ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Potential Drug Candidates for Fast Dissolving Drug Delivery - A Review

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ABSTRACT

Researchers throughout the world are focusing intensively on the methods for the development of new drug delivery systems to enhance patient's compliance. The oral route however still remained as the best administration route of therapeutic agents for its ease of ingestion, pain avoidance and versatility. Hence, fast dissolving tablets become an emerging trend in the pharmaceutical industry. Fast dissolving tablets are ideal for all types of people, including for people who have swallowing difficulties, paediatric, geriatric, and bedridden patients. It is also for active patients who are busy, travelling and may not have access to water. Fast dissolving tablets are also known as orodispersible tablets, mouth-dissolving tablets, orally disintegrating tablets, melt-in mouth tablets, rapimelts, porous tablets, quick dissolving etc. This type of tablets disintegrates quickly once introduced into the mouth in the absence of additional water for easy administration of active pharmaceutical ingredients. Many drugs have the potentials to be made into orodispersible tablets. They vary from analgesics to neuroleptics and anti-psychotic drugs. However only a small percentage of them are researched on and some have been manufactured and marketed. In this review article, drug candidates suitable for fast dissolving drug delivery and the available marketed products have been listed.

Keywords: Fast dissolving tablet (FDT), Marketed fast dissolving tablets, Potential candidates,

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ISSN: 0975-8585

INTRODUCTION

Fast-dissolving drug-delivery systems were initially developed in the late 1970s as an alternative to tablets, capsules, and syrups for paediatric and geriatric patients who experiences difficulties in swallowing traditional oral solid-dosage forms. [1]The speed of solubility of drug affects the rate of absorption of the drug. The faster the drug dissolve into solution, quicker the absorption and onset of clinical effect. They should readily dissolve or disintegrate in the saliva generally within <60 seconds. Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach. The significance of orodispersible dosage forms are progressively being recognized in both, industry and academics. [2]

Orally Disintegrating (OD) Tablet technology has been approved by United States Pharmacopoeia (USP), Centre for Drug Evaluation and Research (CDER). USFDA defined OD tablet as "A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue". Besides, the European Pharmacopeia adopted the term orodispersible tablet for a tablet that disperses or disintegrates in less than 3 minutes in the mouth before swallowing. Such a tablet disintegrates into smaller granules or melts in the mouth from a hard solid to a gel-like structure, allowing easy swallowing by patients. [4]

There are several factors that should be considered while selecting an appropriate drug candidate for development of orally disintegrating dosage forms. The ultimate characteristics of a drug for dissolution in the mouth and pregastric absorption from ODTs include:

- Ability to permeate oral mucosal tissue.
- Good solubility in water and saliva.
- Free from bitter taste.
- Dose lower than 20 mg.
- Ability to diffuse and partition into the epithelium of the upper GIT (log P >1, or preferably>2).
- Small to moderate molecular weight.
- Partially non-ionized at the oral cavity's pH.

However, there are some characteristics of a drug that maybe rendered unsuitable for delivery as an orally disintegrating dosage form, such as drugs with short half-life and frequent dosing, very bitter or unacceptable taste, and drugs which require controlled or sustained release. [3]

A wide range of potential drug candidates suitable for the production of fast dissolving tablets with additional researches done are included in this review along with the list of commercialized products of FDTs which are available in market given in Table 1.

ISSN: 0975-8585

TABLE 1: LIST OF FAST DISSOLVING TABLETS AVAILABLE IN THE MARKET

NO.	DRUG NAME	THERAPEUTIC USE(S)	BRANDS AVAILABLE	MANUFACTURER
1.	Acetaminophen	Pain reliever	Excedrin® QuickTabs	Bristol-Myers Squibb, NY,USA
		Analgesic	TempraQuicksolv®	
			Jr. Tylenol Meltaways	McNeil Consumer Healthcare
2.	Aripiprazole	Anti-psychotics	AbilifyDiscmelt	Otsuka America/Bristol-Myers Squibb
3.	Acyclovir	Antiviral Agents	Acivir DT	Cipla
4.	Alprazolam	Anti-anxiety Agents	Niravam	Schwarz Pharma
5.	Baclofen	Anti-spastic analgesic	Kemstro™	Schwarz Pharma
6.	Clonazepam	Sedation	Klonopin® wafer	Roche
			Clonazepam ODT	Par Pharmaceutical
7.	Clozapine	Anti-psychotics	FazaClo	AzurPharma
8.	Cisapride Monohydrate	Gastrointestinal Prokinetic Agent	Propulsid® Quicksolv ®	Jannsen
9.	Cetrizine HCL	Anti-histamines	Zotacet MD	ZotaPharma
10.	Cefadroxil	Anti-Bacterial Agents	Cefadur DT	Cipla (protec)
11.	Cefixime	Anti-Bacterial Agents	Cefinar DT	ZydusAlidac
12.	Citalopram	Anti-depressants	Citalopram ODT	Biovail
13.	Caffeine	Anorexigenic Agents	Caffeine FD Film	Hughes medical corporation,U.S.A
14.	Carbidopa	Anti-parkinson Agents	Parcopa	Schwarz Pharma
15.	Diphenhydramine citrate	Sinus pressure relief	Benadryl® Fastmelt®	Pfizer Inc.,NY,USA
	Diphenhydramine and Pseudoephedrine	Vasoconstrictor Agents, Sympathomimetic,Bronchodilator Agents	Benadryl Fastmelt	Warner Lambert, NY,USA
16.	Diphenhydramine	Anti-emetics Anti-Parkinson Agents	UNISOM SleepMelts	Chattem
17.	Domperidone	Anti-emetics	Domray MD	Ray Remedies
			Dom DT	Dr.Morepen
			Domestal DT	Torrent Pharmaceuticals, India
18.	Donepezil	Parasympathomimetics	Aricept ODT	Eisai Co.
19.	Desloratadine	Anti-histamines	ClarinexRediTabs	Schering-Plough Corp.,USA
20.	Hyoscyaminesulphate	Anti-ulcer	NuLev®	Schwarz Pharma
21.	Ibuprofen	NSAID	Cibalginadue FAST	Novartis Consumer Health
			Nurofen® Flashtab®	Boots Healthcare
			CibalginaDueFast	Eurand International

22.	Famotidine	Anti-ulcer	Pepeid® ODT	Merck &Co.,NJ,USA
			Gaster D	Yamanouchi
23.	Fexofenadine	Anti-histamines	Allegra ODT	Sanofi Aventis
24.	Fluoxetine	Anti-depression	Fluoxetine ODT	Biovail
25.	Loratadine	Antihistamine	Claritin® RediTabs®	Schering-Plough Corp.,NY,USA
		Allergy	Childrens Dimetapp® ND	Wyeth consumer Healthcare
			DuraSolv® Alavert®	
26.	Loperamide HCL	Antidiarrheal	Imodium Istant Melts	Jannsen
27.	Lansoprazole	Anti-Infectives	PrevacidSoluTab	Takeda Pharmaceuticals
28.	Mirtazapine	Anti-depression	Remeron® Soltab®	Organon Inc.
29.	Mosapride	Gastroprokinetic Agent	Mosid MT	Torrent Pharmaceutical, India
30.	Metoclopramide	Anti-emetics	Metoclopramide Zydis	Salix Pharmaceuticals
			Reglan ODT	Schwarz Pharma
31.	Montelukast	Anti-Asthmatic Agents, Antiarrhythmic Agents	Romilast	Ranbaxy lab. Ltd.,India
32.	Mirtazapine	Anti-depression	Mirtazapine ODT	Teva Pharmaceuticals
			Remeron® SolTab®	OrganonInc
33.	Nimesulide	NSAIDs	Nimulid MD	Panacea Biotec, India
			Nexus MD	Lexus Organics
			Nimex MD	Mexon Health Care
34.	NAcetylcysteine	Mucolitic	Fluimucil	AlpexPharma SA / Zambon Group
35.	Olanzepine	Psychotropic	Zyperxa®	Eli Lilly, Indianapolis,USA
			OlanexInstab	Ranbaxy Lab LTD. New Dehli, India
36.	Olandansetron	Antiemetic	Zofran® ODT	Galaxo Smith Kline
			Vomokind MD	Mankind
			Ondansetron ODT	Teva Pharmaceuticals
37.	Piroxicam	NSAIDs	Feldene Melt®	Pfizer Inc.,NY,USA
38.	Paracetamol	Analgesic, anti-pyretic	Febrectol	Prographarm, Chateauneuf, France
39.	Phloroglucinol Hydrate	Anti-spasmodic	SpasfonLyoc	Farmalyoc
40.	Prednisolone	Inflammatory, auto	Orapred ODT	ScielePharma

		immune condition		
41.	Rizatritpan benzoate	Migrane	Maxalt® -MLT®	Merck & Co, NJ,USA
42.	Resperidone	Schizophrenia	Resperdal® M-TabTM	Janssen
43.	RamosetoronHCl	Anti-emetic	Nasea OD	Yamanouchi
44.	Rofecoxib	NSAIDs	Dolib MD	Panacea Biotec, India
			Orthoref MD	Biochem
			Rofaday MT	Lupin
			Torrox MT	Torrent Pharmaceuticals, India
45.	Selegiline	Parkinsons disease	ZelaparTM	ElanlAmarin corp.
46.	Tepoxelin	Canine NSAIDs	ZubrinTM (Pet drug)	Schering-Plough Corp.,USA
47.	Tramadol HCl	Analgesics	RaliviaFlashDose®	Fuisz Technology, Ltd.
				Biovail
48.	Various combination	Pediatric cold cough,Allergy	Triaminic® Softchews®	Novartis consumer Health
49.	Valdecoxib	NSAIDs	Valus	Glenmark
50.	Zolmitriptan	Anti-migraine	Zomig-ZMT® Rapimelt®	AstraZeneca
51.	Zolpidem tartrate	Sleep disorders	Zolpidem ODT	Biovail

DRUG CANDIDATES SUITABLE FOR FAST DISSOLVING DRUG DELIVERY:

1. ANALGESICS AND ANTI-INFLAMMATORY AGENTS:

Aloxiprin, Auranofin, Azapropazone, Benorylate, Diflunisal, Ketorolac Tromethamine,Etodolac, Fenbufen, Fenoprofen, Calcim, Flurbiprofen, Ibuprofen, Indomethacin, Ketoprofen, Meclofenamic Acid, Mefenamic Acid, Nabumetone, Naproxen, Oxaprozin, Oxyphenbutazone, Phenylbutazone, Piroxicam, Sulindac, Rofecoxib. [39]

Omaima A. Sammour et al investigated to increase the solubility and dissolution rate of Rofecoxib by the preparation of its solid dispersion with polyvinyl pyrrolidone K30 (PVP K30) using solvent evaporation method. It was concluded that the study showed the suitability of PVP K30 as a carrier for the preparation of Rofecoxib solid dispersions. Compared with the experimental optimized preparation, the observed responses were in close agreement with the predicted values of the optimized one, thereby demonstrating the feasibility of the optimization procedure in developing Rofecoxib mouth dissolve tablets. [5]

Sudhir Bhardwaj et al attempted to formulate and evaluate the fast dissolving tablets of Aceclofenac. They concluded that the fast dissolving tablets of the poor soluble drug can be

made by direct compression technique using selective super disintegrants showing enhanced dissolution, taste masking and hence better patient compliance and effective therapy.[6]

Taksande J B. et al formulated and characterized Lornoxicam fast dissolving tablet using natural superdisintegrants. The natural superdisintegrants used were banana powder, soy polysaccharide and synthetic superdisintegrant crospovidone. It was concluded that natural super disintegrants should be preferred as having nutritive value as well as cost benefit in formulation and development of orodispersible tablets than synthetic polymers. [7]

Venkata Naveen Kasagana et al formulated and evaluated fast dissolving Piroxicam tablets using different superdisintegrants, namely crospovidone, sodium starch glycolate and pregelatinized starch. They concluded that FDTs of Piroxicam can be prepared by direct compression method using three superdisintegrants crospovidone, sodium starch glycolate and pregelatinized starch. Crospovidone was found to be a better superdisintegrant for the formulation of Piroxicam Fast Dissolving Tablets. [8]

Cirri M et al developed a tablet formulation based on an effective Flurbiprofen-cyclodextrin system, able to allow a rapid and complete dissolution of this practically insoluble drug. The drug solubility improvement obtained by the different binary systems varied from a minimum of 2.5 times up to a maximum of 120 times, depending on both the cyclodextrin type and the system preparation method. Selected binary systems were used for preparation of direct compression tablets with reduced drug dosage. [9]

Prashant Khemariya et al developed and evaluated mouth dissolving tablets of Meloxicam. These tablets were prepared by wet granulation procedure. Sublimation of camphor from tablets resulted in better tablets as compared to the tablets prepared from granules that were exposing to vacuum. [10]

Amit Modi et al formulated and evaluated fast dissolving tablets of Diclofenac sodium using different superdisintegrants by direct compression method. It was concluded that the batch which was prepared by using combination of crosspovidone and sodium starch glycolate as a superdisintegrant shows excellent disintegration time, enhance dissolution rate, taste masking and hence lead to improve efficacy and bioavailability of drug.[11]

2. ANTHELMINTICS

Albendazole, Bephenium Hydroxynaphthoate, Cambendazole, Dichlorophen, Iverrnectin, Mebendazole, Oxarnniquine, Oxfendazole, Oxantel Embonate, Praziquantel, Pyrantel Embonate, Thiabendazole.[39]

Devendra Revanand Rane et al researched to formulate fast dissolving tablets of Albendazole to achieve a better dissolution rate and further improving the bioavailability of the drug. They concluded that the feat dissolving tablets of Albendazole can be successfully prepared by direct compression techniques using selected superdisintegrants for better patient

compliance and effective therapy. The relative efficiency of these superdisintegrants to improve the disintegration and dissolution rate of tablets was found in order i.e. Crospovidone>Croscarmellose sodium. [12]

3. ANTI-ARRHYTHMICS

Amiodarone, Disopyramide, Flecainide Acetate, Quinidine Sulphate. [39]

Soumya M. et al made an effort to prepare the fast dissolving tablets of Flecainide acetate by direct compression method. The fast dissolving tablets of Flecainide acetate proved to show better release profile in all aspects as compared to marketed formulation. The use of superdisintegrants crospovidone and croscarmellose showed faster disintegration and dissolution profile. [13]

4. ANTI-ASTHMATIC

Deepak Sharma aimed to prepare the fast disintegrating tablet of Salbutamol sulphate for respiratory disorders for paediatrics. The investigation was undertaken with a view to develop a fast disintegrating tablet of Salbutamol sulphate which offers a new range of products having desired characteristics and intended benefits. Superdisintegrants such as sodium starch glycolate was optimized. Different binders were optimized along with optimized superdisintegrant concentration. The tablets were prepared by direct compression technique. [14]

5. ANTI-BACTERIAL AGENTS

Benethamine Penicillin, Cinoxacin, Ciprofloxacin, Clarithromycin, Clofazimine, Cloxacillin, Demeclocycline, Doxycycline, Erythromycin, Ethionamide, Imipenem, NalidixicAcid, Nitrofurantoin, Rifampicin, Spiramycin, Sulphabenzamide, Sulphadoxine, Sulphamerazine, Sulphacetamide, Sulphadiazine, Sulphafurazole, Sulphamethoxazole, Sulphapyridine, Tetracycline, Trimethoprim.

Kamal Saroha et al formulated and evaluated the fast dissolving tablets of amoxicillin trihydrate using synthetic disintegrants. They concluded that formulation (F8) having 10% CCS and showed promising results than formulation (F4) having 10% SSG. FDT of amoxicillin trihydrate in formulation F8 showed extremely fast dissolution rate than that of tablets of formulation F4. [15]

Bhandari Neeraj et al prepared fast dissolving tablets of Cefuroxime Axetil using different superdisintegrants. Different super disintegrants were used such as croscarmellose sodium (CCS), sodium starchglycolate (SSG) and crospovidone (CPVP). They concluded that mouth-dissolving tablets of Cefuroxime Axetil can be successfully prepared by wet granulation technique using selected superdisintegrants for the better patient compliance and effective therapy. [16]

Ravi S Wanare et al prepared Azithromycin Dihydrate using different super disintegrants such as croscarmellose sodium (CCS), sodium starch glycolate (SSG) and crospovidone (CPVP). A direct compression method was failed to formulate dispersible tablet of Azithromycin so wet granulation method was used. They concluded that tablets that were formulated (wet granulation) using crospovidone, crosscarmelose sodium and sodium starch glycolate exhibited quicker disintegration of tablets. [17]

6. ANTI-COAGULANT

Dicoumarol, Dipyridamole, Nicoumalone, Phenindione

7. ANTI-CONVULSANT

Anupama Kalia et al investigated with a view to develop mouth-dissolving tablets of Oxcarbazepine, which offers a new range of product having desired characteristics and intended benefits. In this study, the mouth dissolving tablets were prepared using two different technologies, direct compression method and solid dispersion technology. The results compared for both the technologies showed that the Oxcarbazepine tablets prepared using solid dispersion technology was found to have good technological properties and satisfying and reproducible drug dissolution profiles. [18]

8. ANTI-DEPRESSANTS

Amoxapine, Ciclazindol, Maprotiline, Mianserin, Nortriptyline, Trazodone, Trimipramine Maleate, Acetohexamide, Chlorpropamide, Glibenclamide, Gliclazide, Glipizide, Tolazamide, Tolbutamide.

Danish Kurien et al successfully formulated and evaluated fast dissolving tablets of Escitalopram oxalate by using hydroxyl propyl beta cyclodextrin. Based on wetting time, absorption ratio and percentage drug release of Escitalopram oxalate containing 5% crospovidone is revealed as the best formulation. [19]

9. ANTI-DIABETICS

Glipizide, Tolazamide, Tolbutamide Acetohexamide, Chlorpropamide, Glibenclamide, Gliclazide.

Gnana Chaitanya et al prepared and evaluated oral fast disintegrating tablet formulations of Sitagliptin phosphate using the superdisintegrants for various parameters.It can be concluded that the parameters disintegration time, dispersion time, wetting time and water absorption ratio are inversely related to the disintegrants quantity. Based on the above parameters one formulation was finalized as the optimized formulation which is showing lowest values for the disintegration time, wetting time, and highest values for the water absorption ratio and dissolution rate. [20]

10. ANTI-EMETICS

Basawaraj S. Patil et al attempted to prepare fast dissolving tablets (FDT) of Granisetron Hydrochloride by sublimation technique. The prepared formulations were evaluated for pre-compression and post-compression parameters. They concluded that fast dissolving tablets of Granisetron Hydrochloride are showing enhanced dissolution rate with increasing concentration of subliming agents. [21]

M Koland et al carried out study to formulate and evaluate fast dissolving films of Ondansetron hydrochloride for sublingual administration. They concluded that the use of water-soluble sweeteners, especially mannitol not only enhanced the taste of the Ondansetron containing films, but also increased drug release and drug permeation through oral mucosa. [22]

11. ANTI-EPILEPTICS

Beclamide, Carbamazepine, Clonazepam, Ethotoin, Methoin, Methsuximide, Methylphenobarbitone, Oxcarbazepine, Paramethadione, Phenacemide, Phenobarbitone, Phenytoin, Phensuximide, Primidone, Sulthiame, Valproic Acid. [39]

Swamy P.V. et al had prepared orodispersible tablets of Carbamazepine to enhance patient compliance by direct compression method using full factorial design. They found that the formulation containing 2% w/w Crospovidone and 30%w/w micro crystalline cellulose was more promising. [23]

Shirsand.S.B, et al successfully prepared fast dissolving tablets of Clonazepam by direct compression method by using crospovidone, croscarmellose sodium and mannitol. They concluded that the formulation which was prepared by using 10%crospovidone and 35%w/w microcrystalline cellulose is the best formulation (t50% - 1.8 minutes). [24]

12. ANTI-FUNGAL AGENT

Amphotericin, Butoconazole Nitrate, Clotrimazole, Econazole Nitrate, Fluconazole, Fiucytosine, Griseofulvin, Itraconazole, Ketoconazole, Miconazole, Natamycin, Nystatin, Sulconazole Nitrate, Terbinafine, Terconazole, Tioconazole, Undecenoic Acid.

13. ANTI-GOUT AGENTS

Allopurinol, Probenecid, Sulphinpyrazone

14. ANTI- HISTAMINE

Acrivastine, Astemizole, Cinnarizine, Cyclizine, CyproheptadineHCl, Dimenhydrinate, FlunarizineHCl, Loratadine, MeclozineHCl, Oxatomide, Terfenadine, Triprolidine.

Sandeep D. S. et al formulated and evaluated oral fast dissolving tablets of Promethazine HCL by sublimation method. They concluded that it was sublimation method along with superdisintegrant addition was excellent method in formulation of fast dissolving tablets of Promethazine HCl which gives quick relief from emesis. [25]

Shailesh Sharma et al optimized and formulated Promethazine theoclate fast-dissolving tablets. The solubility of Promethazine theoclate was increased by formulating it as a fast-dissolving tablet containing -cyclodextrin, crospovidone, and camphor, using direct compression method. [26]

Chandan Bisht et al also have made attempts for the development of fast disintegrating tablets of Levocetirizine Dihydrochloride by sublimation method. Their results suggest that suitably formulated fast dissolving tablets of Levocetirizine dihydrochloride containing camphor as a subliming agent can be achieved. The tablets exhibited good in vitro dispersion and wetting properties in presence of subliming agent, sublimation method shows better disintegration and drug release as compared to direct compression. [27]

15. ANTI-HYPERTENSIVE AGENTS

Amlodipine, Carvedilol, Benidipine, Dilitazem, Diazoxide, Felodipine, Indoramin, Isradipine, Nifedipine, Nimodipine, Phenoxybenzamine, Prazosin, Reserpine

C.P. Jain et al prepared fast dissolving tablets of Valsartan using different superdisintegrants by direct compression method. They discovered that the characterization of fast dissolving tablets of Valsartan with formulation containing crospovidone is the most acceptable. [28]

Jeevan T. Naikwade et al formulated and evaluated the fast dissolving tablets of Amlodipine besylate by using co-processed superdisintegrants. Among the designed formulations, the formulation (CP5) containing co processed superdisintegrant (3:1 mixture of crospovidone and sodium starch glycolate)emerged as the overall best formulation based on drug release characteristics in phosphate buffer pH 6.8. From this study, it was concluded that dissolution rate of Amlodipine besylate could be enhanced by tablets containing co-processed superdisintegrant. [29]

Mangesh M. Kumare et al made development of an FDT of Atenolol and to evaluate the effect of co-processed superdisintegrants on its disintegration time and release profile as the prime objective of their research work. They proved that the co-processed superdisintegrants gives the better results than the physical mixture. [30]

R. Margret Chandira et al formulated and evaluated the fast dissolving tablets of Carvedilol. The solubility was enhanced by using β- cyclodextrin as a complexing agent. Tablets were prepared by direct compression technique. They concluded that Carvedilol can be

successfully complexed with Betacyclodextrin to prepare fast dissolving tablets in the ratio of 1: 4. [31]

16. ANTI-MALARIALS

Amodiaquine, Chloroquine, Chlorproguanil, Halofantrine, Mefloquine, Proguanil, Pyrimethamine, Quinine Sulphate.

17. ANTI-MIGRAINE AGENTS

Dihydroergotamine Mesyiate, Ergotamine Tartrate, Methysergide Maleate, Pizotifen Maleate, Sumatriptan Succinate

Mahajan H. S. et al had successfully prepared the mouth dissolving tablets of Sumatriptan succinate by using superdisintegrants sodium starch glycolate, carboxy methyl cellulose, sodium and treated agar by direct compression method.The tablet disintegrates *in-vitro* and *in-vivo* within 10 to 16 second and 12 to 18 seconds respectively. Almost 90% of drug was release from all the formulations within 10 minutes. [32]

18. ANTI-MUSCARINIC AGENTS

Atropine, Benzhexol, Biperiden, Ethopropazine, Hyoscine Butyl Bromide, Hyoscyarnine, Mepenzolate Bromide, Orphenadrine, Oxyphencylcimine, Tropicamide.

19. ANTI-NEOPLASTIC AGENTS & IMMUNOSUPPRESSANTS

Aminoglutethimide, Amsacrine, Azathiopnne, Busulphan, Chlorambucil, Cyclosporin, Dacarbazine, Estramustine, Etoposide, Lomustine, Melphalan, Mercaptopurine, Methotrexate, Mitomycin, Mitotane, Mitozantrone, Procarbazine, Tamoxifen Citrate, Testolactone.

21. ANXIOLYTIC, SEDATIVES, HYPNOTICS & NEUROLEPTICS

Alprazolam, Amyiobarbitone, Barbitone, Bentazeparn, Bromazepam, Bromperidol, Brotizoiam, Butobarbitone, Carbromal, Chlordiazepoxide, Chlormethiazole, Chlorpromazine, Clobazam, Clotiazepam, Clozapine, Diazepam, Droperidol, Ethinamate, Flunanisone, Flunitrazepam, Fluopromazine, Flupenuiixol Decanoate, Fluphenazine Decanoate, Flurazepam, Haloperidol, Lorazepam, Lormetazepam, Medazepam, Meprobamate, Methaqualone, Midazolam, Nitrazepam, Oxazepam, Pentobarbitone, PerphenazinePimozide, Prochlorperazine, Suipiride, Temazepam, Thioridazine, Triazolam, Zopiclone. [39]

Tapan Kumar Giri et al study was undertaken to develop tablets of diazepam-hydroxypropyl-β-cyclodextrin inclusion complex that disintegrate within 3 minutes and release 85% of drug within 30 minutes to provide rapid action of the drug through oro-mucosal route.

Tablets of diazepam were prepared by direct compression method that disintegrated quickly (in 13.3 seconds) and released 85% drug rapidly (in 8.98 minutes). [33]

22. ANTI-PARKINSONIAN AGENTS

Bromocriptine Mesylate, Lysuride Maleate.

23. ANTI-PROTOZOAL AGENTS

Benznidazole, Clioquinol, Decoquinate, Diiodohydroxyquinoline, DiloxanideFuroate, Dinitolmide, Furzolidone, Metronidazole, Nimorazole, Nitrofurazone, Omidazole, Tinidazole. [39]

24. ANTI-PSYCHOTIC AGENTS

R. S. Masareddy et al attempted to study two different methods direct compression and sublimation in formulation of mouth dissolving tablets of Clozapine. The comparative evaluation of two methods showed direct compression method is a better alternative to sublimation method as its formulations rapidly disintegrate in oral cavity. [34]

25. ANTI-THYROIDS AGENTS

Carbimazole, Propylthiouracil

26. β- BLOCKERS

Acebutolol, Alprenolol, Atenolol, Labetalol, Metoptolol, Oxprenolol, Propranolol.

27. CARDIAC INOTROPIC AGENTS

Amrinone, Digitoxin, Digoxin, Enoximone, Lanatoside C, Medigoxin.

28. CORTICOSTEROIDS

Beclomethasone, Betamethasone, Budesonide, Cortisone Acetate, Desoxymethasone, Dexamethasone, Fludrocortisone Acetate, Flunisolide, Flucortolone, Fluticasone Propionate, Hydrocortisone, Methylprednisolone, Prednisolone, Prednisone, Triamcinolone.

29. DIURETICS

Acetazolarnide, Amiloride, Bendrofluazide, Bumetanide, Chlorothiazide, Chlorthalidone, Ethacrynic Acid, Frusemide, Metolazone, Spironolactone, Triamterene.

30. GASTRO-INTESTINAL AGENTS

Bisacodyi, Cimetidine, Cisapride, Diphenoxylate, Domperidone, Famotidine, Loperamide, Mesalazine, Nizatidine, Omeprazole, Ondansetron, Ranitidine, Sulphasaiazine.

Shailendra Kumar et al prepared fast disintegrating combination tablets of Omeprazole and Domperidone by using pertinent disintegrants. From the results obtained, they concluded that the tablet formulation prepared with 4.76% Ac-Di-Sol (internally cross linked form of sodium carboxymethyl cellulose) i.e. 10 mg showed Disintegration time of 15 seconds in vitro. [35]

S. Patra et al developed mouth dissolving tablets of Domperidone with superdisintegrants like crospovidone, croscarmellose sodium and sodium starch glycolate in various concentrations like 3%, 4% and 6% w/w by direct compression method. The formulation F3 (containing 6% w/w concentration of crospovidone) was considered to be the best formulation, having disintegration time of 9 s, wetting time of 15 s and in vitro drug release of 99.22% in 15 min. [36]

31. LIPID REGULATING AGENTS

Bezafibrate, Clofibrate, Fenofibrate, Gemfibrozil,Probucol.

32. LOCAL ANAESTHETICS

Lidocaine

33. MUSCLE RELAXANTS

N.G. Raghavendra Rao et al designed and developed fast dissolving tablets containing Baclofen by direct compression method. Based on the results they concluded that, although differences existed between the superdisintegrants, the fast dissolving Baclofen tablets could be prepared by using any of the superdisintegrants used. Overall results indicates that formulation BD (which contain 9% CP was better one and satisfies all the criteria as fast dissolving tablet. Baclofen showing enhanced dissolution, may lead to improved bioavailability, improved effectiveness and hence better patient compliance. [37]

34. NEURO-MUSCULAR AGENTS

Pyridostigmine

35. NITRATES AND ANTI-ANGINAL AGENTS

Amyl nitrate, Glyceryltrinitrate, IsosorbideDinitrate, IsosorbideMononitrate, PentaerythritolTetranitrate.

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36. NUTRITIONAL AGENTS

Betacarotene, vitamin A, vitamin B2, vitamin D,vitamin E, vitamin K.

37. OPIOID ANALGESICS

Codeine, Dextropropyoxyphene, Diamorphine, Dihydrocodeine, Meptazinol, Methadone, Morphine, Nalbuphine, Pentazocine.

38. PROTEINS, PEPTIDES AND RECOMBINANT DRUGS

Insulin, glucagon, growth hormone (somatotropin),polypeptides or their derivatives,calcitonins and synthetic modifications thereof, enkephalins, interferons, LHRH and analogues (nafarelin, buserelin, zolidex), GHRH, secretin, bradykin antagonists, GRF, THF,TRH, ACTH analogues,IGF (insulin like growth factors),CGRP(calcitoningene related peptide), atrial natriurecticpeptide, vasopressin and analogues(DDAVP, lypressin),factor VIII, G-CSF (granulocyte-colony stimulating factor), EPO (erythropoietin).

39. SEX HORMONES

Clomiphene citrate, Danazol, Ethinyloestradiol, Medroxyprogesterone acetate, Mestranol, Methyltestosterone, Norethisterone, Norgestrel, Oestradiol, Conjugated Oestrogens, Progesterone, Stanozolol, Stiboestrol, Testosterone, Tibolone. Spermicides: Nonoxynol.

40. STIMULANTS

Amphetamine, Dexamphetamine, Dexfenfluramine, Fenfluramine, Mazindol, Pemoline.

41. TOCOLYTIC AGENTS

P. P. Sawarikar et al aimed to investigate development and evaluation of inclusion complex of Isoxsuprine hydrochloride with β-cyclodextrin using kneading and co precipitation methods using DSC. They concluded that the fast dissolving drug delivery system of Isoxsuprine HCl can be successfully formulated. [38]

CONCLUSION

Drug delivery system has become an important subject in the past decade. Development of this system has significantly boosts the pharmaceutical market by extending product life cycles and creating opportunities for many. Researchers are using new advanced

technologies with very interesting features like extremely low disintegration time, exceptional taste masking ability, pleasant mouth feel and sugar free tablets for diabetic patients for the formulation of orodispersible tablets. Pharmaceutical companies are taking advantage of the fast dissolving tablets to extend product line and market the product first. With the rapid growth of fast dissolving tablets, it is just the matter of time for all drugs to be produced in the orodispersible tablet dosage form rather than the conventional tablets.

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