



Review Article

Past Decade work done on fast Dissolving Oral Films

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ABSTRACT

The most popular oral solid dosage forms are tablets and capsules. Many patients find it difficult to swallow tablets and hard gelatin capsules particularly pediatric and geriatric patients and do not take their medicines as prescribed because difficulty in swallowing. To overcome these difficulties, several fast dissolving drug delivery systems have been developed. Fast dissolving oral film is relatively a new dosage form in which thin film is prepared using hydrophilic polymers, which rapidly dissolves on tongue or buccal cavity. An ideal film should be prepared by using different ingredients. A study on different polymers, sweeteners, plasticizers, solubilizers used for fast dissolving oral films are done.

Keywords: Polymers, sweeteners, plasticizers, solubilizers

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1. Introduction

Fast dissolving oral films (FDOFs) or Oral wafers or Oral strips (OS) or sublingual strips or oral thin films (OTF) are the most advanced form of oral solid dosage form due to more flexibility and comfort [1]. It improves the efficacy of

APIs by dissolving within minute in oral cavity after the contact with saliva without chewing and no need of water for administration. It gives quick absorption and instant bioavailability of drugs due to high blood flow and

permeability of oral mucosa is 4-1000 times greater than that of skin [2 and 3]. FDOFs are useful in patients such as pediatric, geriatrics, bedridden, emetic patients, diarrhea, sudden episode of allergic attacks, or coughing for those who have an active life style [4]. It is also useful whether local action desired such as local anesthetic for toothaches, oral ulcers, cold sores or teething. At present Zolmitriptan

is available in the form of tablets, nasal sprays in the market. Patients are non-cooperative with these dosage forms [5]. Hence oral disintegrating films have become important tool to improve the patient compliance. This article gives the information regarding past decade work done on fast dissolving oral films.

2. Excipients used in fast dissolving oral films

Different Polymers Used in Fast Dissolving Oral Films

In FDOFs polymers were used to regulate the release of medicament from the formulation. Among the various polymers, HPMC was extensively used in FDOFs, because it is a nonionic cellulose ether, odorless, soluble in cool water, glacial acetic acid and some organic solvents and water mixtures, not soluble in hot water, ethanol, ether and acetone. Its aqueous solution is of surface activity, high transparency and stability, when heated to certain temperature, the solution becomes cloudy and gelling quickly, however, the solution become clear again after cooling. HPMC has different types varying from its gelling temperature. The solubility is differed from its viscosity, the lower the viscosity, the higher the solubility. However, the solubility in water is not subject to pH value of its aqueous solution. The lower methoxyl content of HPMC, the higher gelling temperature, the lower solubility and surface activity. The various Polymers which were successfully used in preparing fast dissolving oral films were shown in table 1.

Table 1: Various Polymers Used in Fast Dissolving Oral Films

Drug	Polymer	Reference
Sodium diclofenac	Maltodextrin	⁶ Francisco et al., 2011
Amlodipine besylate	Poly Ethylene Glycol (PEG6000) or Poly Vinyl Pyrrolidone (PVP), Sodium Carboxymethyl cellulose (CMC), Hydroxy Propyl methyl cellulose (HPMC)	⁷ Methaq et al., 2013
Montelukast sodium	HPMC, Microcrystalline cellulose and Crospovidone	⁸ Ajaykumaret al., 2011
Zolmitriptan	HPMC E, HPMC E3,	⁹ Sane et al., 2012
Amlodipine Besylate	HPMC, Methylcellulose, PVP k30	¹⁰ Maheswari et al., 2014

Losartan Potassium	HPMC E-5	¹¹ Hemangi et al., 2013
GranisetronHCl	CMC, HPMC and Pullulan	¹² Rawda et al., 2012
Loratidine	HPMC	¹⁴ Narayan et al., 2013
Salbutamol sulphate	Polyvinyl alcohol (PVA)	¹⁶ Mashru et al., 2005
Rizatriptan Benzoate	HPMC15, PVA, Maltodextrin	¹⁷ Karthikyan et al., 2013
Triclosanpoloxamer	HPMC, Xanthan gum and Xylitol	¹⁸ Aditya et al., 2008
Diclofenac sodium	Sodium alginate	¹⁹ Kumaret al., 2013
Verapamil	HPMC E 6, Maltodextrin	²⁰ Kunte et al., 2010
Levocetirizinedihydrochloride	HPMC, PVA	²¹ Prabhakaret al., 2011
Ivabradine HCl	HPMC E-5	²² Ravneet et al., 2012
Propranolol HCl	HPMC15	²⁴ Agaiah et al., 2013
Domperidone	Tri ethyl citrate (TEC), PVA,	²⁵ Rafiet al., 2013
Zolmitriptan	Sodium alginate, Xanthan gum and Sodium starch glycolate, Guar gum	²⁹ Deepthi et al., 2014
Losartan potassium	HPMC15, PVP K30, PVA	³³ Rasoolet al., 2014
Losartan potassium	Maltodextrin, PVA	³⁵ Sumedha et al., 2013
Palonosetron HCl	HPMC, NaCMC, PVP and Pullulan gum-Xanthan gum-HPG	³⁶ Swamy et al., 2014

Montelukast sodium	HPMC	³⁷ Sucrose <i>et al.</i> , 2012
Zolmitriptan	HPMC	³⁹ Prasanna <i>et al.</i> , 2012
Levocetirizine	Pullulan, Xanthan gum	⁴² Dhagla <i>et al.</i> , 2012
Granisetron HCl	HPMC15 cps, PVP K-30	⁴³ Hema <i>et al.</i> , 2013
Amlodipine Besylate	HPMC, NaCMC,	⁴⁴ Methaque <i>et al.</i> , 2013
UAMC01398	HPMC	⁴⁷ Carolien <i>et al.</i> , 2014
Dexamethasone	Hydroxy Propyl Cellulose, Hypromellose	⁴⁹ Minako <i>et al.</i> , 2011
Triclosan	HPMC, Xanthan gum, Xylitol	⁵¹ Aditya <i>et al.</i> , 2008
Caffeine, Riboflavin	PVA	⁵² Xiaoqiang <i>et al.</i> , 2012
Piroxicam	Maltodextrins	⁵³ Francesco <i>et al.</i> , 2008
Diclofenac sodium	Sodium alginate	⁵⁴ Naveen <i>et al.</i> , 2013
Ondansetron HCl	PVA, PVP, Carbopol 934P	⁵⁵ Koland <i>et al.</i> , 2010
Novel sildenafil citrate	PVA, graft copolymer Kollicoat IR, Sodium alginate	⁵⁷ Xu <i>et al.</i> , 2014
Promethazine HCl	Pullulan	⁵⁸ Jigar <i>et al.</i> , 2014
Indomethacin	PVP	⁶⁰ Simonet <i>et al.</i> , 2009
Nicotine hydrogen tartrate	Maltodextrins	⁶¹ Francesco <i>et al.</i> , 2010
Flupentixoldihydrochloride	HPMC E-5, CMC	⁶³ Ahmed <i>et al.</i> , 2014

Different Sweeteners Used In Fast Dissolving Oral Films

Sweeteners were incorporated in mouth dissolving films to mask bitter taste of the drugs. Among the sweeteners, Aspartame and Mannitol were widely used. Researches proved that Aspartame has carcinogenic effect. Mannitol is a polyol, which is widely used in the food and pharmaceutical industries because of its unique functional properties. It is about 50% as sweet as sucrose and has a

desirable cooling effect often used to mask bitter tastes. Mannitol is non-cariogenic and has a low caloric content. Various sweeteners which were used in fast dissolving oral films were shown in table 2.

Table 2: Various sweeteners used in fast dissolving oral films

Drug	Sweetener	Reference
Sodium diclofenac	Sorbitanole ate	⁶ Francesco <i>et al.</i> , 2011
Losartan Potassium	Mannitol	⁷ Hemangi <i>et al.</i> , 2013
Salbutamol sulphate	Mannitol	¹⁶ Mashru <i>et al.</i> , 2005
Rizatriptan Benzoate	Mannitol, Aspartame	¹⁷ Karthikeyan <i>et al.</i> , 2013
Triclosanpoloxamer	Mannitol, Aspartame	¹⁸ Aditya <i>et al.</i> , 2008
Verapamil	Aspartame	²⁰ Kunte <i>et al.</i> , 2010
Levocetirizinedihydrochloride	Aspartame	²¹ Prabhakara <i>et al.</i> , 2011
Ivabradine HCl	Aspartame	²² Ravneet <i>et al.</i> , 2012
Propranolol HCl	Aspartame	²⁴ Agaiah <i>et al.</i> , 2013
Losartan potassium	Aspartame	³³ Rasool <i>et al.</i> , 2014
Losartan potassium	Mannitol	³⁵ Sumedha <i>et al.</i> , 2013
Palonosetron HCl	Aspartame	³⁶ Swamy <i>et al.</i> , 2014
Montelukast sodium	Sucrose	³⁷ Vijaykumaret <i>et al.</i> , 2012
Granisetron HCl	Saccharin sodium	⁴² Hema <i>et al.</i> , 2013
Triclosan	Aspartame, Mannitol	⁵¹ Aditya <i>et al.</i> , 2008
Ondansetron HCl	Mannitol, Sodium saccharin	⁵⁵ Koland <i>et al.</i> , 2010
Promethazine HCl	Aspartame	⁵⁸ Jigar <i>et al.</i> , 2014

Different Plasticizers Used In Fast Dissolving Oral Films

Plasticizers in FDOFs for the flexibility of films. It avoids the cracking and breaking of films. Among the plasticizers used Polyols were popularly used as plasticizer in mouth dissolving films. Among them Poly Ethylene Glycols were popularly used. PEG's below 700 molecular weight occur as clear to slightly hazy, colourless, slightly hygroscopic liquids with a slight characteristic odour. PEG's between 700-900 are semi-solid. PEG's over 1000 molecular weight are creamy white waxy solids, flakes, or free-flowing

powders. Various plasticizers which were used in fast dissolving oral films were shown in table 3.

Table 3: Various plasticizers used in fast dissolving oral films

Drug	Plasticizer	Reference
Sodium diclofenac	Glycerin	⁶ Francesco <i>et al.</i> , 2011
Amlodipine besylate	Glycerin	⁷ Methaq <i>et al.</i> , 2013
Montelukast sodium	PEG400	⁸ Ajayet <i>et al.</i> , 2011
Zolmitriptan	Polyvinyl alcohol, PEG 400	⁹ Sane <i>et al.</i> , 2012
Losartan Potassium	PEG 400	¹¹ Hemangi <i>et al.</i> , 2013
Granisetron HCl	PEG 400	¹² Rawda <i>et al.</i> , 2012
Salbutamol sulphate	Glycerol	¹⁶ Mashru <i>et al.</i> , 2005
Rizatriptan Benzoate	Propylene Glycol	¹⁷ Karthikeyan <i>et al.</i> , 2013
Triclosan poloxamer	PEG, Glycerol	¹⁸ Aditya <i>et al.</i> , 2008
Verapamil	Glycerol	¹⁹ Kunte <i>et al.</i> , 2010
Levocetirizinedihydrochloride	PEG	²¹ Prabhakara <i>et al.</i> , 2011
Ivabradine HCl	PEG 400	²² Ravneet <i>et al.</i> , 2012
Propranolol HCl	PEG	²⁴ Agaiah <i>et al.</i> , 2013
Domperidone	Polyvinyl alcohol, Kollicoat IR, Glycerin	²⁵ Rafi <i>et al.</i> , 2013
Zolmitriptan	PEG 400	²⁹ Deepthi <i>et al.</i> , 2014
Losartan potassium	PEG	³³ Rasool <i>et al.</i> , 2014
Losartan potassium	PEG	³⁵ Sumedha <i>et al.</i> , 2013
Palonosetron HCl	PEG 400	³⁶ Swamy <i>et al.</i> , 2014
Montelukast sodium	Glycerin	³⁷ Sucrose <i>et al.</i> , 2012
Zolmitriptan	PEG	³⁹ Prasanna <i>et al.</i> , 2012
levocetirizine	PEG	⁴² Dhagla <i>et al.</i> , 2012
Amlodipine Besylate	PEG	⁴⁴ Methaq <i>et al.</i> , 2013
UAMC01398 (Anti HIV drug)	PEG 400	⁴⁷ Carolien <i>et al.</i> , 2014

Dexamethasone	PEG	⁴⁹ Minako <i>et al.</i> , 2011
Triclosan	PEG, Glycerol	⁵¹ Aditya <i>et al.</i> , 2008
Piroxicam	Glycerin	⁵³ Francesco <i>et al.</i> , 2008
Ondansetron HCl	PEG 400	⁵⁵ Koland <i>et al.</i> , 2010
Sildenafil citrate	PEG, Glycerol	⁵⁷ Xu <i>et al.</i> , 2014
Promethazine HCl	PEG	⁵⁸ Jigar <i>et al.</i> , 2014
Nicotine hydrogen tartrate	Glycerol	⁶¹ Francesco <i>et al.</i> , 2010

Different Solubilizers Used In Fast Dissolving Oral Films

Various solubilizers were used in fast dissolving oral films. Poloxamer 407 was widely used solubilizer in FDOFs. Most of the common uses of poloxamer 407 are related to its surfactant properties. For example, it is widely used in cosmetics for dissolving oily ingredients in water. It can also be found in multi-purpose contact lens cleaning solutions, where its purpose there is to help remove lipid films from the lens. It can also be found in some mouthwashes. 2-Hydroxypropyl- β -cyclodextrin is the most widely used modified cyclodextrin. The compound has shown to change the physicochemical properties of lipophilic compounds when co-administered.

2-Hydroxypropyl- β -cyclodextrin functions by forming an inclusion complex with the compound being administered for easier diffusion across biological membranes, and its popularity can be attributed to its large 7 glucose unit cavity size. Some advantageous effects are reduction of negative effects, increased aqueous solubility and increased stability. The effects of 2-Hydroxypropyl- β -cyclodextrin have been observed to be dose dependent with both advantageous and disadvantageous results occurring at sporadic concentrations. The compound may also increase the antimicrobial effectiveness of chemical agents by increasing their release rate. Various solubilizers which were used in fast dissolving oral films were shown in table 4.

Table 4: Various solubilizers used in fast dissolving oral films

Drug	Solubilizer	Reference
Amlodipine Besylate	Sodium lauryl sulphate	⁹ Maheswari <i>et al.</i> , 2014
Triclosan poloxamer	Poloxamer407 and Hydroxypropyl- β -cyclodextrin	¹⁸ Aditya <i>et al.</i> , 2008
Triclosan	Poloxamer407, hydroxypropyl- β -cyclodextrin (HPBCD)	⁵¹ Dinge <i>et al.</i> , 2008

3. Conclusion

This study is about past work done on fast dissolving oral films, these films were prepared by using various excipients. From this study it was concluded that the widely

used excipients in FDOFs were polymers (HPMC), sweeteners (mannitol), plasticizer (PEG) and solubilizer (poloxamer 407).

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