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Oral Disintegration of Diclofenac Sodium

Mounika Sathelli*

Department of Pharmacy, St. Mary's College of Pharmacy, JNTUH, Secunderabad, India

Short Communication

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***For Correspondence**

Department of Pharmacy, St. Mary's College of Pharmacy, JNTUH, Secunderabad, 500025, India, Tel: 9290047283; E-mail: mnksatheli@gmail.com

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ABSTRACT

For as long as two decades, there is a moment support increment in the business sector by three-overlay consistently for the patients having more consistence measurement frames. As the improvement for the compound element is higher in the expense, so the pharmaceutical commercial enterprises are focusing on the advancement of the new medication conveyance frameworks for upgrading the bioavailability furthermore viability of the medication. The bioavailability's of the ODT'S is higher than that of the customary measurement structures, for example, the tablets and containers.

Subsequently, in the present study, an endeavor will be made to outline mouth dissolving tablets of Diclofenac ODT (analgesic) with a perspective to give a helpful method for organization to those patients experiencing challenges in gulping, for example, pediatric and geriatric patients and uncooperative rationally sick patients. The mouth dissolving tablets (MDT) of DICLOFENAC will be outlined utilizing co-handled straightforwardly compressible excipients grew in our research centers with the prime target of touching base at expense – successful item. The planned MDT of DICLOFENAC will be assessed for hardness, friability, weight variety, in vitro scattering time wetting time, medication content consistency, in vitro disintegration rate.

INTRODUCTION

In recent advancements in the novel drug delivery systems, the most common and convenient type of administration is the oral route of drug administration. Novel oral drug delivery systems [1] are the type of routes which easily dissolves in the mouth when placed below the tongue, which avoids the problem of swallowing tablets, for improved compliance in patients.

The oral dispersible tablets [2] can be referred as the type of systems which disintegrates with-in a minute time of seconds [3]. In such type of cases, the bioavailability of the compound or drugs can be achieved when resembled with the conventional type of dosage forms which shows the rapid disintegration of the tablets. Various types of direct compression, in-direct compression techniques are developed to increase the porous structure of the tablet and incorporating them in the exact disintegrating agents and also by utilizing high water soluble excipients [4 - 12].

In this way, the oral disintegrating shows the rapid onset of action, by preventing the hepatic first-pass metabolism. The beneficiary terms of increasing the bioavailability, quick onset of action, stability and the patient compliance holds the good position the current trends of market. Controlled-release drug

delivery systems, are the type of dosage forms which totally engulfed to disintegrate the medicaments quickly in the gastro-intestinal tract (GIT).

The most common or conventional methods of oral disintegrating tablets involve:

1) Freeze drying
2) Tablet molding
3) Spray drying
4) Mass extrusion sublimation and
5) Direct compression [13]

As the Oral route of drug administration is the most common and globally accepted route of administration due to its ease of self-administering and compactness, manufacturing etc, similarly it has the drawback of using the oral dosage forms in swallowing them such as tablets and capsules which results in patient in-compliance specifically in the cases of geriatric and pediatric patients and also for the patients who are ailing on the bed. Due to the apparent impact on the patient compliance orally disintegrating tablets (ODTs), the trade for the development of ODT'S has elevated enormously [14, 15].

The ODT'S are obligated by the apparent division of the populations who are facing more difficulties in swallowing, a term called Dysphagia (difficulty in swallowing) which refers to the common problem among the all age groups in regards with the geriatric, pediatric among with the psychiatric patients and also who are suffering from the problems of nausea, vomiting, and motion sickness complications [16]. Some of the ODT'S have bitter in taste which is very difficult in swallowing by various group of people, so such type of ODT'S can be acceptable by adding good taste flavors to it which combines with the formulation of dry and liquid dosage formulation.

ODT'S are explored in increasing their bioavailability of poorly soluble drugs by amplifying the disintegrating profile and also the hepatic metabolism of the drugs [17]. The novel ODT'S confess the high drug loading which has an agreeable taste and also offers the amusing mouth perception, resulting minimum remnants in the mouth after oral administration.

United States pharmacopoeia (USP) approved these dosage forms as ODTs as Orally disintegrating tablets are also called as oral dispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets [18 - 25], rapid dissolving tablets, porous tablets and rapi melts. Recently, European Pharmacopoeia has used the term oral dispersible tablet for tablets that disperses readily and within 3 min in mouth before swallowing [26].

Some of super disintegrates employed in ODTs are [27]

Crosscarmellose:

These are modified cellulose or cross linked type of cellulose, which acts by Wicking due to fibrous structure swelling with minimal gelling (Ac-Di-Sol, Nymce 25 X, Nymcel).

Aliginic acid NF:

These are Cross linked in nature which also acts by wicking mechanism (Satialgine)

Soy polysaccharides:

This is a natural Disintegrant (EMCOSOY).

Sodium starch Glycolate:

This is a modified type of starch which acts by extensive swelling with minimal gelling (Explotab Primogel)

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United States Food and Drug Administration (FDA) defined ODT as "A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue [28]." The disintegration time for ODTs generally ranges from several seconds to about a minute.

Advantages of fast dissolving drug delivery system

Fast dissolving technology offers:-

a. Improved compliance/added convenience,
b. Ease administration for patients
c. No addition of water needed
d. Provide a pleasant mouth feel.
e. No chewing needed
f. Better taste obtained by taste masking
g. Improved stability,
h. Suitable for controlled/sustained release actives
i. Allows high drug loading.

Patented Technologies:

a. *Zydis Technology:*

A Zydis tablet is manufactured by lyophilizing or freeze-drying contains gelatin. The resultant product is weightless and fragile which must be dispensed in a blister pack. The product dissolves on the tongue with-in 2 to 3 seconds.

b. Orasolv Technology 14

In this system active medicament is taste masked.

c. Durasolv technology14

Tablets are prepared by using conventional tableting equipment and have good rigidity consisting of a drug, fillers and a lubricant.

d. Wow Tab Technology15

It is patented by yamanouchi Wow means "without water". Wow tab is an intra buccally soluble, compressed tablets consisting of granules made with saccharine of low and high mouldability.

e. Oraquick16

This technology is patented by K.V Pharmaceuticals. It utilizes taste masking microsphere technology called as micro mask, which provides superior mouth feel, significant mechanical strength, and quick disintegration/ dissolution of product. (Bandari S et al.,2008)

f. Nano Crystal technology14

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Elan's proprietary Nano Crystal technology (NanomeltTM) can improve compound activity and final product characteristics.

g. Pharmaburst technology

SPI Pharma, New castle, patents this technology.

Techniques for preparing ODTS

The various techniques are being utilized or adopted to Prepare ODTs:

- Freeze drying or Lyophilization [29]
- Sublimation
- Mass extrusion
- Melt Granulation
- Spray drying
- Molding
- Nanonization
- Direct compression
- Cotton candy process
- Phase transition process

Freeze drying or Lyophilization: [29]

Freeze drying is the technique in which water is sublimed from the product when it is frozen which shows an amorphous porous construction that can dissolve rapidly. The active ingredient is dispersed in an aqueous solution of a polymer and the mixture is dosed through weight and poured in the wells of the preformed Blister packages. Then these are passed through liquid nitrogen freezing tunnel to freeze the drug Solution which is placed in refrigerated cabinets to continue the freeze-drying. Finally the blisters are packaged and shipped.

Sublimation:

The slow dissolution of the compressed tablet having even highly water soluble components is due to the fact that the low Porosity of the drugs reduces water dispersion into the matrix. After inert volatile solid ingredients like ammonium Bicarbonate, ammonium carbonate, benzoic acid, camphor, hexamethylene tetra mine, naphthalene, phthalic anhydride, urea and urethane were additional too along with other tablet excipients and the blend were compressed into a tablet which is finally subjected to a process of sublimation resulting in exceedingly porosity.

Mass extrusion:

This technology contains softening the active blend using the Solvent mixture of water soluble polyethylene glycol, using Methanol and expulsion of softened mass through the extruder or syringe to get a cylinder designed extrude which finally cut into even segments using heated blade to form tablets. This Process can also be used to coat granules of bitter drugs to mask their taste.

Melt granulation:

Melt granulation system is a process through which Pharmaceutical powders are efficiently agglomerated through a melt able binder. The benefit of this method associated to a Conventional granulation is that no water or organic solvents is necessary. For there is no drying step, the process is

less time consuming and uses less energy than wet granulation. It is a Useful technique to enhance the dissolution rate of poorly water–soluble drugs such as griseofulvin41.

Spray drying:

Spray drying can be used to formulate quickly Disintegrating tablets. This technique is based on a particulate Support matrix, which is equipped by spray drying an aqueous Composition containing support matrix and other components to usage a highly porous and fine powder this is then mixed with active ingredients and compressed into tablets. The Tablets made from this technology are claimed to disintegrate within 20 seconds [30 - 36].

Molding:

The molding of the tablet can be achieved by using the water soluble compounds which dissolves totally and the powder blends are moistened with a alcoholic solvent which are subjected to tablets by molding under pressure which is generally carried out in conventional tablet compression.

Nanonization:

In this technology contains reduction in the particle size of Drug to nano size by milling the drug using a patented wet milling Technique. This system is suitable for poorly water soluble drugs.

Direct compression:

This process is done by using without any preliminary Treatment in which tablets are compressed directly from mixtures of the drug and excipients. This method shows the best advantages than the other manufacturing processes of tablets, such as wet granulation and delivers high Efficiency [5].

Cotton candy process:

This method utilizes an imitables pinning mechanism to Yield floss like crystalline structure which mimics cotton candy.
Phase transition process: This is a combination of low and high melting point sugar alcohols, as well as a phase transition in the manufacturing process, are important.

Taste masking techniques:

Taste masking techniques is defined as a perceived reduction of an undesirable taste that would otherwise exist [36-42]. The ideal solution to reduce or inhibit bitterness is a discovery of a universal inhibitor of all bitter tasting substances that does not effect the other taste modalities such as sweetness or saltiness.

Some of the taste masking techniques is described below:

1. Taste masking by drug particle coating
2. Taste masking by drug microencapsulation [43 - 55]
3. Taste masking by drug resin complexation
4. Taste masking by rheological modifications

OUTLOOK

Various examples are taken into account regarding the massive clinical trials administered for safe Drug analysis which covers the broad scope the recent laws of pharmacovigilance in European and US [2], Pharmacovigilance teaching strategies in the major countries [3, 4], Biosimilars in Pharmacovigilance [5],

Pharmacogenetics Therapies development [6], SAR Studies [7], ADR studies [8 - 10], Alcohol Medication Interactions [11, 12].

Safety signal initiative by WHO regarding Pharmacovigilance has developed as a system [13, 14]. Patient Safety have evolved at rate in all the Countries on the primary focus of drug safety in clinical perspectives [15, 16], the trends, scope ,future initiatives, Modern developing technologies have wide scope for the enhancement of Pharmacovigilance career [17 - 21].

PHARMACOVIGILANCE VS ADVERSE DRUG INTERACTIONS

The safety of drug is peculiar when in the case of adverse drug interaction appears such as clinical pharmacists major role and the correct quality dosage, the various reports illustrated are [22 - 29], the adverse drug interactions being the main obstacle for the Pharmacovigilance, thus including several steps.

Recent Pharmacovigilance studies use the reliable software of SAS (Statistical Analysis System) for the early and fast retrieval of large clinical data in number of Individuals participating. Even the Pharmacovigilance have evolved in the economic field rapidly with global advancements and approaches [30 - 33].

Adverse reactions effect lead to serious consequences which result in drug- drug interaction, drug to foreign substance interaction, etc.

Hence a clear study with safety measures in use with well developed and highly professional individual's presence is required. Careful review on the adverse drug reactions must be clear as adverse drug reactions are undesirable impacts on the drug which badly affect the drug influence in treatment.

Special Technologies are used for drug safety with upcoming development in technology such as use of Apple's Research Kit a recent innovation for medical research data collection, where retrieval of absolute details in less time is possible.

Several Excipients used in drug development are carefully scrutinized for its further non interaction with drug main active ingredients.

Physician's views and concerns regarding several cases they handle may give us the idea regarding the adverse drug reactions and hence the knowledge of Pharmacovigilance at present can be noticed.

Recently Pharmacovigilance for Novel Oral Anticoagulants have been studied which show that physicians should be precise regarding the pharmacology of NOACs, dose adjustments, contra-indications, drug-drug interactions.

They should have a complete record of patients with the Anticoagulants treated with adverse reactions reported if any.

Safety and efficacy assessment is prime importance in Pharmacovigilance. Clinical trials are framed as such maintaining a set of regulations and procedures that determine the safety and effectiveness of medications, devices, diagnostic products and treatment regimens intended for human use.

Special regulations are followed in Pharmacovigilance which are mentioned by Food & Drug Administration organisation, where every clinical trial is followed with utmost care and importance towards studies of Adverse Drug Interactions are studied and well defined terms are illustrated for the improvement of clinical trials in each and every stage starting from Clinical Trial-I to Clinical Trial-III, and

Clinical Trial IV after releasing into market with the effective and strong documented suggestions by persons excelled in Pharmacovigilance.

Pharmacovigilance hence developed into a major research interest today in pharmacy professional with more employment opportunities in Multinational organizations as the the field is related to scientific arena of science and technology requiring developing of knowledge in the fields of software development tools coupled with scientific knowledge.

Drug safety is hence a very crucial factor as the drug starting from its formulation, quality checks, approval by FDA in preliminary stages, Quality Assurance, clinical trials and then into the market all at last gives or based on result of Drug Safety.

If Safety province of Drug is not maintained it may lead to vain of all works done starting from formulation to release in market, which results in heavy money loss and financial crisis.

CONCLUSION

Diclofenac sodium is an analgesic used as Pain killer. The concept of formulating mouth dissolving tablets containing Diclofenac sodium offers a suitable and practical approach in serving desired objective of faster disintegration and dissolution characteristics with increased bioavailability [55 - 63]. Numerous patients think that it hard to swallow tablets and hard gelatin cases and along these lines don't follow medicine, which brings about high rate of resistance and insufficient treatment [64 - 65]. Late advances in novel medication conveyance frameworks (NDDS) intend to upgrade security and adequacy of medication particle by planning a helpful measurements structure for organization and to accomplish better patient consistence [66]. One such approach is mouth dissolving/apportioning tablet detailing. In the present work, mouth dissolving tablets of Diclofenac sodium were outlined with a perspective to upgrade tolerant consistence [67]. Distinctive clumps of plans were arranged utilizing super-disintegrant to be specific, crospovidone [68 - 70]. The arranged groups of tablets were assessed for hardness, friability, medication content consistency, wetting time, water retention proportion, in vitro scattering time.

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