The Role Of Dissolution Test in Evaluation Of Ibuprofen Oral Dosage Form Availablein Iraqi Market

Aumaima Tariq Abid[1], Rusul M Alhilo[2], Hajer Alaa Obeid[1], Saif M. Hassan[1*], Saly Naser Abbas[1], Mohammed Jasim Jawad[1], Najah R. Hadi[3]

Department of Pharmacy, Al-Zahrawi University College, Karbala, Iraq[1]
Al-Zahraa University for Women, Karbala, Iraq[2]
Department of Pharmacology and Therapeutics, Faculty of Medicine, University of Kufa, Iraq[3]

Corresponding author: 1*

ABSTRACT— The aim of this study was to assess the quality of some selected ibuprofen products in community pharmacies in Iraq. Different parameters of quality control of pharmaceutical products can guarantee the quality and bioavailability and optimal therapeutic activity. Used quality control parameters, i.e., the variation of weight, friability, disintegration time, dissolution time were tested in vitro. The weight range was (0.56-0.60) g, (0.26-0.33) g, (0.48-0.54) g for Apifen (Ajanta) (400), Apifen (Ajanta) (200), and ibuprofen (flamingo) (400) respectively. Disintegration time was (18min, 17min, and 13min) for Apifen (Ajanta) (400), Apifen (Ajanta) (200), and ibuprofen (flamingo) (400) respectively. Dissolution time at 0.1 N HCL 12.9, 12.2, 18.5, For Apifen (Ajanta) 200 mg, Apifen (Ajanta) 400mg, Ibuprofen 400mg and the dissolution time at Phosphate buffer pH6.8 88.7, 86.6, 90.2 Apifen200mg, Apifen 400 mg, Ibuprofen 400mg. The results showed that all products fulfill the given specification of pharmacopeia (USP-NF) which its dissolution rate was less % in USP (85%after 30min) in phosphate buffer and in 0.1N HCL (18% after 30 min) for ibuprofen(flamingo). Disintegration of ibuprofen 400(flamingo) showed the quickest disintegration while Apifen (400) the slowest.

KEYWORDS: Ibuprofen, dissolution, disintegration, friability, dosage form.

1. INTRODUCTION

Ibuprofen is (2RS)-1[4-(2-methyl propyl) phenyl] Propanoic acid Ibuprofen was the first member of Propanoic acid derivatives to be introduced in 1969 as a better alternative to Aspirin. Gastric discomfort, nausea and vomiting, though less than aspirin or indomethacin, are still the most common side effects [1]. Ibuprofen is the most commonly used and most frequently prescribed Non-steroidal anti-inflammatory drugs(NSAIDs) [1], [2]. It is a non-selective inhibitor of cyclo-oxygenase-1 (COX-1) and Cyclooxygenase-2 (COX-2) [3]. Although its anti- inflammatory properties may be weaker than those of some other NSAIDs, it has a prominent analgesic and antipyretic role. Its effects are due to the inhibitory actions on cyclooxygenases, which are involved in the synthesis of prostaglandins. Prostaglandins have an important role in the production of pain, inflammation and fever [4], [5]. Ibuprofen is supplied as tablets with a potency of 200 to 800 mg. The usual dose is 400 to 800 mg three times a day [6]. It is almost insoluble in water having pKa of 5.3.8 It is well absorbed orally; peak serum concentrations are attained in 1 to 2 hours after oral administration. It is rapidly bio-transformed with a serum half-life of 1.8 to 2 hours. The drug is completely eliminated in 24 hours after the last dose and eliminated through metabolism [7], [8]. The drug is more than 99% protein bound, extensively metabolized in the liver and little is excreted unchanged [9]. Although highly bound to plasma proteins (90-99%), displacement interactions are not clinically significant, hence the dose of oral anti coagulants and oral hypoglycemic needs not be altered [10]. More

than 90% of an ingested dose is excreted in the urine as metabolites or their conjugates, the major metabolites are hydroxylated and carboxylate compounds [11], [12]. Old age has no significant effects on the elimination of ibuprofen [13]. Renal impairment also has no effect on the kinetics of the drugs, rapid elimination still occur as a consequence of metabolism [14]. The administration of ibuprofen tablets either under fasting conditions or immediately before meals yield quiet similar serum concentrations-time profile. When it is administered immediately after a meal, there is a reduction in the rate of absorption but no appreciable decrease in the extent of absorption [11], [15].

2. Material and method

For standard curve of Ibuprofen, first of all stock solution was prepared by taking 20 mg of Ibuprofen in 100 ml solvent (phosphate buffer pH 6.8) in a volumetric flask. The drug was dissolved in the solvent by magnetic stirrer. Five different dilutions were prepared of the stock solution (0.2 mg/ml) having concentrations, 0.1 mg/ml, 0.05 mg/ml, 0.025 mg/ml, 0.0125 mg/ml and 0.0062 mg/ml respectively. These prepared dilutions were then analyzed by UV-Visible Spectrophotometer at 264 nm. The values of absorbance were plotted against concentrations and a slope was developed as given in figure (1).
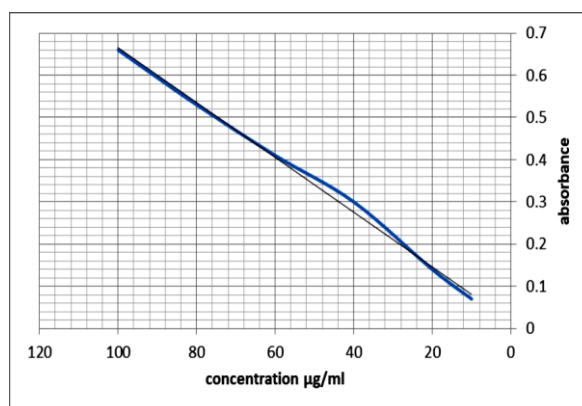

Figure 1: calibration curve of ibuprofen

A-Weight variation: For each brand, 20 tablets were randomly selected and weighed individually using an analytical balance. The average weights were calculated and the percentage deviations from mean values were calculated. Then the standard deviations, and percentage of related standard deviation (RSD)was determined [16].

B-Hardness test: Hardness test Tablet hardness is defined as the force required breaking the tablet in a diametric compression test. If the tablet is too hard, it may not disintegrate in the required period of time to comply with the dissolution specification. Conversely, the hardness must not be so low that the tablets are soft and friable. To get a satisfactory quality tablet hardness should be between 4 and 8 kg 6 [17].

C-Friability test: It is defined as the percentage of weight loss of powder from the surface of the tablets due to mechanical action and the test is performed to measure the weight loss during transportation. in friability test the tablets are prone to abrasion hence enabling us to check for the tablet strength under application of force in different manner [18].

D-Disintegration time test: Six tablets were subjected to this test. One tablet was introduced into each tube of disintegration apparatus with addition of a disc. The assembly was suspended in the beaker containing distilled water 37°C and the apparatus was operated for 15 minutes. The assembly was removed from the

liquid and detected for any fragment of tablet remains [19].

E-In vitro dissolution rate studies: Paddle dissolution Apparatus was used for the in vitro drug release studies of Ibuprofen, the study was carried according to the, USP method. Two different Medias were used. The dissolution tests were performed at 50 rpm, in 900 mL of 0.1 N HCl, phosphate buffer pH 6.8, at 37C (3 replicates). The drug dissolved is determined by UV absorbance (Lambda 264 UV) on filtered portions of the dissolution media. The percentage of drug released after 30 min was recorded using the linear regression equation of the calibration curve. These test in the tablet and suspension [20].

3. Results

The weight range was (0.56-0.60) g, (0.26-0.33) g, (0.48-0.54) g for Apifen (Ajanta) (400), Apifen (Ajanta) (200), ibuprofen (flamingo) (400) respectively, as shown in the table below.

Table 1: weight variation measurement (n=10)

Brand	Minimum weight(g)	Maximum weight(g)	Average weight(g)	Standard Deviation (SD)	%Relative Standard (RSD)
Apifen (400)	0.56	0.60	0.571	0.008	1.046
Apifen (200)	0.26	0.33	0.292	0.009	1.401
Ibuprofen(flamingo) (400)	0.48	0.54	0.494	0.010	1.402

Disintegration time was (18min, 17min, and 13min) for Apifen (Ajanta) (400), Apifen (Ajanta) (200), and ibuprofen (flamingo) (400) respectively. Dissolution time at 0.1 N HCL 12.9, 12.2, 18.5, For Apifen (Ajanta) 200mg, Apifen (Ajanta)400mg, Ibuprofen 400mg and the dissolution time at Phosphate buffer pH6.8 88.7, 86.6, 90.2 Apifen200mg, Apifen 400mg, Ibuprofen 400mg.

Table 2: results of quality test

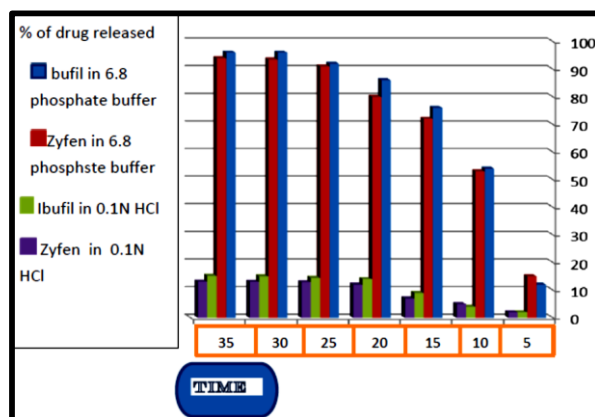| brands	hardness	friability	Disintegration time (min)	Dissolution test (%)of drug released	
				0.1N HCl	Phosphate buffer pH= 6.8
Apifen200mg	6.59±0.2	2.9±0.4	17±0.2±0.1	12.9±0.2	88.7±0.1
Apifen 400mg	13.4±0.1	2.85±0.2	18±0.1±0.3	12.2±0.1	86.6±0.4
Ibuprofen400mg	12.75±0.1	0.54±0.4	13±0.4±0.1	18.5±0.3	90.2±0.1

Figure 2: dissolution test of suspension dosage form

4. Discussion

Ibuprofen is one of the commonly used medicines as it is effective, available, and reasonably priced, and it has multiple pharmaceutical forms, so it can be used for all ages. This is what prompted us to make an evaluation of some of the products we have available to several companies. We used the conventional evaluation methods for grains, and our results show the best product and give expected result is ibuprofen400 (flamingo) depending on pharmacopeia (USP-NF). We saw the dissolution test is the most important way to study, under in vitro conditions, the release of a drug from a solid dosage form, and thus represents an important tool to determine factors that affect the bioavailability of a drug from a tablet dosage form. It is an evaluation as to whether or not a tablet releases its drug contents when placed in the environment of the gastrointestinal tract. The rate of dissolution may thus be directly related to the efficacy of the oral solid dosage form, as well as to bioavailability differences between formulations. The test is conducted using a specially designed instrument (dissolution apparatus) with selected pharmacopeia specification. The dissolution performance of ibuprofen if as tablet or suspension is tested when poured in the dissolution vessel only 20% of the active dissolve at low PH in 60 min whereas ibuprofen dissolves in few minutes in PH6.8 buffer, confirming that the solubility of ibuprofen strongly depends on the PH of the solution. The second important thing we used in evaluation two different companies for two suspension and this only method can use in evaluation of suspension and saw the ibuprofen dissolution quickly when the acidity low. Depending on the result we should protect the ibuprofen from the acid of GI to get good dissolution and disintegration therefore good bioavailability product.

5. Conclusion

Ibuprofen is a commonly prescribed analgesic and anti-inflammatory drug. Currently many generic and multinational brands of this drug are available in the Pharma market in the gulf region. it has been observed that multi sourcing of a drug product might lead to variability in clinical responses and eventually dissatisfaction among prescribers and consumers. Small differences in manufacturing process, different formulation factors such as type and amount of excipients, packaging or storage factors and substandard as well as counterfeit products could alter the disintegration, dissolution and other parameters that consequently lead to variation in therapeutic response. The results showed that all products fulfill the given specification of pharmacopeia (USP-NF) which its dissolution rate was less % in USP (85%after 30min) in phosphate buffer and in 0.1N HCL (18% after 30 min) for ibuprofen(flamingo). Disintegration of ibuprofen 400(flamingo) showed the quickest disintegration while Apifen (Ajanta) (400) the slowest.

6. Recommendation

We advise any person to do the search about ibuprofen to sure from availability of matter because the difficulty that we faced when search about the active constituent of ibuprofen. the old devices second problem we faced you made us repeat the test more than once so we advise the researchers to use more development devices for get more accurate results.

7. References

[1]   Tripathi K. Non steroidal anti inflammatory drugs and anti pyretic analgesics. Essentials of medical pharmacology. 2003;5:176

[2]   Mohsin MM, Jawad MJ, Hassan SM, Awad SM, Hussain YA, Hadi NR. Synthesis and Evaluation of The Thrombolytic Activity of Novel Condensed Pyrimidine Sulfonamide Derivatives. European Journal of Molecular & Clinical Medicine. 2020;7(2):220-4

[3]   Chavez ML, DeKorte CJ. Valdecoxib: a review. Clinical therapeutics. 2003;25(3):817-51

[4]   Wahbi AA, Hassan E, Hamdy D, Khamis E, Barary M. Spectrophotometric methods for the determination of Ibuprofen in tablets. Pakistan journal of pharmaceutical sciences. 2005;18(4):1-6

[5]   Jawad MJ, Hassan SM, Ahjel SW, Hadi NR, Awad SM. Synthesis of Novel Pyrimidine Derivatives as Bioisosters of Nifedipine and In Vitro Evaluation of their Antihypertensive Activity. Latin American Journal of Pharmacy. 2021;40(1):131-40

[6]   Insel PA. Analgesic-antipyretic and antiinflammatory agents and drugs employed in the treatment of gout. The Pharmacological Basic of Therapeutics. 1996:617-57

[7]   Antal E, Wright III C, Brown B, Albert K, Aman L, Levin N. The influence of hemodialysis on the pharmacokinetics of ibuprofen and its major metabolites. The Journal of Clinical Pharmacology. 1986;26(3):184-90

[8]   Ahjel SW, Hassan SM, Hussein SF, Hadi NR, Awad SM. Antineoplastic Effect of New Synthesized Compounds of 2-Thiouracil Sulfonamide Derivatives against Ovarian and Breast Carcinoma Cells" In Vitro Study". Systematic Reviews in Pharmacy. 2020(4)

[9]   Abukhalaf IK, Deutsch DAv, Ansari NA, Alsharif A. Nonsteroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs, and agents used in gout. Handbook of Drug Interactions: Springer; 2012. p. 415-75

[10]   Bushra R, Aslam N. An overview of clinical pharmacology of ibuprofen. Oman medical journal. 2010;25(3):155

[11]   Ebenezer V, Babu A. Effectiveness of Ibuprofen as an Anti-inflammatory Drug on the Post Opeperative Sequelae following Transalveolar Extraction of Impacted Lower Third Molars. Indian Journal of Multidisciplinary Dentistry. 2013;3(2)

[12]   Olive G. Analgesic/Antipyretic treatment: ibuprofen or acetaminophen? An update. Therapie. 2006;61(2):151-60

[13]   Crampton E, Glass R, Hind I, Rees J. The pharmacokinetics of ibuprofen in elderly and young subjects. Boots Research Report DT 84041; 1984

[14]   Krasniqi D, Thaqi E, Berisha D, Bibaj G, Kryeziu F. The use of Ibuprofen and our knowledge about it. 2019

[15]   HASSAN SM, AL-JAF ANA, HUSSIEN YA, AWAD SM, ABDULKHALEQ MA, HADI NR. Effect of new synthesized compounds of 2-Thiouracil Sulfonamide Derivatives against colon and liver carcinoma cells "In Vitro Study. International Journal of Pharmaceutical Research. 2020;12(4)

[16]   Eraga SO, Arhewoh MI, Chibuogwu RN, Iwuagwu MA. A comparative UV− HPLC analysis of ten brands of ibuprofen tablets. Asian Pacific Journal of Tropical Biomedicine. 2015;5(10):880-4

[17]   Abbaspour M, Sadeghi F, Garekani HA. Design and study of ibuprofen disintegrating sustained-release tablets comprising coated pellets. European journal of pharmaceutics and biopharmaceutics.

2008;68(3):747-59

[18]   Gryczke A, Schminke S, Maniruzzaman M, Beck J, Douroumis D. Development and evaluation of orally disintegrating tablets (ODTs) containing Ibuprofen granules prepared by hot melt extrusion. Colloids and surfaces B: biointerfaces. 2011;86(2):275-84

[19]   Swain RP, Satish P, Subudhi B, Panda S. Formulation and optimization of orodispersible tablets of ibuprofen. Int J Pharm Pharm Sci. 2015;7(2):441-7

[20]   Rivera-Leyva J, García-Flores M, Valladares-Méndez A, Orozco-Castellanos L, Martínez-Alfaro M. Comparative studies on the dissolution profiles of oral ibuprofen suspension and commercial tablets using biopharmaceutical classification system criteria. Indian Journal of Pharmaceutical Sciences. 2012;74(4):312