15 to offering higher patient compliance and excellent effectiveness of the drug. PEG-400 and propylene glycol were used as plasticizers, tween-80 as solubilizing agent, aspartame and menthol as sweetener and pineapple flavor as taste masking agent.

3.3 Past work carried on solid dispersions (SDPs)

Yamashita et al., 2003 had established new method of preparation for SDP formulation of Tacrolimus (poorly water soluble drug) without the use of solvent to enhance its solubility. To select the appropriate carrier, three different SDPs with PEG-6000, PVP and HPMC were prepared. Similarly, Kim et al., 2006 prepared SDP of Felodipine using a solvent wetting method. Rate of dissolution of drug was found to be faster when PVP, HPMC and poloxamer used as hydrophilic carrier. In addition, Dehghan and Jafar, 2006 had worked for improving dissolution of Meloxicam using preparation of SDP and to investigate the effect of different types of carriers on in-vitro dissolution of Meloxicam. SDPs of Meloxicam were prepared by using co-grinding, physical mixing and solvent evaporation methods with PEG-6000 as hydrophilic carrier.
Likewise, Shavi et al., 2010 made an attempt for enhancement of dissolution and bioavailability of Gliclazide by preparation of SDP with different water soluble polymers such as PEG-4000, PEG-6000 using fusion method and PVP-K30 by solvent evaporation method. In the same way, Kothawade et al., 2010 formulated SDP of Telmisartan to improve its solubility and dissolution rate. SDPs were prepared using PVP, PEG-1500 and PEG-4000 to increase its aqueous solubility. In addition, Dehghan and Shareef, 2010 had worked for enhancement of dissolution and anti-inflammatory effect of Meloxicam using SDPs by $3^2$ factorial designs. SDP of Meloxicam was prepared using hydrophilic carriers like PVP and PEG-6000 to solve the solubility problem. PEG-6000 and PVP in varying amounts was the independent variables.

Further, Kumar et al., 2011 prepared SDP of Irbesartan by solvent evaporation method and physical mixing using various superdisintegrants such as SSG, crospovidone, croscarmellose sodium and MCC for enhancing its solubility and dissolution rate. Results revealed faster disintegration within two minutes in comparison with the pure drug. Similarly, Gupta et al., 2011 prepared SDP of Ibuprofen (BCS class II drug) by using different methods to achieve its enhanced dissolution rate and improved oral bioavailability. In addition, Kshirsagar et al., 2011 used modified solvent method for preparation of SDPs of Oxcarbazepine and Quetiapine using PEG-6000 as a carrier to improve the dissolution properties. Likewise, Someshwar et al., 2011 had worked for dissolution enhancement of poorly water soluble drug Famotidine using water soluble carriers like urea, mannitol and sorbitol. SDPs showed improved dissolution when compared with the pure drug.

Furthermore, Bhise et al., 2011 had prepared SDP of Telmisartan by fusion method using polymers like Poloxamer-407, PVP-K30, HPMC-E4 and PEG-6000 to enhance its solubility. Aleti et al., 2011 prepared SDP of Cefixime (BCS class-II drug with low oral bioavailability) using natural polymer. Various techniques used for preparing solid dispersions are physical mixing, kneading and solvent evaporation methods using different drug to polymer ratio. Similarly, Dewan et al., 2012 formulated SDPs of Carvedilol (poorly water soluble drug) by both fusion and solvent evaporation method using different polymers such as PEG-6000, poloxamer-407, HPMC-6cps and SSG.
In addition, **Mogal et al., 2012** had used SDP technique for improving solubility of Paracetamol. Several carriers such as methyl cellulose, urea, lactose, citric acid, PVP PEG-4000 and PEG-6000 were used. Whereas, **Kaushik and Pathak, 2012** had used solvent (ethanol) wetting method for preparation of SDP of Felodipine. The dissolution rates of Felodipine with PVP, HPMC and poloxamer SDPs were found to be much faster for the physical mixtures. Similarly, **Kumar et al., 2012** prepared SDP of Tadalafil (BCS class-II drug) using water soluble polymers like PVP-K30 and PEG-6000 for improvement of its dissolution and bioavailability. SDPs were further evaluated for drug content, *in-vitro* drug release, FTIR, DSC, XRD and SEM analysis.

In addition, **Rao et al., 2012** formulated SDPs of Carvedilol (BCS class-II drug) by solvent evaporation method using different carriers like mannitol, lactose, urea and PEG-4000 in different ratios for enhancement of its dissolution rate. The dissolution rate was substantially improved for Carvedilol SDPs as compared with pure drug sample. Likewise, **Bhyan et al., 2013** had prepared SDP of Carvedilol by solvent evaporation and fusion methods using nicotinamide and PVP-K30 to improve its solubility, dissolution properties and stability. DSC, XRD and SEM study suggested amorphous state of drug in SDP form. Similarly, **Ibrahim and Badry, 2014** formulated SDP of Famotidine using Gelucire 50/13 and Pluronic-F127 to enhance its dissolution. SDPs were characterized by DSC, which indicated that there were no signs of interaction of the drug with the carriers. Moreover, **Begam et al., 2014** developed co-ground mixtures and SDPs of Aripiprazole with hydrophilic carriers such as guar gum and HPMC. FTIR studies revealed no chemical interaction between drug and carriers.

### 3.4 Past work carried on fast dissolving oral film (FDFs)

**Repka et al., 2005** had prepared thin film of Lidocaine by hot melt extrusion technology using cellulosic polymers HPC and HPMC. Results suggested that the mechanism of drug release from both of the films was predominantly diffusion of the drug through the polymer matrices. Similarly, **Dinge and Nagarsenker, 2008** had formulated fast dissolving films for delivery of Triclosan to the oral cavity using poloxamer-407 and hydroxyl propyl-β- cyclodextrin (HPBCD) to improve drug solubility.
In addition, Shimoda et al., 2009 had prepared fast dissolving oral thin film of Dexamethasone using MCC, PEG, HPMC, polysorbate-80 and low-substituted HPC as base materials. The film was disintegrated within 15 seconds after immersion into distilled water. The dissolution test showed that approximately 90% of Dexamethasone was dissolved within 5 minutes. Likewise, Nishimura et al., 2009 had prepared Prochlorperazine oral disintegrating film using MCC, PEG and HPMC as the base materials. The dissolution test revealed a rapid disintegration property in which most of Prochlorperazine dissolved within 2 minutes after insertion into the dissolution medium.

In addition, Cilurzo et al., 2010 had studied the feasibility of formulation of Nicotine fast dissolving films made of maltodextrins. Particular attention was given to the selection of the suitable taste masking agent and characterization of the flexibility under different mechanical stresses. In the same way, Kulkarni et al., 2010 had prepared oral strip by solvent casting method using various hydrophilic polymers like HPMC-E15, HPMC-K4M, HPMC-E5, PVA, PVP, gelatin, eudragit-RL100 and pullulan. Among all polymers pullulan and HPMC-E15 showed desired film forming capacity.

Similarly, Garsuch and Breitkreutz, 2010 had compared different film forming materials used for the preparation of fast dissolving oral films with and without caffeine and caffeine citrate. All films were found to be dissolved within 40 seconds. HPMC was found to be the most suitable film forming material, providing fast dissolution films. Further, Patel et al., 2010 had done review on fast dissolving films and suggested that sublingual or buccal delivery of a drug in form of FDF has the potential to provide fast onset of action, decrease the dose and thus enhance safety and efficacy of drug. In addition, Murata et al., 2010 had prepared FDFs from natural polysaccharides such as pullulan without heating, controlling the pH or adding other materials. All films were found to be readily swelled in dissolution medium, released the incorporated compound and subsequently disintegrated. In the same way, Meshad and Hagrasy, 2011 prepared orodispersible film of Mosapride by solvent casting method and optimized using D-optimal design to study the effect of polymer ratio and plasticizer type and their level on film mechanical properties, disintegration time and dissolution rate.

Furthermore, Gupta et al., 2011 worked for enhancement of dissolution rate and oral bioavailability of Meclizine HCl by preparing rapidly dissolving oral film with β-cyclodextrine. The FDFs were prepared by solvent casting method with suitable
appearance, mechanical strength and disintegration time using methocel-E5 as a primary film former. Whereas, *Cilurzo et al., 2011* had prepared FDF of Diclofenac for suppression of bitterness by a taste sensing system. The bitterness intensity of Diclofenac and the masking effect were evaluated by an electronic tongue. However, *Prasanthi et al., 2011* developed sublingual FDF for an antiasthmatic drug by solvent evaporation technique using different water soluble polymers. In this study tween-80 was used as a solubilizing agent and aspartame as a sweetener. Likewise, *Saini et al., 2011* formulated oral fast dissolving anti allergic film of Levocetrizine Dihydrochloride by solvent casting method using Maltodextrin & HPMC-E15 as film forming polymers. To decrease the disintegration time, concentration of maltodextrin & HPMC-E15 were optimized by using $2^2$ factorial designs.

Furthermore, *Ghorwade et al., 2011* formulated FDFs of Montelukast sodium by solvent casting method using gelatin as a film base, different concentrations of superdisintegrants like MCC and crospovidone and PEG-400 as plasticizer. Similarly, *Tomar et al., 2012* had prepared FDFs of Dicyclomine for buccal delivery by solvent casting method using HPMC, PVA and Eudragit-RL100. Films were evaluated for mechanical properties, morphology study, swelling properties, disintegration time, dissolution time and *in-vitro* drug release. In addition, *Bhyan and Jangra, 2012* developed fast dissolving sublingual films of Rizatriptan benzoate to bypass first pass metabolism and provide rapid onset of action of the drug. The FDFs were prepared by solvent casting method using low viscosity grade HPMC-E15, maltodextrin as polymer and SSG as disintegrating agent.

Furthermore, *Nagar et al., 2012* had formulated matrix type mouth dissolving films of Aripiprazole by solvent evaporation technique using HPMC-3cps. The mouth dissolving film was found to be bioequivalent to the conventional solid dosage form. Similarly, *Patel et al., 2012* formulated mouth dissolving film of Domperidone by solvent casting technique and its *in-vitro* performance was evaluated by the usual pharmacopoeial and unofficial tests. The mouth dissolving film formed was found to be disintegrated within 1 minute. While, *Figueroa et al., 2012* prepared HPMC films containing BCS Class-II drug (Naproxen, Fenofibrate and Griseofulvin) nanoparticles for enhancing their dissolution rate. The influence of the drug molecule on the film properties was also investigated. However, *Panchal et al., 2012* prepared mouth
dissolving film of Ropinirole Hydrochloride by solvent casting method using pullulan as polymer and PEG-400 as plasticizer.

Furthermore, Rubia et al., 2012 formulated FDFs of Citalopram Hydrobromide by solvent casting technique using HPMC-E5 as polymer, propylene glycol as plasticizer and sorbitol as sweetener. Drug excipient compatibility study was performed using FTIR studies. In addition, Jadhav et al., 2012 prepared fast dissolving oral film of Levocetirizine Dihydrochloride using HPMC and sodium CMC to improve its bioavailability. The films were designed using optimal design and numerical optimization technique was applied to find out the best formulation. Likewise, Chouhan et al., 2012 prepared FDFs of Nicotine Hydrogen Tartrate for smoking cessation therapy. The films were prepared using HPMC-E3 or E5 by solvent casting method. All formulations exhibited rapid release during the initial few minutes followed by a relatively slow release, finally approaching a plateau level in about 10 minutes.

In addition, Vijaya et al., 2012 formulated fast dissolving oral thin films of Montelukast Sodium by solvent casting method using different film forming agents like HPMC and PVP, PEG-400 and glycerol as a plasticizer and mannitol as sweetener to bypass first pass metabolism, enhance the convenience and compliance for the elderly and pediatric patients. Similarly, Bansal et al., 2013 prepared fast dissolving film of Losartan Potassium by solvent casting method using PVA and maltodextrin in different ratio, propylene glycol as a plasticizer to improve oral bioavailability of drug. Whereas, Low et al., 2013 had studied the effect of type and ratio of solubilising polymer on characteristics of hot melt extruded orodispersible films. Concentration of drug and the interaction between drug and polymer was found to be the main factors which affected the mechanical strength of the film.

Furthermore, Nalluri et al., 2013 prepared mouth dissolving films of Salbutamol Sulfate by wet film applicator to casting the solution which was prepared using HPMC of different viscosity grades along with film modifier, PVP-K30 and SLS to enhance convenience and compliance to the elderly and pediatric patients for better therapeutic efficacy. Similarly, Farhana et al., 2013 prepared Caffeine containing fast dissolving oral thin film using HPMC-15cps, sodium alginate and kollicoat® IR white in various proportions to achieve quick onset of action and improved bioavailability. Cumulative percent drug release of film was found to be near about 100% within 120 seconds which
was remarkable in comparison to other formulations. In addition, Chaudhary et al., 2013 had developed fast dissolving orodispersible films of Granisetron Hydrochloride by two factor, three level Box-Behnken design to achieve rapid onset of action and improved bioavailability.

Similarly, Methaq, 2013 had prepared FDFs of SDP containing Amlodipine Besylate. Drug dissolution was found to be increased with increase in the drug to PEG-6000 or PVP ratio for SDP. Likewise, Riana et al., 2013 developed orally disintegrating film for delivery of probiotics in the oral cavity. The film formulations were composed of Lactobacillus acidophilus entrapped in a matrix composed of carboxymethyl cellulose, gelatin and starch. In addition, Raju et al., 2013 formulated FDFs of Loratidine by solvent casting method using low viscosity grades of HPMC as film forming polymers, sweeteners, flavors and citric acid to mask the bitter taste of Loratidine.

Furthermore, Pamula et al., 2013 developed mouth dissolving films of Chlorpheniramine Maleate using HPMC (3cps and 5cps), methyl cellulose and Kollicoat IR with suitable plasticizers like PEG-400 and glycerin. Superdisintegrant was also included in the formulation to improve the release characteristics. Likewise, Kumar et al., 2013 prepared oral dissolving films containing Sumatriptan Succinate by using different grades of HPMC-E3, E6, E15, maltodextrin DE6, xanthan gum and other polymers by solvent casting method to improve its bioavailability. In addition, Malah and Nazzal, 2013 studied the dissolution and mechanical properties of FDFs prepared from a tertiary mixture of pullulan, PVP and hyperomellose. Disintegration studies were performed in real time by probe spectroscopy to detect the onset of film disintegration. Whereas, Kapadia et al., 2013 developed sublingual film of Asenapine Maleate to achieve avoidance of first pass metabolism, improved bioavailability of drug and improved patient compliance. Different formulations were prepared by varying concentration of HPMC-K4M and ethanol: water ratio by solvent casting method.

Furthermore, Kumar et al., 2014 formulated oral films of Enrofloxacin with the aim of increasing solubility and bioavailability. Films exhibited excellent uniformity, mechanical properties, swelling properties. SEM analysis revealed uniform distribution of drug in polymer matrix. Likewise, Xu et al., 2014 formulated Sildenafil Citrate
containing orally dissolving films using PVA-PEG graft copolymer by solvent casting method to improve its dissolution, bioavailability and provide faster onset of action.

In addition, Preis et al., 2014 studied mechanical strength of orodispersible buccal films. Maximum limit for mechanical strength of the film was set up to 0.06N/mm² based on the obtained results of standard formulation. However, Ketul et al, 2014 developed fast dissolving film of Telmisartan using pullulan as film forming agent and microcrystalline cellulose as disintegrant to achieve faster onset of action and improved bioavailability. Likewise, Sindhu et al., 2015 developed fast dissolving films of Telmisartan (BCS Class-II drug) SDP to increase the oral bioavailability. Formulations were evaluated based on tensile strength, thickness, weight variation, folding endurance, drug content uniformity, surface pH and all exhibited satisfactory results.

Furthermore, Zhao et al., 2015 prepared oral thin film of Meclizine Hydrochloride by solvent casting method to improve its bioavailability. A commercial product (Zentrip) was developed for people who suffered from motion sickness. OTF characteristics were evaluated using micrometer and auto stripping tester. Similarly, Woertz and Kleinebudde, 2015 had prepared orodisperisible polymeric films containing poorly water soluble drugs (Loperamide Hydrochloride and Ibuprofen) with the objective of improved drug loading, storage stability, improved dissolution and bioavailability. HPMC and three different types of HPC were used as film forming polymers. Whereas, Woertz and Kleinebudde, 2015 prepared Loperamide Hydrochloride containing orodisperisible polymeric films with attention on its crystalline form. HPMC and HPC in varying concentrations were used as film forming polymers whereas arabic gum, xanthan gum and tragacanth served as thickening agents. Films were characterized with respect to the content uniformity, morphology, thermal behavior and crystallinity.

In addition, Visser et al., 2015 developed a versatile casting solution suitable for the extemporaneous production of orodispersible films (ODF) for water soluble (Enalapril Maleate) and poorly water soluble drug (Diazepam). The composition of optimized casting solution was hypromellose, carbomer, glycerol, disodium EDTA and trometamol. Whereas, Visser et al., 2015 prepared orodispersible films (ODFs) with application of the quality by design (QbD) approach for optimizing the formulation
using Design-Expert software. Disintegration time was found to be sensitive to the percentage of hypromellose. However, Maghsoodi et al., 2016 prepared mucoadhesive sublingual films of Sumatriptan and combination of Sumatriptan with Metoclopramide separately using solvent casting method with HPMC as polymer and propylene glycol as plasticizer to achieve improved efficacy, patient compliance and improved bioavailability.

Whereas, Patel et al., 2016 had formulated fast dissolving film of Cetirizine and Dextromethorphan using solvent casting method without the use of organic solvent with HPMC-E5 LV, PEG-400 and aspartame-neotame-citric acid-menthol ion exchange resins for taste masking of Dextromethorphan. In addition, Reddy et al., (2016) prepared fast dissolving buccal films of Zolmitriptan by solvent casting method using HPMC-E5, E15 and E50 (film former) and propylene glycol (plasticizer) to increase bioavailability and avoid first pass effect. Best film formulation found to be disintegrated within 56 seconds and released 99.89% of drug. Similarly, Pathan et al., 2016 prepared fast dissolving oral film of Promethazine Hydrochloride by solvent casting method using HPMC-E15, PEG-400, SLS, MCC, sucrose and strawberry flavor to achieve quick onset of action and improved bioavailability. Likewise, Gorle and Patil, 2017 had formulated fast dissolving film containing Amlodipine Besylate using solvent casting method with the use of HPMC and SSG to achieve faster onset of action, improved bioavailability, ease of administration and avoidance of dysphasia. Fast disintegration time of films was achieved at low concentration of HPMC and high concentration of SSG.

Furthermore, Prabhudessai et al., 2017 prepared Orciprenaline Sulphate fast dissolving oral films using different polymers to achieve improved bioavailability, quick onset of action and improve patient compliance. Results of the various studies revealed improved bioavailability, quick release rate of drug and stable formulation. Likewise, Galgatte et al., 2017 designed fast dissolving sublingual wafer of Tamsulosin Hydrochloride with the application of $3^2$ factorial designs to treat benign prostatic hyperplasia with improved bioavailability. Similarly, Alhalabi et al., (2017) developed fast dissolving oral film of SDP of Meloxicam by solvent evaporation methods using HPMC-E6. SDP of drug was prepared by melting method using poloxamer-188 and gelucire 44/14 as hydrophilic polymer to enhance the solubility of drug and it exhibited 5-8 fold increased solubility.
In addition, **Buddhadev and Buddhadev, 2017** prepared fast dissolving films of Etophylline by solvent casting method using HPMC and PVA to achieve rapid onset of action, increased bioavailability, ease for administration and avoidance of problem of dysphasia. Films indicated fast disintegration time and faster dissolution of drug which might provide quick onset of action. Likewise, **Sarangi et al., 2017** developed fast dissolving oral films of Losartan Potassium by solvent casting method. Films indicated uniform drug content, 78-96% drug release within 5 minutes with first order release kinetics. Similarly, **Thonte et al., (2017)** prepared fast dissolving films of SDP (with PEG-6000) of Glibenclamide by the solvent casting method using HPMC-K15, HPMC-E15, HPMC-K100, PEG-400, tween-80 and citric acid. Films exhibited fast disintegration and fast mouth dissolving time of 26 seconds and 2 minutes respectively with acceptable film endurance.

Furthermore, **Jaafar, 2017** prepared fast dissolving oral film of Metoclopramide Hydrochloride by solvent casting method using different types and concentration of polymer and plasticizer to improve patient compliance by avoiding problem of dysphasia. In the same way, **Sharawy et al., 2017** prepared buccoadhesive films of Duloxetine Hydrochloride by solvent casting method using HPMC and PVA to improve its oral bioavailability and avoid first pass effect. Pharmacokinetic study of optimized films revealed high Cmax as compared with that of marketed formulations. Likewise, **Joshua et al., 2017** had prepared oral thin films of Propranolol Hydrochloride to improve its bioavailability and avoiding first pass metabolism. Best film formulation showed fast disintegration time (47 seconds), fast drug release (93%) up to 20 minutes, ex-vivo permeation (91%) and smooth surface with little pores in SEM analysis.

Moreover, **Tamer et al., 2018** developed fast dissolving oral film of practically insoluble Bromocriptine Mesylate by solvent casting method using HPMC, PVA, pectin and gelatin (film formers), PEG-400, propylene glycol and glycerin (plasticizer), poloxamer-407 (surfactant) and crospovidone (superdisintegrants) to achieve improved solubility, enhanced bioavailability, avoidance of pre systemic metabolism and quick onset of action. In addition, **Bawane et al., 2018** prepared fast dissolving film of Bisoprolol Fumarate by solvent casting method using hydrophilic polymers to achieve quick onset of action. Films found to be disintegrated rapidly and exhibited fast drug release.