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Quality Control Assay of Three Pharmaceutically Important Sulphur Drugs Commonly Dispensed at Nigerian Defence Academy Medical Centre, Kaduna-Nigeria

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Abstract: A total of 36 samples of three sulphur containing drugs, viz.: chlorpropamide, Ampicillin and frusemide from three different companies labelled A, B and C commonly dispensed to officers, cadets and civilian staff of the Nigerian Defence Academy were tested for their potency using the U.V spectrophotometer assay method. The total drug content, percentage active ingredients, chemical assay and dissolution rate studies for the drugs were evaluated. The specified chemical tests were carried out on the samples analysed and the results were in conformity with that described in BP 1993. The drug contents and percentage active ingredients were found to be within acceptable limit of the monograph. The dissolution rate study of chlorpropamide using the BP 1993 method and pH dependent dissolution rate studies of Ampicillin and Frusemide were investigated on physiological buffer solution pH 6.8. The results obtained demonstrated very good dissolution rate profiles and are discussed in the light of high rate of faking, adulteration and manufacture of substandard drugs and their implication.

Key words: Sulphur, drugs, ingredients, defenee academy, Nigeria

INTRODUCTION

One of the objectives of pharmaceutical analyst in quality control is to be able to know the actual strength of drug product. This can be achieved by using an appropriate individual ingredient. The selection of any specific analytical method will be based on a number of criteria which include, reliability sensitivity, selectivity, specificity and convenience[1].

Some commonly used analytical techniques in drug analysis, from both biological and non-biological samples include: Gravimetric analysis, Titrimetric analysis, Palarography, chromatography techniques (GC, HPLC, TLC) and spectroscopic techniques (IR, MS, Fluorimetry, UV visible and collorimetry).

There have been reports of influx of imitation drugs into our country and analysis by some pharmaceutical companies showed that most of the drugs contained lower and in very few studies higher percentage of the active ingredient[2].

The need to ascertain that pharmaceutical product quality is within acceptable limits cannot be overemphasised. This is even more important these days when the problems of faking, adulteration and production of sub-standard drugs are becoming very serious globally[3].

Since pharmaceuticals are products that affect human lives, the concept of a little to much or a little less cannot be accepted. It is important that pharmaceuticals be prepared right in both their active medicaments and other excipients.

Ampicillin, chlorpropamide and Frusemide are some important sulphur containing drugs, which are used constantly in the treatment of various disease conditions at the Nigerian Defence Academy medical centre.

For these drugs to be therapeutically effective, the pharmaceutical dosage forms must contain the stated amount of the active chemical substances as the official standards.

Due to the economic and health hazards posed by sub-standard and fake drugs on officers, staff and cadets of the Nigerian Defence Academy, the institution which serves as training ground for future leaders and protectors of the territorial integrity of Nigerian nation, this study is therefore designed to carry out an invitro analysis on the quality of chlorpropamide, Ampicillin and Frusemide, which are commonly used sulphur drugs.

MATERIALS AND METHODS

Drugs and chemicals:

- Twelve samples each of chloropropamide (Diabenese) tablets, Frusemide (lasiz) tablets and Ampicillin Trihydrate capsules from different companies.

- Ampicillin standard supplied by WHO Centre for Chemical reference Substances, Solnaz, Sweden, control No. 274001.
- Hydrochloric acid-Analar grade (BDH Chemicals Poole England)
- Methonal (G.R.P Hopkin and William, Chadwell, Heatu, Essex England).
- Sodium hydroxide pellets (BDH) (f) Acetone (BDH) (g) Ethanol (BDH) (h) sodium nitrate (BDH) (i) Chloroform (BDH), (j) Dichloromethane (BDH) (k) Ninhydrin (BDH) (l) Boric acid (BDH), (m) Imidazole crystals) BDH) (n) Mercury (II) Chloride (BDH) (o) 1,4-dioxan (BDH) (p) N-(1-Napthyl) ethylene diaminehydrochloride (BDH (q) Potassium dihydrogen orthophosphate (BDH).

Equipments:

- SP8-100 ultimate spectrophometer, Pye Unicam
- Analytical balance, Type H35 AR melter, GallenKamp.
- Silica Curvettles B.S 3875, 310 mn F.O.
- Thermometer 31/3 Quick fit.
- Melting point determination apparations, Gallenkamp.
- pH meter-kent (Electronic Instrument Ltd., Model 7060).
- Erweka dissolution apparatus.
- Water bath.
- Stop clock.
- Reflux condenser
- Magnetic stirrer.

Sampling: The products were supplied by the pharmacy department of the medical centre. A total of three types of each of the drug products from three companies were tested. For each drug product, four batches were selected and from each batch, twenty tablets and capsules were randomly selected. All the samples tested were still within their shelf life.

Identification of frusemide, ampicillin and chlorpropamide in the samples: To ascertain the presence of Frusemide, Ampicillin and chlopropamide in the samples, they were subjected to melting point determination and both thin layer chromatography audultraviolet spertrophotometric analysis as described by BP 1993.

Chemical assay of frusemide, ampicillin and chlorpropamide samples

Chemical assay of frusemide BP 1993: Twenty tablets of Frusemide were weighed and powdered. 0.2 g of the powdered Frusemide was shaken with 30 mL of 0.1 M sodium hydroxide for 10 min, sufficient 0.1 M sodium hydroxide was then added to produce 500 mL. The suspension was then filtered. 5 mL of the filtrate was pipetted and diluted to 250 mL with 0.1 M sodium hydroxide. The absorbance of the resulting solution was then measured at the maximum of 271 nm. The percentage content of Frusemide was calculated taking the value of A (1%, 1cm) to be 580 by using the formula:

$$\% \text{ Content} \quad \frac{\text{Actual Amount}}{\text{Theoretical Amount}} \times 100$$

Chemical assay of ampicillin: 0.17 g of Ampicillin Trihydrate capsules equivalent to 0.15 g of Ampicillin was dissolved in 500 mL of distilled water. This was shaken for 30 min using an electric shaker. The solution was then filtered using a sintered glass number zero under pressure. 10 mL of the resulting solution was transferred to a 100 mL graduated flask and 10 mL of boric acid buffer (pH9.0) was added. 1 mL of acetic anhydride-dioxan solution was added, the whole content of the flask was allowed to stand for 5 mm and sufficient water added to produce 100 mL. 2 mL aliquots of the solution were placed in 2 stoppered tubes labelled A and B. To one tube, 10 mL of imidazole-mercury reagents was added. The tube was carefully stoppered and immersed in water bath at 60°C for 25 min with occasional swirling. After wards, the tubes was removed from the water bath and cooled rapidly in an ice-bath to 20°C (Solution A.) To the second tube was added 10 mL of water. (Solution B) and mixed. The absorbance of solution A and B was measured at 325 nm using a mixture of 2 mL of water and 10 mL of imidazole-mercury reagent as blank for solution A and water for solution B.

The above procedure was repeated using 0.17 g of the standard Ampicillin sample. The content of Ampicillin was calculated from the difference obtained from the standard sample. The percentage content of Ampicillin was calculated using the formula: -

$$\% \text{ Content} \quad \frac{\text{Absorbance of Sample}}{\text{Absorbance of Standard}} \times 100$$

Chemical assay of chlorpropamide samples B.P 1993: Twenty Chlorpropamide tablets was accurately weighed and average weight determined. They were powered and a quantity of the powder equivalent to 0.25 g of Chlorpropamide was weighed and added to 40 mL of methanol in a 50 mL volumetric flask and shaken for 20 min. Sufficient methanol was added to produce 50 mL, mixed and filtered 5 mL of the filtrate was diluted to 100 mL with 0.1 M-hydrochloric acid and mixed and the absorbance of the resulting solution was measured at 252 nm. The percentage content of Chlorpropamide was

calculated taking 598 as the value of A (1%, 1cm) at the maximum at about 232 nm. Where A (1%, 1cm) is the specific absorbance solution of the absorbing solution.
The percentage content was calculated using the formula:-

$$\% \text{ Content} \quad \frac{\text{Actual amount}}{\text{Theoretical amount}} \times 100$$

Dissolution tests for frusemide, ampicillin and chlorpropamide

Dissolution test for frusemide: One litre of physiological buffer solution pH 6.8 as the dissolution medium was introduced into the vessel and immersed in a constant temperature water bath maintained at 37±0.5°C. One Frusemide tablet was placed in a basket, which was lowered into the medium. The apparatus was operated and the basket rotated at 100 revolutions per minutes. 10 mL of the sample was withdrawn after 45 min and the sample filtered at 37°C and the amount of active ingredients present in the sample was determined by measuring the absorbance of the diluted sample at 271 nm.

Dissolution test for ampicillin: One litre of physiological buffer solution pH 6.8 as the dissolution medium was introduced into the vessel and immersed in a constant temperate water bath maintained at 37±0.5°C. One Ampicillin capsule was placed in the basket which was lowered into the medium. The dissolution apparatus was operated and the basket rotated, at 100 revolution per minute. 10 mL of the sample was withdrawn after 45 min and filtered. The amount of the active ingredient present in the sample was determined by measuring the absorbance of the diluted sample at 325 nm.

Dissolution test for chlorpropamide BP 1993: One litre of a 0.68%$^{W}/_{V}$ solution of potassium dihydrogen orthophosphate (pH 6.8) as the dissolution medium was introduced into the vessel and immersed in a constant temperature water bath maintained at 37±0.5°C. One tablet was placed in the basket immersed into the medium. The motor was started at a rotational speed of 100 revolutions per minutes. A sample 10 mL of the dissolution medium was withdrawn after 45 min and filtered. The absorbance of the filtered sample was measured after diluting 100 times at a maximum of 230 nm. The dissolution procedure was performed thrice. The total content of chlorpropamide in the medium was calculated taking 469 as the value of A (1%, 1cm) at the maximum, at about 230 nm using the formula:

$$\frac{\text{Absorbance}}{\text{Weight of drug in gram x A (1\%, 1cm)}} \times \text{dilution factor}$$

RESULTS AND DISCUSSION

Identification tests: The identification test result obtained for the sample of frusemide tablets analysed confirms the presence of frusemide in all. This is shown by the exhibition of absorption maxima of the samples solution at between 270-274 nm compared to 271 nm for the BP 1993 methanol method.

The melting points of the recrystallized precipitate of chlorpropamide samples was between 141-144°C compared to the BP value of 143°C. This confirms the presence of chlorpropamide in all the samples. Equally, the solution of the samples obtained in the BP 1993 assay method exhibits absorption maxima at between 230-233 nm compared to 232 nm for the BP 1993 value.

The TLC result obtained confirms the presence of Ampicillin in all the samples. This is shown by the presence of a principal spot due to each of the samples on the chromatogram which corresponds to that of the standard Ampicillin. The Rf values of the spot were between 0.625-0.635 compared to 0.620 for the standard. These identification results indicate that the drugs were pure and unadulterated.

Chemical assay: The values of the drug content and percentage composition of the three sulphur drug samples analysed using the BP UV Spectrophotmetric method are given in Table 1, 2 and 3 for frusemide, Ampicillin and Chlorpropamide, respectively. The result obtained show that the sulphur drugs tested complied with the BP 1993 specification of drug content: (95-105%). For frusemide and (92.5-107.5%) for both Ampicillin and Chlorpropamide, respectively.

Table 1: Percentage drug content of frusemide samples

	Companies/Percentage content (%)		
Sample	A	B	C
1	99.00	103.00	102.00
2	98.75	96.00	102.00
3	101.25	98.00	101.95
4	102.00	99.75	100.65

Table 2: Percentage drug content of ampicillin samples

	Companies/Percentage content (%)		
Sample	A	B	C
1	98.0	100.72	97.95
2	97.62	99.34	100.11
3	99.43	98.10	103.25
4	101.35	97.30	98.33

Table 3: Percentage drug content of chlorpropamide samples

	Companies/Percentage content (%)		
Sample	A	B	C
1	104.30	102.60	100.80
2	102.60	99.60	101.10
3	104.30	95.85	104.00
4	99.00	97.80	101.80

Table 4: Dissolution of frusemide tablets in phosphate buffer pH 6.8

	Companies/Percentage content (%)		
Sample	A	B	C
1	90.10	85.20	94.00
2	90.00	80.10	78.37
3	90.20	78.33	90.50
4	91.70	90.10	91.70

Table 5: Dissolution of ampicillin capsules BP 1993

	Companies/Percentage content (%)		
Sample	A	B	C
1	96.40	101.33	95.79
2	90.33	99.24	90.30
3	98.25	97.68	98.10
4	97.64	101.84	102.50

Table 6: Dissolution of chlorpropamide tablets BP 1993

	Companies/Percentage content (%)		
Sample	A	B	C
1	93.20	103.40	101.30
2	98.40	99.80	98.75
3	99.70	99.70	99.10
4	90.30	96.90	101.10

Dissolution rate studies: The amount of active ingredient in solution after the dissolution test were between 78.33 and 103.4% in all the three sulphur drugs analysed Table 4, 5 and 6. These values complied with the BP specification that the amount of active ingredient in solution per tablet should not be less than 70% of the stated amount. The dissolution rate profiles of the three different sulphur drugs analysed released maximum percentage of active ingredients in less than 30 minutes, which complied favourably with the BP specification for dissolution rate test.

CONCLUSION

The identification tests, chemical assay and dissolution rate studies on the three sulphur drugs analysed showed that chemical equivalence between the different brands of the sulphur drugs conformed with the general manufacturing practice by the different manufacturers. Chemical equivalence may not infer bio-equivalence, however, taking other factors into consideration, one can say that the different generic products of chlorpropamide, frusemide and ampicillin being dispensed at the Nigerian Defence Academy Medical Centre may infer similar bioavailability data upon administration, therefore, possibly therapeutically equivalent.

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