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Past Decade work done on fast Dissolving Oral Films

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A B S T R A C T
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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CONTENTS

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 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]Francesco *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]Ajaykumar*et 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]Narayana*et al.*, 2013
Salbutamol sulphate	Polyvinyl alcohol (PVA)	[16]Mashru *et al.*, 2005
Rizatriptan Benzoate	HPMC15, PVA, Maltodextrin	[17]Karthikeyan *et al.*, 2013
Triclosanpoloxamer	HPMC, Xanthan gum and Xylitol	[18]Aditya *et al.*, 2008
Diclofenac sodium	Sodium alginate	[19]Kumar*et al.*, 2013
Verapamil	HPMC E 6, Maltodextrin	[20]Kunte *et al.*, 2010
Levocetirizinedihydrochloride	HPMC, PVA	[21]Prabhakar*et 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]Rafi*et 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]Rasool*et 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 *et al.*, 2012
Zolmitriptan	HPMC	[39]Prasanna*et al.*, 2012
Levocetirizine	Pullulan, Xanthan gum	[42]Dhagla*et al.*,2012
Granisetron HCl	HPMC15 cps, PVP K-30	[43]Hema *et al.*, 2013
Amlodipine Besylate	HPMC, NaCMC,	[44]Methaq*et al.*, 2013
UAMC01398	HPMC	[47]Carolien *et al.*,2014
Dexamethasone	Hydroxy Propyl Cellulose, Hypromellose	[49]Minako *et al.*, 2011
Triclosan	HPMC, Xanthan gum, Xylitol	[51]Aditya *et al.*, 2008

Caffeine, Riboflavin	PVA	[52]Xiaoqiang *et al.*, 2012
Piroxicam	Maltodextrins	[53]Francesco*et al.*,2008
Diclofenac sodium	Sodium alginate	[54]Naveen *et al.*, 2013
Ondansetron HCl	PVA, PVP, Carbopol 934P	[55]Koland *et al.*, 2010
Novel sildenafil citrate	PVA, graft copolymer Kollicoat IR, Sodium alginate	[57]Xu *et al.*, 2014
Promethazine HCl	Pullulan	[58]Jigar *et al.*, 2014
Indomethacin	PVP	[60]Simon*et al.*,2009
Nicotine hydrogen tartrate	Maltodextrins	[61]Francesco *et al.*,2010
Flupentixoldihydrochloride	HPMC E-5, CMC	[63]Ahmed *et al.*,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	Sorbitanolate	[6]Francesco *et al.*, 2011
Losartan Potassium	Mannitol	[7]Hemangi *et al.*,2013
Salbutamol sulphate	Mannitol	[16]Mashru *et al.*, 2005
Rizatriptan Benzoate	Mannitol, Aspartame	[17]Karthikeyan *et al.*, 2013
Triclosanpoloxamer	Mannitol, Aspartame	[18]Aditya *et al.*, 2008
Verapamil	Aspartame	[20]Kunte *et al.*, 2010
Levocetirizinedihydrochloride	Aspartame	[21]Prabhakara *et al.*, 2011
Ivabradine HCl	Aspartame	[22]Ravneet *et al.*, 2012
Propranolol HCl	Aspartame	[24]Agaiah *et al.*, 2013
Losartan potassium	Aspartame	[33]Rasool *et al.*, 2014
Losartan potassium	Mannitol	[35]Sumedha *et al.*,2013
Palonosetron HCl	Aspartame	[36]Swamy *et al.*, 2014
Montelukast sodium	Sucrose	[37]Vijaykumar*et al.*,2012
Granisetron HCl	Saccharin sodium	[42]Hema *et al.*, 2013
Triclosan	Aspartame, Mannitol	[51]Aditya *et al.*, 2008
Ondansetron HCl	Mannitol, Sodium saccharin	[55]Koland *et al.*, 2010
Promethazine HCl	Aspartame	[58]Jigar *et al.*, 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 *et al.*, 2011
Amlodipine besylate	Glycerin	[7]Methaq *et al.*,2013
Montelukast sodium	PEG400	[8]Ajay*et al.*,2011
Zolmitriptan	Polyvinyl alcohol, PEG 400	[9]Sane *et al.*, 2012
Losartan Potassium	PEG 400	[11]Hemangi *et al.*,2013
GranisetronHCl	PEG 400	[12]Rawda *et al.*,2012
Salbutamol sulphate	Glycerol	[16]Mashru *et al.*,2005
Rizatriptan Benzoate	Propylene Glycol	[17]Karthikeyan *et al.*,2013
Triclosanpoloxamer	PEG, Glycerol	[18]Aditya *et al.*,2008

Verapamil	Glycerol	[19]Kunte*et al.*, 2010
Levocetirizinedihydrochloride	PEG	[21]Prabhakara *et al.*,2011
Ivabradine HCl	PEG 400	[22]Ravneet *et al.*,2012
Propranolol HCl	PEG	[24]Agaiah *et al.*,2013
Domperidone	Polyvinyl alcohol, Kollicoat IR, Glycerin	[25]Rafi *et al.*, 2013
Zolmitriptan	PEG 400	[29]Deepthi *et al.*, 2014
Losartan potassium	PEG	[33]Rasool *et al.*,2014
Losartan potassium	PEG	[35]Sumedha *et al.*,2013
Palonosetron HCl	PEG 400	[36]Swamy *et al.*,2014
Montelukast sodium	Glycerin	[37]Sucrose *et al.*, 2012
Zolmitriptan	PEG	[39]Prasanna*et al.*, 2012
levocetirizine	PEG	[42]Dhagla *et al.*, 2012
Amlodipine Besylate	PEG	[44]Methaq *et al.*, 2013
UAMC01398 (Anti HIV drug)	PEG 400	[47]Carolien *et al.*,2014
Dexamethasone	PEG	[49]Minako *et al.*,2011
Triclosan	PEG, Glycerol	[51]Aditya *et al.*,2008
Piroxicam	Glycerin	[53]Francesco *et al.*,2008
Ondansetron HCl	PEG 400	[55]Koland *et al.*,2010
Sildenafil citrate	PEG, Glycerol	[57]Xu *et al.*,2014
Promethazine HCl	PEG	[58]Jigar *et al.*, 2014
Nicotine hydrogen tartrate	Glycerol	[61]Francesco *et al.*, 2010

Table 4: Various solubilizers used in fast dissolving oral films

Drug	**Solubilizer**	**Reference**
Amlodipine Besylate	Sodium lauryl sulphate	[9]Maheswari *et al.*,2014
Triclosanpoloxamer	Poloxamer407 and Hydroxypropyl-β- cyclodextrin	[18]Aditya *et al.*,2008
Triclosan	Poloxamer407, hydroxypropyl-β- cyclodextrin (HPBCD)	[51]Dinge *et al.*,2008

3. Different Solubilizers

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 antimicrobialeffectiveness of chemical agents by increasing their release rate. Various solubilizers which were used in fast dissolving oral films were shown in table 4.

4. 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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