Drug Quality Control Work in Drug Analysis and Research Unit: Observation During 1991-1995

I.O. KIBWAGE*, J.K. THURANIRA, LILY GATHU, I.M. GITHIGA, J.M. NGUYO, J.K. NGUGI AND O. KING'ONDU.

Drug Analysis and Research Unit, Department of Pharmaceutical Chemistry, University of Nairobi, P.O. Box 19676, Nairobi Kenya.

The Drug Analysis and Research Unit received and analyzed 262 drug samples over a five-year period 1991 to 1995. Samples were obtained from regulatory authorities, local industry, non-Governmental organizations, Hospitals and private practitioners. The samples analyzed, constituted 59.4% local and 40.6% imported. Failure to comply with quality specifications as set out in respective monographs was overall 17.5% representing 19.9% of local and 14.2% of imported products.

Key Words: Drugs, quality, DARU work.

INTRODUCTION

Both the regulatory authorities and consumers demand that drug products on the market be of good quality. A drug that is of good quality is the most effective armamentarium against disease. When manufacturers release products into the market, it is expected that they have followed good manufacturing practices and that their products are indeed of quality. Analysis of drug products from the Kenyan Market has previously shown varying levels of quality [1-5]. Analysis of intravenous infusions from local sources [6], tetracycline finished products and raw materials [7] and Co-trimoxazole preparations [8] on the Kenyan market show variable degrees of quality.

During this period Drug Analysis and Research Unit (DARU) devolved from being a University of Nairobi and Ministry of Health joint venture to full-fledged Unit in the then Department of Pharmacy when the National Quality Control Laboratory (NCQL) was established in 1993. In the years 1991 and 1992 the core staff of the NDCQL operated independently of University activities and their observations have already been published [5]. Their findings are not included in this paper which extends the series of observations and discusses the drug quality control findings in DARU between 1991 - 1995.

MATERIALS AND METHODS

Samples

The samples analyzed at the DARU were obtained from various sources; regulatory authority, hospitals, manufacturers and consumers. Details of procedures and requirements for receiving samples in DARU have been discussed previously. [1, 2]

Samples were of both local and foreign origin.

Method

The methods and other procedures that were used in the quality control of the drug products are those set out in respective monographs in the relevant pharmacopoeia. Drug products were therefore expected to conform to official compendia specification in British Pharmacopoeia (BP) [9], United States Pharmacopoeia (USP) [10], European Pharmacopoeia (Ph. Eur.) [11] or Indian Pharmacopoeia [12]. Products which are not subject to official compendia monograph were analysed using manufacturers method and to his specifications.

RESULTS

The purpose of analysing samples was to verify label claims and to ensure that they conform to official compendia or manufacturer's own specifications. The results are given in table 1.

Unlike previous reports, some analysed samples were purposively selected by the DARU to check on complaints voiced in various fora.

A total of 262 samples were evaluated for quality. 156 (59.4%) were local and 106 (40.6%) were imported. The overall failure to meet quality specifications was 46 (17.5%) of samples. When samples of local origin are considered, 31 samples (19.9%) failed compared to 15 (14.2%) of imported samples. The apparent higher failure rate amongst local product could be explained as consequent of some local manufacturers seeking a second opinion following in-house results and the Unit targeting complaint products.

The major cause of failure was low content of the active ingredient(s). These included, ferrous sulphate 2-products, NaCl/glucose preparation -1, phenoxymethyl penicillin - 1, ethambutol - 1, gentamicin - 1, isoniazid - 1, piperazine - 1, nystatin - 1 and ergometrine - 2. Others were the multi-component preparations, di-iodohydroxyquinoline and hydrocortisone -2 (low hydrocortisone content), throat lozenges-2 (low content of eucalyptus-1 and both low benzocaine and eucalyptus-1) and Promethazine /codeine/ephedrine -1 (low Promethazine).

TABLE 1: Therapeutic and chemical classification of drugs analyzed by the DARU between January 1991 and December 1995

Class and Subclass	Number of Requests for Analysis	Number of Drugs Passed test and source		Number failed test and source	
		Local	Imported	Local	Imported
1. Alimentary system					
a) Antacid					
(i) Magaldrate	1	-	-	-	1
(ii) Compound magnesium trisilicate	5	4	1	-	-
(iii) Magnesium and Calcium Carbonate	1	-	1	-	-
(b) Antispasmodics					
(i) Hyoscine-N-butyl bromide	4	1	-	3	-
(c) Stimulant laxatives					
(i) Biscodyl	1	1	-	-	-
(e) H2-receptor Antagonist					
(i) Famotidine	1	-	1	-	-
(f) Antidiarrhoes					
(i) Loperamide	1	1	-	-	-
2. Allergic disorders					
(a) Antihistamines					
(i) Chlorpheniramine maleate	3	3	-	-	-
(ii) Promethazine	1	1	-	-	-
3. Cardiovascular system					
(a) Atihypertensives					
(i) Atenolol	2	-	2	-	-
(ii) Dilitiazem	1	-	1	-	-
(iii) Nifedipine	2	-	2	-	-
4. Endocrine system					
(a) Corticosteroids					
(i) Betamethasone	1	1	-	-	-
(ii) Hydrocortisone	4	1	2	1	-
(iii) Prednisolone	1	1	-	-	-
5. Infections					
(a) Antibiotics					
(i) Chloramphenicol	2	1	1	-	-
(ii) Erythromycin	3	3	-	-	-
(iii) Penicillins	30	16	8	6	-
(iv) Rifampicin	2	-	1	-	1
(v) Tetracyclines	6	5	1	-	-
(vi) Gentamycin	8	7	-	1	-
(vii) Framycetin	1	-	1	-	-

Class and Subclass	Number of Requests for Analysis	Number of Drugs Passed test and source		Number failed test and source	
		Local	Imported	Local	Imported
(b) Sulphones and sulphonamides					
(i) Co-trimoxazole	40	18	12	3	7
(ii) Pyrimethamine & Sulphadoxine	3	-	3	-	-
(c) Anthelmitics					
(i) Mebendazole	1	1	-	-	-
(ii) Niclosamide	2	-	2	-	-
(iii) Piperazine	1	-	-	1	-
(d) Antiprotozoal drugs					
(i) Amodiaquine	1	1	-	-	-
(ii) Chloroquine	13	10	3	-	-
(iii) Metronidazole	7	5	2	-	-
(iv) Tinidazole	1	-	1	-	-
(e) Anti-tuberculosis					
(i) Ethambutol	3	1	1	1	-
(ii) Isoniazid	1	-	-	1	-
(ii) Pyrazinamide	1	-	1	-	-
(f) 4-Quinolones					
(i) Norfloxacin	6	-	6	-	-
(g) Antifungals					
(i) Nystatin	1	-	-	1	-
(h) Oxytocics					
(i) Ergometrine	2	-	-	-	2
6. Nervous System					
(a) Analgesics					
(i) Aspirin	6	4	2	-	-
(ii) Indomethacine	2	-	2	-	-
(iii) Paracetamol	7	4	3	-	-
(b) Tranquilizers					
(i) Chlorpromazine	5	3	2	-	-
(i) Fluoxetine	1	-	1	-	-
(iii) Haloperidol	2	-	2	-	-
(c) Sedative hypnotics					
(i) Diazepam	2	2	-	-	-
(ii) Phenobarbitone	1	1	-	-	-
7. Nutrition and blood					
(a) Antianaemics (haematinics)					
(i) Folic acid	1	1	-	-	-
(ii) Ferrous sulphate	4	-	-	2	2

Class and Subclass		Number of Requests for Analysis	Number of Drugs Passed test and source		Number failed test and source	
			Local	Imported	Local	Imported
(b)	*Electrolyte and water replacement*					
(i)	I.V. fluids	7	4	1	1	1
(ii)	Dextrose/glucose	4	3	1	-	-
(iii)	Sodium Chloride	3	1	2	-	-
(c)	*Vitamins*	1	-	-	1	-
8.	**Ophthalmic drugs**					
(i)	Tetrahydrazoline	1	-	1	-	-
9.	**Respiratory System**					
(a)	*Allergic emergencies*					
(i)	Adrenaline	3	2	-	1	-
(b)	*Expectorant & Cough suppressants*					
(i)	Bromohexine/Pseudoephedrine	2	-	2	-	-
(ii)	Dextrometorphan	1	-	1	-	-
(iii)	Promethazine, codeine, ephedrine	5	4	-	1	-
(c)	*Bronchodilators* (Bronchial spasm relaxants)					
(i)	Aminophylline	-	-	-	-	-
(ii)	Pentoxifylline	1	-	1	-	-
(iii)	Etophylline & Theophylline	14	-	14	-	-
(d)	*Cough /cold Preparations*					
(i)	Dextromethopharm/Phenylpropanolamine/ Chlorpheniramine	1	-	1	-	-
(ii)	Diphehydramine	1	-	1	-	-
(iii)	Paracetamol/Chlorpheniramine/ Phenylpropanolamine	1	-	1	-	-
(e)	*Throat Lozenges*					
(i)	Benzocain/Eucalyptus/Menthol	8	5	-	3	-
(ii)	Benzocaine/Cetylpyridinium	1	-	1	-	-
10.	**Skin preparations**					
(a)	*Antiseptics/anti-infective*					
(i)	Compound Benzoic acid powder	3	3	-	-	-
(iv)	Tetracycline	1	1		-	-
(b)	Dermatologicals					
(i)	Clobetasole	2	1	-	-	1
(ii)	Di-iodohydroxy quinoline & Hydrocortisone	4	2	-	2	-
(iii)	Hydroxyquinoline	2	-	-	2	-
11.	**Miscellaneous**					
(c)	*Paracetamol/codeine*					
(i)	Doxylamine and Caffeine	1	-	1	-	-
TOTAL		262	125	91	31	15

However, a number of samples failed because the content was above the allowed limits. These included included atropine sulphate preparation-1, ferrous sulphate products-2, IV fluid -1 (potassium content), benzyl pencillin-2 ampicillin-1, rifampicin-1, and hydrocortisone. The atropine sulphate, which failed also, had a pH outside acceptable limits.

In the dematological group, 1 quinoline cream had a content 10 times the declared value while clobetazole propionate cream had no active ingredient at all; a true counterfeit for a leading brand.

During this period, work on the quality of intravenous fluids (IVs) locally manufactured [5], and tetracyclines [6] were carried out and the finding are already published. The findings are not included in the above table. The Analysis of IVs shows failure rates of about 16% sterility. This increases to 50% in 1 year of storage [5].

The performance of most of the co-trimoxazole has been discusses previously [7].

Drugs on the market still show a significant percentage of poor quality. For those which intended for registration but failed, the manufacturer was advised to review his formulation and/or standard operating procedures.

Others already registered, means they have been vetted and were acceptable. However, it will be wrong to assume these were batch defects. No follow-up of the batches of the same product was evaluated. It is recommended that the regulatory authority institute well structured comprehensive and systematic evaluation of pharmaceuticals on the market whereby all available drugs in a therapeutic/chemical class are evaluated and the element of batch defects investigated. Those found to have consistent quality problem should be withdrawn, registration cancelled and the manufacturer undergo a GMP audit.

ACKNOWLEDGEMENTS

VILR-ABOS, of the Belgium Government for financial support through research grants No. 1579911. Miss Gladys Ngarika for secretarial assistance. Other DARU staff for various inputs.

REFERENCES

[1] C.K. Maitai, W.M.K. Tsekpo, E.Wakori, C.Wangia, L.Mkoji, and I.M. Githiga, E. Afr. Med. J. 59: 399, 1982.

[2] J.O. Ogeto, C.K. Maitai, C. Wangia, M.L. Mkoji, E. Wakori, G.K. Rutere,R.W. Mithamo, A. Ochieng, and I.M.Githiga, E. Afr. Med. J. 60: 438, 1983.

[3] I.O. Kibwage, J.O. Ogeto, C.K. Maitai, G. Rutere, J.K. Thuranira, and. E. Afr. Med. J. 69: 577-580 1992.

[4] K. O. Mang'era, G.K. Rutere, J. K. Thuranira, R. Mithamo, A. Ochieng, S. Vugigi,E. Ogaja, and I.O. Kibwage, Pharm. J. of Kenya. 4(3): 66-69, 1992.

[5] S. Vugigi, I.O. Kibwage, E. Ogaja, K.O. Mang'era, H.K. Chepkwony, A.N. Machine,and J. Kathanzu, Pharm. J. of Kenya. 8(2): 23-25, Dec.1997.

[6] J.W. Muritu, I.O. Kibwage, C.K. Maitai, and J. Hoogmartens, J. Pharm. Biomed. Anal. 12: (1994) 1483-1488.

[7] I.O. Kibwage, C. Ondari I.G. Mureithi, J.K. Thuranira, and J. Hoogmartens, J. East Cent. Afr. J. Pharm. Sci. 1: (1998) 34 - 38.

[8] J.A. Aluoch-Orwa C.O. Ondari, I.O. Kibwage, and J. Hoogmartens, E. Afr. Med. J. 72: (1995) 800-804.

[9] British Pharmacopoeia. Her Majesty's Stationery Office, London ,UK.

[10] United States Pharmacopoeia.23, National Formulary 18. United States Pharmacopoeia

[11] European Pharmacopoeia,. Council of Europe, Strasbourg CEDEX 1.

[12] Pharmacopoeia of India, Controller of Publications. Government of India, Civil Lines, Delhi.