Assessment of physicochemical properties of furosemide (40mg) tablets marketed in Syria

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ABSTRACT

There are several generics of furosemide tablets available within the drug delivery system globally. Numerous brands of furosemide (40 mg) are available in the Syrian drug market. The objective of this study is to determine the biopharmaceutical and chemical equivalence of three brands of furosemide tablets marketed in Syria. The physicochemical equivalence of three brands of furosemide tablets were assessed through the evaluation of both official and non-official standards such as weight variation, friability, hardness, content uniformity, and dissolution rate. All the brands complied with the official specifications for weight variation and friability tests. The result indicates that all two brands passed the non-official test of crushing strength/hardness. two brands had values within the range specified (90-110%) for content uniformity in the USP while brand C failed the test. all brands released more than 80% drug in 60 minutes therefore, all formulations passed this acceptance pharmacopeia criterion (USP).

Keywords: furosemide, hardness, friability, weight variation, content uniformity, dissolution test.

1. INTRODUCTION

Quality control of drugs have become important subject in the field of giving drug since the existing of many pharmaceutical industries that produce the same dosage form for the same active ingredient. The evaluation of pharmaceutical form differs from each one to another, for example, there are many examinations that should be done on tablets which are considered solid dosage form. This examinations involve tests for physical properties such as hardness, friability, weight variation, test for the uniformity of content and dissolution test. Tablets should pass this tests to ensure that patient will receive the required therapeutic efficacy, and the drug is safe for the patient throughout the expiration date (Köhler, 2009, Ansel, 2000).

Furosemide (figure 1) is a potent diuretic with a rapid action. Like the other loop or high-ceiling diuretics it is used in the treatment of edema associated with heart failure including pulmonary edema, and with renal and hepatic disorders and may be effective in patients unresponsive to thiazide diuretics. It is also used in high doses in the management of oliguria due to renal failure or insufficiency. Furosemide is also used in the treatment of hypertension either alone or with other anti-hypertensives Furosemide inhibits the reabsorption of electrolytes primarily in the thick ascending limb of the loop of Henle and also in the distal renal tubules. It may also have a direct effect in the proximal tubules. Excretion of sodium, potassium, calcium, and chloride ions is increased and water excretion enhanced. It has no clinically significant effect on carbonic anhydrase (Gulbis, 2006; Rudy, 1991; Dormans, 1996)

Furosemide is fairly rapidly absorbed from the gastro intestinal tract; bioavailability has been reported to be about 60 to 70% but absorption is variable and erratic. The half-life of furosemide is up to about 2 hours although it is prolonged in neonates and in patients with renal and hepatic impairment. Furosemide is up to99% bound to plasma albumin, and is mainly excreted in the urine, largely unchanged. There is also some excretion via the bile and non-renal elimination is considerably increased in renal impairment. Furosemide crosses the placental barrier and is distributed into breast milk (Benet, 1979, Ponto, 1990).
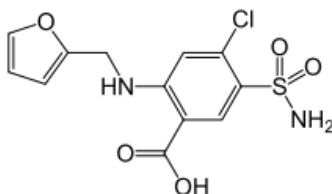

Figure.1.Structure of furosemide

Furosemide tablets is marketed in one strength in Syria (40 mg), and is considered a common prescribed drug doctors. This study aims at evaluating the physical and chemical characterizes of three commercial types of furosemide tablets marketed in Syria.

2. MATERIALS AND METHODS

Three commercial brands (A, B, C) of furosemide were randomly selected. Furosemide brands having label strength of 40 mg were purchased from registered pharmacies in Lattakia, Syria. All tests were performed within product expiration dates. The reagents used were sodium hydroxide (BDH Chemicals, UK) and potassium di hydro orthophosphate (BDH Chemicals, UK). Freshly distilled water was used throughout the work.

Mechanical Resistance Tests: This include hardness and friability tests. For the test of hardness we choose 10 tablets from each commercial brand, after that each tablet was located singly in the Erwerka hardness tester machine. The machine record the power that essential to destroy the tablet.

For friability test a Sample from 20 tablets were chosen of each brand, and put in the Roche friabilator after weighing them together. The friabilator was regulated to 25 rpm for 4 minutes. Then tablets were weighed again after cleaning from dust. By using this formula: % of Friability = [(Wi − Wf)/ Wi] x 100 The friability was evaluated. The loss in weight shouldn't left over 1% according to BP.

Weight Variation: 20 tablets were taken from each brand. Each tablet was weighed individually. Then the average weight was calculated for every brand. The individual weight was compared with an average weight. Not more than two of the individual weights deviated from the official standard (limit ±7.5%).

Calibration Curve of Furosemide in Sodium Hydroxide at 271 nm: A standard curve was created for furosemide using pure drug powder diluted to 5 known concentrations (range between 0.40 and 2.04 mg/100ml). These standard curves were established to verify accurate analysis of the drug.

Uniformity of Content: 10 tablets were taken from each brand. We crushed and dissolved each tablet singly in 100 ml sodium hydroxide. The samples were filtrated through a membrane filter. The samples of each solution were assayed for drug concentration using spectrophotometer at 271 nm. The calculation of content for each tablet was determined using the standard curve.

Several measures were calculated in order to determine the amount and acceptability of variations in drug content. The percent of label claim was used in the expression of the drug content for each tablet. Each tablet should contain not less 90% and not more than 110% of the active substance (proxy USP specification for drug content).

Dissolution Test|: Firstly, A standard curve was made using pure drug powder of furosemide solved in phosphate buffer (PH=5.8), diluted to 5 known concentrations (range between 0.19and 1.96mg/100ml).

Dissolution test was determined using a 7-compartment Veego dissolution test apparatus (paddle type) containing 900ml of the buffer solution, temperature 37 ±0.50C, speed 50rpm. Samples of 5ml were withdraw at the intervals of 5, 10, 15, 30, 45 and 60 minute, and directly replaced by 5ml of dissolution medium. Each of the withdrawn samples was filtered with syringe filter 0.45μm, the filtrate diluted, and the assayed using spectrophotometer at wavelength 274nm. The aim of doing dissolution study for test and reference product was to assess the product's dissolution profiles. For passing the test all furosemide immediate release tablets must release 80% of drug within 60 minutes.

3. RESULTS AND DISCUSSION

Hardness and Friability Tests: Crushing strength test shows the ability of tablets to withstand pressure or stress during handling, packaging and transportation. It is a property of a tablet that is measured to assess its resistance to permanent deformation. This result also indicates that all brands passed the non-official test of crushing (Table 1).

The result of tablet friability test shows that virtually all the tested brands had impressive friability values ranging from 0.43% to 0.92%w/w (Table 1). According to BP no batch should have a friability value greater than 1.0%w/w; therefore, all the brands passed the test.

Table.1.Hardness and friability of metformin tablets

Brand	Hardness(KP±SD) N=10	Friability (%) N=20
A	7.31 ±0.65	0.43
B	6.98 ±0.33	0.68
C	4.09 ±0.87	0.92

Weight Variation: Mass uniformity can be used in the way to evaluate the uniformity of dosage form for the studied brands, the deviation of weight from the official standard less than±7.5%, as a result all commercial types passed the pharmacopeia requirements for weight variation (table 2).

Table.2.Weight variation of metformin tablets

| Brand	Measured weight mean (mg) N=20	Deviation range (%)	RSD (%)
A	169.3	-1.22-3.98	3.01
B	200.7	-3.43-2.57	2.13
C	201.1	-2.98-4.01	3.78

Calibration Curve of Furosemide in Sodium Hydroxide at 271 nm: A linear relationship between the absorbance and the concentration of furosemide in sodium hydroxide at 271 nm in the concentration range of 0.40-2.04mg/100ml is observed. The regression equation is Y= 0.4132X+0.0234 and the correlation coefficients (r) of the linear regression of the calibration curves is 0.9999.

Content Uniformity: The results obtained from the assessment of the percentage content of active ingredient in the three brands of furosemide tablets showed that two brands (A, B) gave values within the monograph specifications (90-110%), while brandC failed the test with values outside of proxy USP specification in 7 tablets. Tablets of brand A have the largest content 39.01 mg (see table 3).

Table.3.Content uniformity of furosemide tablets

Brand	Measured drug content mean (mg) N=10	Percent of content range (%) N=10	RSD (%)	Outside of proxy USP specification
A	39.01	96.12-98.65	2.12	0
B	37.54	92.87-94.76	2.01	0
C	34.87	85.97-90.65	4.89	7

Dissolution Test: Firstly, there was a linearity relationship in the range of 0.19-1.96 mg/100ml when standard curve for furosemide in phosphate buffer was prepared. The regression equation is $Y=0.3435x+0.1404$ and the correlation coefficients (r) of the linear regression of the calibration curves is 0.9985. The dissolution of solid dosage forms like as tablets that are taken orally are essential conditions to can be absorbed. Dissolution test reflect the behavior of product in vivo (Papadopoulou, Valsami, 2008). Consequently, dissolution test is currently used as an in vitro bioequivalence (BE) test. We studied three commercial types of furosemide (40 mg) tablets. To assess the dissolution profiles, dissolution curve (based on mean percentages of drug released) of test products was combined and depicted in figure 2. In this study, it was observed that for all products, at least 80% release in60 minutes took place. Therefore, all formulations passed this acceptance pharmacopeia criterion (USP).
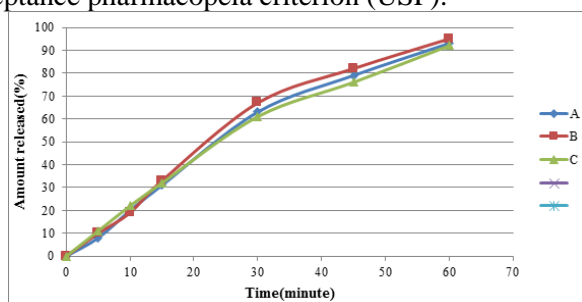
Fig.2.Dissolution profiles of furosemide tablets

4. CONCLUSION

On the whole, all studied commercial types passed the non-official test of hardness and passed the pharmacopeial requirements for friability (less than 1%), and weight variation tests (deviation less than $\pm7.5\%$). Two brands (A, B) passed the USP requirements for content uniformity, while brand C failed the test with values outside of proxy USP specification. In this study, it was observed that for all products, at least 80% release in 60minutes took place.

ACKNOWLEDGEMENT

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