ISSN: 2287-6898
International
Journal of Bio-Pharma Research
Volume 9, Issue 3 (2020) pp. 2645-2650
Review Article
Open Access

A short review of bioavailability studies on various drug profiles

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Abstract: Novel Drug Delivery System is driving towards increasing safety and efficacy of existing drug molecule through novel concepts like Oral Drug Delivery System. therein the essential approach utilized in the event of the oral dispersible tablets by using different superdisintegrants. Tablets containing Atenolol with superdisintegrants like sodium starch glycolate, cross carmellose sodium, cross povidone were prepared by direct compression method. The formulated tablets were evaluated for pre-formulation and post formulation parameters and that they were found to be satisfactory. The formulated oral dispersible tablets possess good drug releasing property, good mouth feel and improved drug bioavailability with better patient compliance.

Keywords: Superdisintegrants; Oral dispersible tablets; Direct compression method; Disintegration time; Dissolution studies

Introduction

The oral route of administration is taken into account because the foremost generally accepted route because of its convenience of self-administration, compactness and direct manufacturing. But the foremost evident drawback of the commonly used oral dosage forms like tablets and capsules is difficulty in swallowing, resulting in patients incompliance particularly just in case of paediatric and geriatrics patients but it also applies to parents that are ill in bed and to those active working patients who are busy or traveling, especially people that haven't any access to water.

Over a decade, the demand for development of orally disintegrating tablets (ODTs) has enormously increased because it's significant impact on the patient compliance. Orally disintegrating tablets are appreciated by a huge segment of population particularly who have difficulty in swallowing [1].

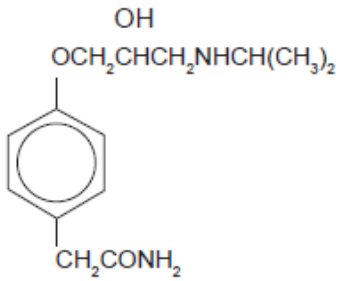

Figure 1. Structure of Atenolol

Dysphagia (difficulty in swallowing) is common among all age groups and more specific with paediatric, geriatric population in conjunction with institutionalized patients, psychiatric patients and patients with nausea, vomiting, and ketosis complications. ODTs with quality and flavour increase the acceptability of bitter drugs by various groups of population [2]. This dosage form combines the benefits of dry and liquid formulation. Some novel ODT technology allow high drug loading, have an appropriate taste, offer a satisfying Mouth felling, leaving minimal residue within the mouth after oral

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administration are investigated for his or her potential in improving bio availability of poorly soluble drug through enhancing the dissolution profile of the drug and hepatic metabolism drugs. Orally disintegrating tablets also are called as or dispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, and rapimelts. However, of all the above terms, us pharmacopoeia (USP) approved these dosage forms as ODTs [3]. European Pharmacopoeia has used the term or dispersible tablet for tablets that disperses readily and within 3 min in mouth before swallowing, sort of super disintegrants employed in ODTs.

US 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. The disintegration time for ODTs generally ranges from several seconds to a few of minute.

Literature Review

Rapidly dissolving dosage form the studies of Purvis *et al.*,[4] rapidly dissolving formulations of the poorly water-soluble drug repaglinide using ultra-rapid freezing technique (URF), and investigated the influence of quite excipients on repaglinide stability. Repaglinide compositions containing differing types and levels of excipients and different drug potencies (50%-86%) were produced by the URF technology. Surfactants, including sodium dodecylsulfate, and alkalizing agents like diethaanolamine (DEA) and tromethamine (TRIS)were incorporated into the compositions. Forced degradation of repaglinide was conducted under stressed conditions (e.g., elevated temperature, exposure to peroxide) to work out the stableness of the drug in such environments. it had been concluded that the solubility of repaglinide increased as a function of accelerating pH; therefore, incorporation of an alkalizing agent into the URF formulations increased the drug's solubility. Drug Instability resulted when the drug was exposed to pH values above 9. URF formulations containing alkalizing agents showed no degradation or spontaneous re-crystallization within the formulation, indicating that increased stability was achieved by processing.

Ciper *et al.*,[5] prepared novel capsule-based fast disintegrating dosage forms for the oral cavity (Fastcaps). Films were casted from various additive-containing gelatine solutions and evaluated with reference to disintegration time and mechanical properties to identify suitable formulations for the capsule preparation. The disintegration time of films decreased with decreasing bloom strength and may be further decreased by the addition of sugars or PEGs. Fast disintegrating capsules were successfully prepared by a dipping process, where parameters a bit like the viscosity and temperature of the dipping solution and thus the dipping velocity of the steel pins were optimized. the specified viscosity range of the dipping solution for Fast cap manufacturing was 500–600 clog. The addition of the hydrophilic additives (xylitol, sorbitol or PEG 1500) didn't significantly affect the viscosity and gelation temperature of the dipping solution. The in vitro disintegration of Fastcaps (30–45 sec) was twice as rapid because the one among regular hard gelatine capsules. Vivo, Fastcaps disintegrated rapidly (9–13 sec) and their content was spread throughout the mouth within seconds. Lactose and/or microcrystalline cellulose were suitable fillers for Fast caps.

Ciper *et al.*,[6] prepared fast disintegrating capsules for administration within the mouth either by perforation or by vacuum-drying of

conventional hard capsules. When compared to other fast disintegrating dosage forms (e.g. lyophilized sponges or tablets), these capsules exhibited various advantages, especially, a high drug loading capacity and no compression steps. The disintegration time of conventional hard gelatine capsules (HGC) was reduced from 91 to 39 sec by introducing 6-10 small holes (diameter =25-50 micron) into the capsule shell. Vacuum-drying of conventional hard gelatine capsules resulted in brittle capsules, which broke rapidly within the mouth. The brittleness of the hard gelatine capsules correlated well with their moisture content. The critical moisture value for sufficient brittleness of hard gelatine capsules was lactose > Avicel PH112 > mannito.

Al-khattawi *et al.,*[7] studied the pharmacokinetics of ketoprofen from a fast-dissolving lyophilized tablet (LT), as compared to a moment release (IR) tablet as reference after single oral dose (25 mg) administration in six healthy subjects aged between 25-40 years employing a randomized crossover design. the speed of absorption of ketoprofen from LT was significantly faster than that of IR tablet and had significantly higher Cmax (by about 50%) and earlier tmax (by 15 min), whereas the extent of absorption expressed by AUC was about 68% higher as compared to the IR tablet. The relative bioavailability of the LT compared with the IR tablet was 168%. The difference between the formulations for half-life and MRT were statistically significant value.

Van Schaick *et al.,* evaluated the bioequivalence of a fast-disintegrating oral tablet of risperidone with conventional oral tablet. A randomized, open-label, 2-way crossover trial was taken during which healthy volunteers received two 0.5-mg tablets of a fastdisintegratingoral risperidone formulation and two 0.5-mg tablets of conventional oral risperidone, each during one administration. The plasma concentration-time profiles of the active moiety, risperidone, and 9-hydroxy-risperidone were similar after intake of the formulations. The fast-disintegrating tablet and thus the normal tablet showed bioequivalence with reference to the active moiety, risperidone, and 9-hydroxy-risperidone. A single administration of two 0.5-mg fast-disintegrating risperidone tablets was bioequivalent to a minimum of one administration of two 0.5-mg conventional risperidone tablets.

Mishra *et al.,*[8] studied the suitability of spray dried excipient base within the formulation of orally disintegrating tablet containing Valdecoxib (low aqueous solubility drug) and Metoclopramide (high aqueous solubility drug). Spray dried excipient base was prepared using Scientech spray drier. Super disintegrants (such as Ac-Di-Sol, Kollidon CL, sodium starch glycolate), diluent (mannitol) in conjunction with sweetening agent (aspartame) were utilized in the formulation of tablets. The tablets were evaluated for hardness, friability, water absorption ratio, disintegration time and in vitro drug release. Using an equivalent excipient, the tablets were prepared by direct compression and evaluated. Maximum drug release and minimum disintegration time were observed with Kollidon CL excipient bases compared to tablets prepared by direct compression, showing the prevalence of the spray dried excipient base technique over direct compression technique., crospovidone, croscarmellose sodium, and sodium starch glycolate. Tablets of etoricoxib prepared using L-HPC exhibited the tiniest amount friability and disintegration time (approximately 65 sec). Sublimation technique was utilized within the preparation of ODTs. The addition of camphor lowered the disintegration time (to 30 sec), but the percent friability was increased. A 32 full factorial design was

employed to review the joint influence of the number of super disintegrants (L-HPC) and thus the number of sublimating agent (camphor) on the percent of friability and thus the disintegration time. The results of multiple linear statistical method revealed that for obtaining an efficient ODT of etoricoxib, higher percentages of L-HPC and camphor should be used.

Gohel *et al*.,[9] developed mouth dissolve tablets of nimesulide. Granules containing nimesulide, camphor and crospovidone were prepared by wet granulation technique. Camphor was sublimed from the dried granules by exposure to vacuum. The tablets were evaluated for friability, wetting time, and disintegration time. A 32 full factorial design was wont to investigate the joint influence of amount of camphor and crospovidone. The results of multiple rectilinear regression analysis revealed that for obtaining a rapidly disintegrating dosage form, tablets should be prepared using an optimum concentration of camphor and a much better percentage of crospovidone. Sublimation of camphor from tablets resulted in superior tablets as compared with the tablets prepared from granules exposed earlier to vacuum.

Van Schaick *et al.*,[10] evaluated the bioequivalence of a fast-disintegrating oral tablet of risperidone with conventional oral tablet. A randomized, open-label, 2-way crossover trial was taken during which healthy volunteers received two 0.5-mg tablets of a fast disintegrating oral risperidone formulation and two 0.5-mg tablets of conventional oral risperidone, each during one administration. The plasma concentration-time profiles of the active moiety, risperidone, and 9-hydroxy-risperidone were similar after intake of the formulations. The fast-disintegrating tablet and thus the normal tablet showed bioequivalence with reference to the active moiety, risperidone, and 9-hydroxy-risperidone. A single administration of two 0.5-mg fast-disintegrating risperidone tablets was bioequivalent to a minimum of one administration of two 0.5-mg conventional risperidone tablets.

Al-khattawi *et al.*,[11] formulated orally disintegrating tablets (ODTs) of etoricoxib. Tablets were prepared using direct compression method employing superdisintegrants like low substituted hydroxypropyl methyl cellulose, low substituted hydroxyl - propyl cellulose, crospovidone, croscarmellose sodium, and sodium starch glycolate. Tablets of etoricoxib prepared using L-HPC exhibited the tiniest amount friability and disintegration time (approximately 65 sec). Sublimation technique was utilized within the preparation of ODTs. The addition of camphor lowered the disintegration time (to 30 sec), but the percent friability was increased. A 32 full factorial design was employed to review the joint influence of the amount of super disintegrants (L-HPC) and thus the number of sublimating agent (camphor)on the percent of friability and thus the disintegration time. The results of multiple linear regression analysis revealed that for obtaining an efficient ODT of etoricoxib, higher percentages of L-HPC and camphor should be used.

Ishikawa *et al.*,[12] prepared rapidly disintegrating tablets using microcrystalline cellulose (Avicel PH-M series) within the formulation of tablets to decrease the feeling of roughness when a tablet, which is rapidly disintegrated by saliva containing acetaminophen or vitamin C as model drugs. Tablets prepared using spherical microcrystalline cellulose, PH-M-06, with the tiniest particle size (mean value, 7μ) had sufficient crushing strength (approximately, 8 kg) and rapidly disintegrated (within 15 sec) when the blending ratio of PH-M-06 to

low-substituted hydroxypropyl cellulose (LHPC) was 9:1. Sensory evaluation by volunteers showed that PH-M-06 was superior to PH-102 in terms of the sensation of roughness within the mouth. Consequently, it had been found that particle size could also be an important factor for tablet preparation using microcrystalline cellulose. Drugs like acetaminophen and vitamin C (concentration of approximately 50%) might be incorporated within the tablet form using PH-NM-06 in combination with L-HPC as an honest disintegrants at a coffee compression force (1-6 kN).

Fukami *et al.*,[13] formulated a quick disintegrating compressed tablet using amino acids, such as L-lysine Hcl, L-alanine, glycine and L-tyrosine as disintegration accelerator. The tablets having the hardness of about 4 kg were prepared and thus the effect of amino acids on the wetting time and disintegration time within the mouth of tablets was examined on the thought of surface free energy of amino acids. The wetting time of the tablets increased within the order of L-lysine Hcl, L-alanine, glycine and L-tyrosine, whereas the disintegration time within the mouth of the tablets increased within the order of L-alanine, glycine, L-lysine Hcl and L-tyrosine. The behaviour wax analysed by the introduction of surface free energy which revealed that when the polar component of aminoalkanoic acid was large value or the dispersion component was small value, faster wetting of tablet was observed. When the dispersion component of aminoalkanoic acid was large value or the dispersion component was small value, faster disintegration of tablet was observed, expect of L-tyrosine tablet.

Conclusion

This review represents importance of oral dosage forms in various drugs. Fast dissolving oral drug delivery system are solid dosage form which disintegrate or dissolve within seconds when placed within the mouth without need of water or chewing. First developed fast dissolving dosage form in formulation and therefore the rapid disintegrating properties were obtained through a special procedure or formulation modification, hence mouth dissolving film is proved to be better alternative in such cases. This fast dissolving drug delivery system is fitted to the drugs which undergo high first pass metabolism and is employed for improving bioavailability. Mouth dissolving film consists of thin oral strip; which release active ingredients immediately after uptake into mouth. In present investigation it was concluded that availability of larger area that results in rapid disintegrating and dissolution within the mouth.

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Cite this article as:

Prashanthievangelin M., VamsiKrishna G., Elisha Y., Radhika G., B. Chandra Sekhar, Pravallika. A short review of bioavailability studies on various drug profiles. *International Journal of Bio-Pharma Research*, Volume 9, Issue 3 (2020) pp. 2645-2650.

http://dx.doi.org/10.21746/ijbpr.2020.9.3.1

Source of support: DST-NRDMS; **Conflict of interest**: Nil.