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The impact of some processing and formulation on dissolution rate of aspirin in different dosage form

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ABSTRACT— Most studies had been used dissolution test since it is one of the most important quality control tests performed on pharmaceutical dosage forms and is now developing into a tool for predicting bioavailability, and in some cases, replacing clinical studies to determine bioequivalence. Dissolution behavior of drugs has a significant effect on their pharmacological activity. In fact, a direct relationship between in vitro dissolution rate of many drugs and their bioavailability has been demonstrated and is generally referred to as in vitro-in vivo correlation, IVIVC. In an attempt to study the possible changes that can improve the bioavailability of aspirin, decrease gastric side effect and provide a rapid effect in our study, we tried to collect many researches and benefit from previous experiences. Practical plan of the study was designed, and dissolution test was the corner stone of our plan. The study path was changed during COVID-19 pandemic existence to a theoretic review. The study is designed in a way to explore, in a comparative manner, the impact of excipients and dosage form formulations on aspirin's dissolution rate and aimed to provide prospective studies with the required information that mirror the effect of formulation changes on the in vivo performance via dissolution studies.

KEYWORDS: Aspirin, dissolution, coated tablet, dosage form.

1. INTRODUCTION

Aspirin, which is well known as acetyl salicylic acid (ASA), is one of the oldest and commonly used drugs in the world, with approximately 35,000 tons produced and consumed annually [1]. It is a non-steroidal anti-inflammatory drug (NSAID) used for treating fever, pain, and inflammation in the body. At low doses, aspirin is used to prevent heart attacks, strokes, and blood clot formation in people at high risk [2]. There is also increasing evidence that regular aspirin use is associated with a decreased incidence of developing cancer [3]. Although aspirin effectively relieve symptoms, such as pain, the relief comes at the expense of important side effects and drug resistance. Currently several studies revealed that various factors such as formulation, excipients and manufacturing process may affect the therapeutic and side effects of the drug. Research on aspirin yielded interesting results in clinical pharmacology and drug behavior. However, in individual patients the available tests are of no particular use to predict reliably drug outcome or to guide in making therapeutic decision. Prospective laboratory trials seem necessary to reach such conclusions [4], [5]. Dissolution tests are widely used in the pharmaceutical industry for developing new drug products [6]. It can be used also to evaluate batches and used as a guide to develop new and existing formulations and possibly to assess the impact of certain changes in the formulation. From a quality assurance point of view, a more discriminative dissolution method is preferred, because the test will indicate possible changes in the quality of the product before in vivo performance is affected [7], [8].

2. Overview of the studies

We identified articles, researches, reviews, technical reports and other original papers that suggest different formulas of aspirin, the majority of these investigating the effect of formula on dissolution test directly or as a part of bioequivalence test, table (1).

- An article, in Pharmaceutical Technology, published in 2001 demonstrated a relatively simple ASA formulation using a combination of microcrystalline cellulose and partially pregelatinized starch. Microcrystalline cellulose provides the compatibility needed for producing a tablet for aqueous enteric film coating and starch provides the necessary dissolution characteristics to the formulation. Dissolution test revealed that more than 80% of acetylsalicylic acid released in less than 20 min. for formulas with suitable excipients, this can be considered as a good parameter for excipients role [9].

- In an attempt to reduce gastrointestinal side effect, a lyophilized aspirin-chitosan HCl complex was prepared. This novel complex demonstrated a successful and simple method to enhance aspirin aqueous solubility and dissolution rate. This complex also exhibited exceptional stability in comparison with pure drug. This study submitted special recommendations about studying the nature of aspirin-chitosan interaction [10], [11].

- In 2011, Meenakshi K. D and his colleagues formulated new aspirin tablets which have optimum physicochemical properties for more compliance and palatable melt in mouth, by direct compression method using super disintegrants. They concluded that the new formula of aspirin produced fast dissolving tablet in comparison with that of marketed tablet formulation of aspirin [12].

- In University of Karachi, a study attended to formulate aspirin tablets by direct compression method using fewer excipients (lactose, corn starch and aerosi) and to compare this formulation with the other brands. As one of the evaluation tests, dissolution of trial batches was found to be better than most of commercial brands tested, this might be due to the use of few excipients. Rapid disintegration of tablets favors high dissolution rates [13].

- In the beginning of the past decade, A new 500 mg aspirin tablet formulation containing micronized active ingredient and an effervescent component has been developed for potential improvement in the onset of action for acute pain treatment. This paper describes the dissolution and the pharmacokinetics of the new formulation in comparison with regular aspirin tablets, aspirin granules and aspirin effervescent tablets. The micronized aspirin tablet formulation was dissolved better than the time the aspirin standard tablet at 15 min [14].

- A new orally disintegrating tablet formulation of low-dose ASA (81 mg) was designed as a fast-acting and quick-dissolving solid dosage form for routine daily use in preventing myocardial infarction and cardiovascular events. Rojeab Y. et al., aimed to evaluate the in vitro dissolution characteristics and the absorption kinetics of ASA from the new product. Orally disintegrating tablet formulation of low-dose ASA characterized by fast dissolution compared to other formulas [15].

- Aspirin floating tablets were prepared (to improve the bioavailability) by a direct compression method using Methocel, NaHCO3, Ethocel, Aerosil, and dicalcium phosphate anhydrous as excipients. Tablets were evaluated by different methods. In vitro dissolution study was determined using USP apparatus II, this study came to sum up that "the dissolution of aspirin was influenced by the excipients in the tablet" [16].

- A certain work emphasized on the formulation and development of sustained release dosage forms for the therapy of various chronic diseases, also investigating the effects of polymers on the sustained action. The dissolution was carried out for 8 hrs. This was done to get a simulated picture of drug release in the in vivo condition. Karim et al., in this work demonstrated that the pattern of release was sustained due to the use of polymers in the formulation. The release characteristics were considerably influenced by the properties and amount of polymers used It was evident that hardness increased with the increase of concentration of polymers [17].

- Seven brands of ASA (300 mg) tablets were purchased from different pharmacy outlets in Benin City, Edo State, Nigeria. All the brands of ASA tablets passed the dissolution test, as a part of quality evaluation tests. Results showed that 70% of the drug (from different brands) was dissolved within 45 min. Dissolution test gives an indication of assessing the bioavailability of drugs as the rate and extent of the drug absorbed depends on the dissolution rate of drug particles [18], [19].

Table (1): overview of studies

	Invention disclosed	Year ofpublication	Type of apparatus	Media	Method of tablet manufacturing	Dosage form	Formula (additives)
(9)	Formulation of Acetylsalicylic Acid Tablets for Aqueous Enteric Film Coating	2001	USP Apparatus I (Basket)	acetate buffer (pH=4.5)	Compression and coating	enteric film coated tablet	Aspirin Stearic acid, starch Microcrystalline cellulose Croscarmellose sodium Sodium starch glycolate
(10)	Preparation and Characterization of Aspirin-Chitosan Complex: An Attempt for Its Solubility and Stability Improvement	2010	axed in a molar ratio of (1:1)	dissolved in 500 ml of purified water	simple mixing of previously dried aspirin and chitosan powders	1:1 aspirin chitosan HCl mixture	Aspirin chitosan hydrochloride salts
(12)	Design of aspirin formulation for rapid pain relief	2011	USP type-II apparatus (paddle)	500 ml of phosphate buffer (pH 4.5)	Direct compression	Fast dissolving tablet	Aspirin, iodine214, iodine254, mannitol croscarmellose, talc microcrystalline cellulose,
(13)	FORMULATION OF ASPIRIN TABLETS USING FEWER EXCIPIENTS BY DIRECT COMPRESSION	2011	USP type-II apparatus (paddle)	0.05M acetate buffer solution 500 mL (pH 4.5) at 50 rpm	Direct compression	Rapid release tablet	Aspirin Lactose, CornstarchAerosil
(14)	Dissolution of micronized aspirin formulation	2011	USP general test	pH of 4.5.	Direct compression	micronized Tablet	micronized aspirin
(15)	in vitro dissolution of ASA from a new orally disintegrating tablet formulation of low dose ASA (ODA)	2011	USP apparatus II (paddle method)	0.1 N HCl	Direct compression	orally disintegrating tablet	Starch, Croscarmellose sodium, Hypromelloses, Cellulose, Corn, Microcrystalline, Mineral oil, Titanium Dioxide
(16)	In vitro release modeling of aspirin floating tablets	2015	USP apparatus II (paddle method)	SGF without pepsin pH 1.2	Direct compression	floating tablet	Aspirin Methocel K4M CR, NaHCO3, Ethocel, Aerosil, Dicalcium, phosphate anhydrous
(17)	In Vitro Evaluation of Aspirin Sustained Release Tablets Using Hydrophilic Polymer	2016	USP apparatus-II (paddle)	phosphate buffer, pH 6.8	Direct compression	sustained release dosage forms	Aspirin, Ethyl cellulose HPMC-K15 MCR, Lactose & povidone K-30 magnesium stearate

(18)	Comparative Study of The Physicochemical Properties and Dissolution Profiles of Some Brands of Acetylsalicylic Acid Tablets Marketed In Benin City, Edo State, Nigeria	2019	USP dissolution apparatus (rotating basket)	(800 ml of 0.1N HCl)	Direct compression	Coated tablet	AsA (1) Biophar ma ASA (2) Emprin ASA (3) Kunimed ASA (4) Disprin ASA (5) Anacin ASA (6) Aspirin caplet ASA (7) Propon (Seven different brands)

3. Discussion

Among various routes of drug administration, the oral route is the most widely used for systemic delivery of drugs via pharmaceutical dosage forms including the conventional and advanced drug delivery systems [20]. The most widely used oral route of drug administration is natural, uncomplicated, convenient and safe due to its ease of administration, patient acceptance and cost-effective manufacturing process [21]. Low-dose aspirin is in routine use today in preventing myocardial infarction and cardiovascular events and its main adverse effects are the gastro intestinal disturbances and ulcers when administered orally and to reduce the adverse effects, it can be formulated as sustained release which could provide a more constant plasma concentration with less frequent administration. Aspirin has low solubility in water (1:300) [22], [23], therefore, dissolution is one of the rates limiting step in their absorption and bioavailability [24], [25]. A major challenge of pharmaceutical formulation activity is increasing the efficacy of the product by achieving faster dissolution and faster absorption which may lead to a faster onset of action in acute pain [26]. Dissolution testing is a critical component of quality control procedures and in the pharmaceutical industry; it is used to ensure that the final solid dosage forms have consistent dissolution properties. After studying all researches, we found that all experiments had an impact on dissolution rate. The type and amount of the excipients added had a special effect on dissolution rate as mentioned in a study and concluded that Microcrystalline cellulose decrease the rate while Starch 1500 may increase it [9], aspirin chitosan complex increase dissolution and reduce irritation of gut [10], Lactose, Cornstarch, Aerosil also increase dissolution rate [13] and by addition of Methocel, NaHCO3, Ethocel, Aerosil, and dicalcium phosphate anhydrous as excipients in Aspirin floating tablets ,the dissolution of was influenced by the excipients [16]. These findings came to agree with the fact that realizes the effect of drug formula (excipients) on dissolution rate. The impact of dosage form on dissolution rate was obviously observed and coincided with the increase in drug release as seen in micronized tablets (14) and orally disintegrating tablet (This is because the formed ASA-containing solution/suspension will start getting absorbed from the oral cavity first) [27]. while for sustain released tablet that Were prepared with different ratios of Ethyl cellulose and hydroxypropyl methyl cellulose, the release rate decreased with the increase of polymers [28]. Dissolution test is one of the most important bioequivalence tests, by taking different brands of aspirin, certain study found that all the brands had the same results and dissolution rate came to satisfy all the brands.

4. Conclusion

Dissolution test is one of the most important quality control tests used to predict drug bioavailability, to determine bioequivalence and to determine the effect of formula and comparison between different dosage forms.

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