UTILISATION PATTERNS OF INFORMATION SOURCES IN PHARMACY LIBRARY OF UNIVERSITY OF UYO

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ABSTRACT

The study assessed the utilisation patterns of information sources in Pharmacy Library, University of Uyo, Akwa Ibom State. The study population comprised all registered Faculty of Pharmacy Library users (i.e., students and staff of the Faculty) in 2009/2010 academic session. The study involved the use of research question and hypothesis. The number of users and the type of information sources consulted formed the instrument for analysis. The study design was ex-post-facto; it used data collected over a period of one year. Data were analyzed using Pearson Product Moment Correlation. The finding showed significant relationship between utilisation and type of information sources consulted. The analyses also identified the types of information materials that were heavily, moderately and lightly used throughout the one-year period. The study recommends that the stock of heavily-used and moderately-used resources should be increased to multiple copies in order to satisfy user needs.

KEYWORDS: Utilisation patterns, Library use, Pharmacy libraries, Pharmacy information sources and use.

INTRODUCTION

The concept of which information sources meet user needs lends itself to what the researchers describe as the '3As,R&C' of information quality. 3As,R&C translates into Availability, Adequacy (of volumes), Accessibility, Relevance and Currency. Users are interested in information sources that meet their needs in answering specific questions and solving specific problems.

Information sources, according to Olabisi (2002), provide reliable information and form the cornerstone for building the awareness, expertise and practical strategies necessary to solve problems in order to improve the world's health and the physical, technical, mental and scientific development of humanity. Losee (1994) observed that scientists use information not only to solve problems, but also to clear uncertainties.

The most difficult aspect of library service is to provide and organize information sources to enable users make maximum and effective use of resources for present and the future users. Webb (1995) suggested that anyone providing this service must ensure its appropriateness to users' needs and to be ready to adapt promptly as those needs change. This is true in particular for medical practitioners, researchers, students and others in allied fields who frequently need up-to-date information in education programmes, diagnostic procedures and research in various fields of treatment for ailments (Rees, 1993).

In order that resources are maximized and these resources be made available (the first 'A', *availability*), university librarians use book selection policies that cater to the diversities of fields of specialization in the universities. This suggests broad-spectrum acquisition and selection policies, which take care of every discipline in departments and specialty areas in the university. Availability means that the range of available resources has to be in-depth, and the materials and services should not jeopardise the expectation of the patrons and the mother institution. This is necessary and expedient for, as Akusu (1987) observed, information utilisation differs according to areas of specialisation. University libraries and especially pharmacy libraries' collections are organised primarily to meet the needs of pharmacy scholars and to promote and expand the frontier of pharmaceutical knowledge so as to support learning, teaching and research needs. This claim is supported by Mahajan (2009) who found that utilisation patterns are different among users and opined that libraries must understand information seeking behaviours of users so as to re-engineer their services and provide information effectively.

Library collections are developed and organised through procurement, donations, bequests and exchange of the information sources. *Adequacy* (the second 'A') has to do with adequacy of number of volumes. Users could be discouraged from the use of the Pharmacy Library if the resources, though available, are not adequate in number of volumes. Earnest and urgent attention to volumes facilitates effective use of library and pharmaceutical inquiry. Sufficient volumes enhance collection utilisation. The last (the third) 'A' of collection quality for utilisation is *accessibility* which, according to Lancaster (1979), is one of the most important features that determines whether or not a particular information service is used.

The time of the user should not be wasted according to Ranganathan (1988). The 'R' of utilisation quality is concerned with relevance. Information science and relevance align together and underlie the effectiveness of the information communication process. It was Saracevic (1970) who found that there is a formal relationship between the quality of retrieved material and their relevance. Information that is not relevant to the users' needs is as bad as not being available at all.

The last letter of the information utilisation model is 'C', which is currency. As new publications come into circulation in large quantities day by day, and as knowledge expands in every field, books that were published only a few years ago tend to cease to meet current tastes and demands. Where demand has declined for certain books and these are not discarded, the library soon faces the problem of obsolescence, and users will lose interest in such collections. Sometimes some sources, though not very current, may be very useful to users. Some of these items in the collections pose problems during re-organisation and weeding. In this case, user evaluation of used resources becomes paramount. According to Ntecki (1996), it is the user who can tell the worth of books or information sources; the assessment of how well a library succeeds depends on the user as a judge of quality.

Opeke, Osunkunle and Okwilagwe (2002) also affirmed that scientists' (pharmaceutical) need orientation to basic skills in information gathering, information management and information use in order to improve resourcefulness in their information gathering activities. A study by Ajayi (2004) of medical students' library seeking patterns showed that the library was most frequently used for studying and for making photocopies of materials. The respondents relied on textbooks and handouts for current information. Thus the light use of library information resources raises the concern that students are not developing adequate retrieval skills for finding information.

The holdings of an academic library reflect the extent of excellent academic performance in the mother institution. This is one of the reasons Nigerian University Commission (NUC) cannot accredit courses for which the library does not have adequate information sources to support the academic work. Certain characteristics in libraries lend themselves for user utilisation and or non-utilisation. Ajidahun (1990) maintained that users would utilise information if it meets their needs. Udofia (1998) suggested that library stock should bear direct relevance to its tertiary level in all relevant fields and be suitable for research and instructional activities as well as being fit to supplement and complement lectures. Some information sources may be so limited in quantity that users do not find adequate volumes. This is partially due to increase in student enrolments. This was observed by Marriott and Feather (1993) who said that having very few copies in a collection may hinder utilisation due to the problem of non-corresponding enrolments and volume availability. The same observation was made by Tysome (1996) and Sumsion (1997). The library as the heart of the institution has the duty of making information adequately available, relevant, current and accessible to users. Ajayi and Adetayo (2010) noted that the effectiveness of a library as an instrument of learning is determined by the success with which it is able to provide the user with the information he seeks.

The perception of the library in terms of its quality has direct relevance with utilisation. Udoh (2003) found that there is relationship between quality of information sources and utilisation. Besides utilisation of the sources, patterns of use are necessary and are achieved through evaluation of the collection. Udoh (2008) noted that it is the worth of a collection that results in its use and graduates steadily toward user satisfaction. It is such material, those in which the user finds satisfaction, that will be heavily used; and the ones that do not provide satisfaction will be lightly used.

This study concerned itself with the Faculty of Pharmacy Library, University of Uyo where printed pharmacy–related materials are kept. The problem the study sought was to determine utilisation patterns in the Faculty of Pharmacy Library collection, and to determine those areas (classification) of heavily-utilised, moderately-utilised and lightly-utilised material. It sought to assess and analyse the Pharmacy Library collection so as to ex-ray utilisation patterns within the collection. The research question concerned itself with the type of materials which are utilised, and the study hypothesized on whether there is significant relationship between utilisation of

materials and types. This study is very significant, as patterns of used materials are elicited to guide weeding, re-organisation and procurement of information sources by the mother institution.

MATERIALS AND METHODS

The research design of this study was ex-post facto. The researchers preferred this method because the research was based on normal, annual statistical compilation of utilisation in the Library. They explored extensively the annual compilation of statistical data made available through daily use of the Pharmacy Library which opens from 9 am - 4 pm on week days. The head count of registered users was made through the checking of library ticket. The books consulted were recorded by their classification as they were picked from the users' tables for re-shelving. Re-shelving of consulted/used resources is done two times a day: 12 noon - 1 pm and 3.30 - 4 pm.

The information sources in Pharmacy Library range from "general medicine" (R) to "other systems of medicine" (RZ), plus some in the pure sciences and mathematics (Q, QA-QD, QH-QP, QR), "pharmacy/chemical industry" (H-HX) and "environmental sanitation/technology" and "chemical technology (TD & TP), as well as "food sciences" (TX). "General dictionaries" (AG) are also included in the Pharmacy Library's collection.

Main Hypothesis of the Study

The null hypothesis states that there is no significant relationship between utilization and types of materials consulted. In order to test the hypothesis, two variables were identified as follows: types of materials as the independent variable and utilisation of the materials as the dependent variable. Pearson Product Moment Correlation analysis was used to analyse the data in order to determine the relationship between the two variables.

RESULTS

Table 1 shows frequency of one year's (2010) distribution of use by the library users, ranging from *RM* sources (which were used 1388 times), to *AG* general dictionaries, which were consulted 24 times in the same year. The table clearly shows the total number of head count (users) on monthly basis and a total number of five thousand nine hundred and seventeen (5,917) users in the year 2010.

Other data are the types of materials consulted by the users; these were tabulated in order to know the rate of high-demand, moderate-demand and low-demand materials consulted by students and staff. From the above, we observed that materials under Therapeutics and Pharmacology (*RM*) were highly used by one thousand three hundred and eighty-eight (1,388) users for the year 2010, while the least consulted material for the year was General Dictionaries (*AG*), consulted by twenty-four (24) researchers in the same year (Table 2).

Table 3 presents the obtained r-values as 0.574, 0.529, 0.517, 0.896, 0.898, 0.735, 0.815, 0.625, 0.832, 0.964, 0.615, 0.741, 0.789, 0.878, 0.838, 0.459, 0.509, 0.112 and 0.276 for *R, RA, RB, RC, RD-RE, RG, RJ, RK, RL, RM, RS-RZ, H-HX, Q, QA-QD, QH-QP, QR, TD-TP, TX, and AG* respectively.

These values were tested for significance by comparing them with the critical r-value (0.576) at 0.05 level with 10 degree of freedom. The obtained r-values were greater

than the critical r-value for classifications: *RC, RD-RE, RG, RJ, RK, RL, RM, RS-RZ, H-HX, Q, QA-QD, QH-QP.* Hence, the result was significant. However, the obtained r-values for *R, RA, RB,* the library materials and most of the types of material consulted in the Pharmacy Library. In view of the fact that the relationship between utilisation of most material was found significant, the null hypothesis was rejected, while the alternate one was retained.

QR, TD-TP, TX and *AG* were lower than the critical r-value. The result therefore showed significant relationship between utilisation of

These findings were represented in Fig 1, which used bar chart to represent heavily used, moderately used and lightly used information sources.

Table 1: Head Count and Checklist of Books Consulted by Staff and Students, 2009/2010 Session

MONTH	UTIL	R	RA	RB	RC	RD_RE	RG	RJ	RK	RL	RM	RS_RZ	H_HX	Q	QA_QD	QH_QP
	Y	X1	X2	X3	X4	X5	X6	X7	X8	X9	X10	X11	X12	X13	X14	X15
JAN.	760	46	67	46	61	44	3	11	33	65	152	129	3	13	64	88
FEB.	1,159	30	67	45	106	50	64	57	26	136	245	109	66	64	106	79
MARCH	85	5	3	9	20	2	6	4	4	9	38	3	2	5	4	5
APRIL	299	14	15	15	35	14	19	15	18	17	87	28	18	19	15	29
MAY	234	11	9	32	16	15	2	4	1	1	49	56	3	1	40	50
JUNE	584	31	28	60	42	29	12	7	5	14	121	111	6	11	65	63
JULY	543	49	29	69	40	13	9	15	4	8	120	101	3	5	46	67
AUGUST	327	30	11	36	13	5	6	6	2	2	103	90	1	1	34	40
SEPT.	343	26	12	48	6	5	1	0	0	0	116	121	0	0	21	33
OCT.	477	29	18	40	23	14	3	6	2	4	119	135	6	0	7	59
NOV.	582	54	37	51	27	21	18	16	3	7	118	109	0	0	61	68
DEC.	524	36	28	65	38	15	7	10	4	2	120	124	0	3	41	52
TOTAL	5,917	361	324	516	427	227	182	151	102	268	1388	1116	108	122	504	633

Key: UTIL = total utilized; R, RA, RB, etc. = Library of Congress subject classification codes

Table 2: Patterns of Utilization for Heavily-, Moderately- and Lightly-Used Information Sources.

RM Therapeutics Pharmacology Pharmacogenetics Pharmacokinetics	1388

RS-RZ Pharmacy Materia medica Pharmaceutical biochemistry Pharmaceutical calculations Pharmaceutical chemistry Pharmaceutical dosage forms Pharmaceutical economics Pharmaceutical ethics Pharmaceutical laboratory technology Pharmaceutical supplies Pharmaceutical telecommunication Pharmaceutical technology Pharmaceuticals, Delayed action Pharmacists Pharmacy technicians Formularies Pharmacopeias Pharmacognosy Plant drugs Assay Nursing Eclectic medicine Homeopathy Other systems of medicine	1116
QH-QP Biology Botany Human anatomy Comparative histology Physiology Animal Biochemistry Experimental pharmacology	633
RB Pathology	514
QA-QD Mathematics Physics Chemistry	504

RC Internal medicine	427
QR Microbiology Pharmaceutical microbiology	383
R General medicine	361
RA Public aspects of medicine Toxicology Biochemical toxicology Pharmaceutical policy Pharmaceutical services Pharmacies, Hospital	324
RL Dermatology	268
RD-RE Surgery Ophthalmology	227
RG Gynecology Obstetrics	182
TD-TP Environmental technology/sanitation Chemical technology	166
RJ Pediatrics	151
Q General science	122
H-HX Pharmacy & chemical industries	108
RK Dentistry	102
TX Food engineering	79
AG General dictionaries	24

DISCUSSION

The results of the findings showed that RM (1,388 times consulted) and RS-RZ (1,116 times consulted) were very heavily used. Those resources moderately consulted were *R, RA, RC, RD-RE, RL, QA-QD, QH-QP, QR.* Those least consulted or lightly utilized resources were *H-HX, RG, RJ, RK, Q, TD-TP, TX* and *AG.* It should be noted that even though use levels were not significant, they were still utilised by researchers.

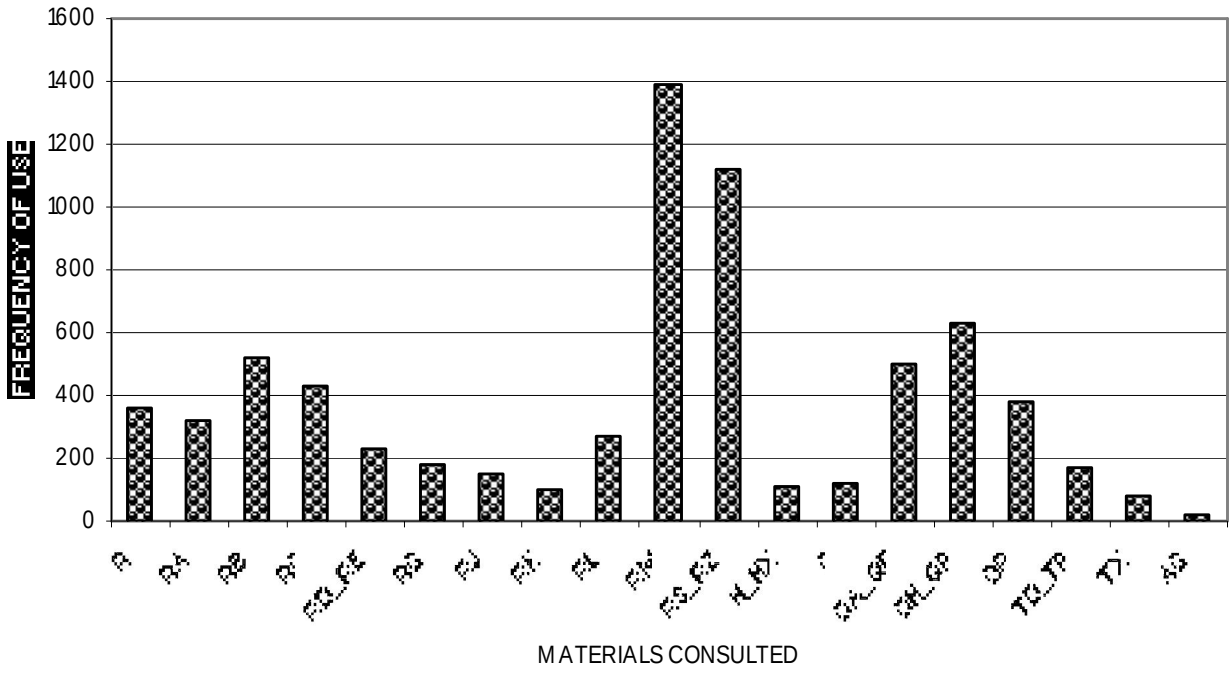

FIG. 1: BAR CHART REPRESENTING HEAVILY USED, MODERATELY USED AND LIGHTLY USED INFORMATION SOURCES

The use of such results is important to library service. If the quantity of heavily-used materials is not increased, there is a tendency for overuse of such material, which results in wear and tear and mutilation of that material. If copies of heavily used materials are inadequate and users have to wait for few copies, this contradicts the third low of Ranganathan, which concerns saving the time of the user. The results also indicate that the lightly-used materials should be retained, as some were found to be significant.

CONCLUSION AND RECOMMENDATIONS The study showed that there is significant relationship between utilisation of pharmacy information resources and types of information sources in the Pharmacy Library, University of Uyo. Some

information sources were heavily, moderately and lightly utilised by the users. Similar results were found by Mahajan (2009) who concluded that libraries must understand information utilization for efficient information delivery. Libraries must understand utilisation levels of their collections so that they can acquire relevant materials that would meet users' needs. It is through this type of data analysis that the true situation of utilization patterns is revealed.

Table 3: Pearson Product Moment Correlation Analysis of the Relationship Between Utilization and Types of Materials Consulted in Pharmacy Library.

Variable		$\sum x$	$\sum x^2$	$\sum xy$	r
		$\sum y$	$\sum y^2$		
Materials R	(χ_1)	722	143670	2340516	0.574^{Δ}
Materials RA	(χ_2)	648	118636	213131	0.529^{Δ}
Materials RB	(χ_3)	1032	292114	3336590	0.517^{Δ}
Materials RC	(χ_4)	854	205438	2810836	0.896*
Materials RD-RE	(χ_5)	454	58312	1496520	0.898*
Materials RG	(χ_6)	332	38274	1189784	0.735*
Materials RJ	(χ_7)	302	27130	1005260	0.815*
Materials RK	(χ_8)	204	12584	675246	0.625*
Materials RL	(χ_9)	533	95249	1819066	0.832*
Materials RM	(χ_{10})	2776	2116678	9050592	0.964*
Materials RS-RZ	(χ_{11})	2232	1368652	7232883	0.615*
Materials H&Hx	(χ_{12})	216	16448	732386	0.741*
Materials Q	(χ_{13})	244	19692	823308	0.789*
Materials QA&QD	(χ_{14})	1008	284578	3309431	0.878*
Materials QH&QP	(χ_{15})	1266	439996	4117237	0.838*
Materials QR	(χ_{16})	766	163550	2484011	0.459^{Δ}
Materials TD&TP	(χ_{17})	332	32578	1089613	0.509^{Δ}
Materials Tx	(χ_{18})	158	8542	515871	0.112^{Δ}
Materials AG	(χ_{19})	48	694	156730	0.276^{Δ}
Utilization (y) 38784464					11834

*Significant at 0.05 level; not significant at 0.05 level; df = 10; N = 12; Critical r-value = 0.576

The researchers conclude by presenting the following recommendations:

stock of heavily-used and moderately-used resources should be increased to multiple copies in order to satisfy user needs; resources not heavily used should be evaluated for currency and relevance to the core courses in the Pharmacy Faculty; basic reference sources, whether used heavily or not, should be retained; other auxiliary libraries and resource centres in the University of Uyo system should evaluate their collections for the '3As,R&C' of information quality, so as to provide effective and efficient collection development and management; orientation to the library resources relevant to the faculty's pharmacy courses should be given to lecturers and students.

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Impact of Rutile mining on water quality in Mogbwemo, Southwestern Sierra Leone

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ABSTRACT

A study to assess the impact of Rutile mining on the quality of surface and well waters in Mogbwemo was conducted. Results showed significant levels ($p<0.05$) of heavy metals (Cd, Cu, Fe, Pb, Ti and Zn) in the water bodies. A four stage sequential extraction procedure according to Tessier protocol applied to sediment of the water bodies for the metals Cu, Fe and Zn revealed about 1% and 15% for the exchangeable and bioavailable fraction respectively of the total metal within the sediment. The bioavailable metal fraction in the sediment correlated strongly to the level of metals present in the water bodies for Fe ($R^2 = 0.66$), but a much weaker correlation for zinc ($R^2 = 0.34$) and no correlation for Cu. It was concluded that pollution in the water bodies of Mogbwemo could possibly have originated from the mining activities of Rutile.

KEYWORDS: Chemical speciation, heavy metals, pollution, sediment

INTRODUCTION

Sierra Leone has a number of useful mineral deposits including iron ore, bauxite, rutile, gold, chromite ilmenite, columbite, kimberlite and cassiterite (Gwynne-Jones *et al*., 1978). Rutile (TiO_2) and ilmenite ($FeTiO_2$) are mined by the Sierra Rutile mining company operating in the Impere Chiefdom, Bonthe District in the Southern province of Sierra Leone. The mining activities have resulted in mine spoil heaps and sand tailings covering very large areas of land that was once organic-rich. Another consequence of the mining operations in the region is the change in the physical properties (e.g. colour, taste etc.) of the fresh water resources reported by inhabitants living in and around the site.

Mogbwemo is a fairly large settlement in the neighbourhood of Sierra Rutile Mines. Residents of Mogbwemo and surrounding communities around the Rutile mines depend on water from nearby streams and wells for various domestic purposes. The presence of significant quantities of toxic metals in these bodies of water may pose a real threat to the survival of the inhabitants of the region both in the short and long term. However, where heavy metal poisoning occurs, the effect cannot be easily detected or diagnosed in the short term. Consequently, local residents will be expected to face long-term metal pollution effects as a result of regular consumption of water in their environment. Although, the level

of metal pollution is important, they do not provide adequate information about their impact on the environment (i.e. their interaction with sediments, bioavailability or toxicity) (Alonso *et al*., 2004). For instance, the bioavailability of a metal and metal toxicity for aquatic organisms is dependant on the physical and chemical form (e.g. the amount of free metal ions and very labile complexes under diverse range of environmental conditions) of the metal (Allen and Hansen, 1996; Mota and Simoes, 1996). In view of this, this study aim to assess the potential impact of the mining activities on the quality of surface and well waters in Mogbwemo.

MATERIALS AND METHODS

Study area and sample collection

Sierra Rutile is located in the south-western province of Sierra Leone. It holds mineral leases over an area of 224 square miles (Lee Peck communication, 1991). This area includes the Gambia, Jagbahun, Nyandehun, Sembehun and Taninahun Boka prospects. The area around the plant site no longer holds mineral deposits for the past five years. It is already mined out and consists of mine spoils, sand tailings and ponds. Water samples for this research were collected from some of the bodies of water in these mined out areas (S1, S2, S3) and from two wells (W1 and W2), all within approximately 1km radius of the plant site where secondary ore processing was carried out. The water bodies S2 and S3 are very large ponds, which are used by local residents for domestic purposes such as laundry as well as cooking and drinking after chlorination. These are provided with hand pumps. Site S1 is a much smaller pond than S2 and S3 and is not used in any way by local residents. S1 is also closest to the central processing plant (~100m) compared to the others. W1 and W2 are deep aquifer wells approximately 10m deep. Approximately 200ml of water samples were collected using a sampling bottle with a wide mouth made of polyethylene material. The bottle was tied to a string carrying a weight and then lowered into the water. Water samples were collected at various depths ranging from ½m to 1m below the surface of each of S1, S2, and S3, and at intervals of about 25m along the length of the pond. The small volumes of samples were then added to obtain representative samples from each water body. In the case of well water W1 and W2, small volumes of ~50ml collected in batches making up to 200ml were collected using a hand pump.

About 500g sediment samples were collected from the banks of each of the sample sites to determine speciation of the metals, pH and conductivity. The soil samples/sediments were dug out from three different levels within 6-12 inches (i.e. surface, ~6inches and ~12inches from six different locations at each site. The three categories of soil/sediments from the banks of each water body were added to form a uniform mixture from which a representative 1g sample was withdrawn for the study of speciation of the metals in the sediments.

Analytical determination

All physico-chemical analysis was carried out according to standard methods (APHA, 1998). For each determination, number of replicate

samples was three. Conductivity and pH of the water samples and solutions of the soil were measured by means of a conductivity meter (JENWAY 4320) model and HACH Sension 1 pH meter respectively after calibration of the instrument.

The following elements: titanium (Ti), cadmium (Cd), copper (Cu), Iron (Fe), zinc (Zn) and lead (Pb) were determined quantitatively using a portable data logging spectrophotometer (HACH DR 2010 model) following qualitative confirmation of their presence in water and soil/sediments samples according to standard methods as outlined in Vogel (1995).

Sequential extraction techniques to assess the types of associations between metals and sediment was carried out using the established Tessier sequential extraction scheme as described in Gumgum and Ozturk (2001). The scheme divides metals into five fractions: exchangeable, carbonate-bounded, Fe /Mn oxides-bounded, organic matter-bounded and residual. The residual fraction was calculated by difference (i.e. total metal concentration – sum of exchangeable, carbonate-bounded, Fe /Mn oxides-bounded and organic matter-bounded fractions).

Statistical analysis

A one-way analysis of variance (ANOVA, $p<0.05$) was performed using Microsoft excel to determine differences between levels of metals in the water samples collected from the various locations . The Spearman rank correlation was used to test the relationships between level of metals in the water samples and sediments.

RESULTS

Level of pollutants

Table 1.0 presents results of physico-chemical parameters of water samples from sites S1, S2, S3, W1 and W2. pH of all water samples investigated were acidic and well below WHO standard of 6.8-6.9 for drinking water as well as the European Union (EU) standard of 6.5-8.5 for surface water (Sowa, 1994). Values of pH for water samples from the various locations were significantly different from each other ($p<0.05$) with S1 been the most acidic. Conductivity values for water samples from the different locations are significantly different from each other ($p<0.05$) with conductivity of S1 a factor of 3 – 12 times more than the conductivity of the others. Conductivity values for water samples from the different locations exceeded the EU limit of 1000 mS^{-1} for surface water used for potable abstraction (Sowa, 1994).

For all metals investigated, there was no significant difference ($p>0.05$) in level between locations. However, there was significant difference ($p<0.05$) in levels between the different metals within a given location. Average levels of Ti, Cd and Fe are 3-4 times higher than Pb, Cu and Zn (Table 1). Highest level of metals was found in S1 as in the case for pH and conductivity.

Table 1.0: Summary of physical and chemical characteristics of waters from the various locations. Values represent Mean± standard error for three replicates.

Parameters	S1	S2	S3	W1	W2
pH	3.52±0.3	5.05±0.2	5.58±0.3	4.55±0.5	4.77±0.4
Conductivity ($\mu S\ cm^{-1}$)	154.6±6.4	19.7±4.8	12.1±0.4	48.5±5.4	27.4±9.7
Ti ($mg\ L^{-1}$)	0.17±0.1	0.18±0.1	0.19±0.1	0.21±0.1	0.14±0.1
Pb($mg\ L^{-1}$)	0.03±0	0.05±0	0.03±0	0.08±0	0.03±0
Zn($mg\ L^{-1}$)	0.035±0	0.036±0	0.035±0	0.038±0	0.036±0
Cd($mg\ L^{-1}$)	2.33±2.0	0.38±0.2	0.32±0.2	0.36±0.3	0.39±0.2
Fe($mg\ L^{-1}$)	0.43±0.2	0.18±0.1	0.15±0.1	0.01±0	0.01±0
Cu($mg\ L^{-1}$)	0.07±0	0.04±0	0.05±0	0.05±0	0.06±0

Table 2a: Result of chemical speciation for site S1

Fractions	Concentration ($mg\ Kg^{-1}$)		
	Fe	Cu	Zn
Exchangeable	2.0±0	48.4±2.4	0
Carbonate-bound	0	56.1±2.8	0
Fe-Mn bound	194.1±9.7	274.0±13.7	88.1±4.6
Organic	210.0±	258.2±12.9	92.0±4.6
Residual	3626.0	2964.0	972.0
Total	4032.3±201.6	3600.1±180	1152,3±57.6

Table 2b: Result of chemical speciation for site S2

Fractions	Concentration ($mg\ Kg^{-1}$)		
	Fe	Cu	Zn
Exchangeable	2.0±0.1	22.0±1.0	62±3.0
Carbonate-bound	4.1±0.1	10.0±0.4	6.0±0.3
Fe-Mn bound	210.1±10.4	366.1±17.3	20.1±0.9
Organic	422.0±21.0	280.2±13.8	28.0±1.4
Residual	9442.0	4218.0	3484.0
Total	10080.1±501.4	4896.0±244.8	3600.0±179.0

Table 2c: Result of chemical speciation for site S3

Fractions	Concentration ($mg\ Kg^{-1}$)

	Fe	Cu	Zn
Exchangeable	10.1±0.5	38.1±1.9	24.0±1.1
Carbonate-bound	4.0±0.2	2.0±0	0
Fe-Mn bound	390.2±18.7	338.1±16.7	0
Organic	366.2±18.1	210.0±10.4	28.3±1.4
Residual	6862.0	4572.0	5468.0
Total	7632.1±387.2	5160.0±257.9	5520.3±267.3

Table 2d: Result of chemical speciation for site W1

Fractions	Concentration (mg Kg^{-1})		
	Fe	Cu	Zn
Exchangeable	126.1±6.5	46.0±2.3	0
Carbonate-bound	10.0±0.4	2.0±0	4.0±0.1
Fe-Mn bound	522.0±26.1	612.2±30.5	416.2±21.0
Organic	262.1±13.2	234.1±11.7	128.0±6.4
Residual	7000.0	3906.0	4012.0
Total	7920±397.0	4800.0±192.0	4560.0±228.0

Table 2e: Result of chemical speciation for site W2

Fractions	Concentration (mg Kg^{-1})		
	Fe	Cu	Zn
Exchangeable	20.0±1.0	252.0±12.6	28.0±1.4
Carbonate-bound	26.0±1.3	12.0±0.7	6.0±0.3
Fe-Mn bound	410.0±20.5	726±36.3	8.0±0.4
Organic	228.0±11.4	160.0±8.0	400.0±20.0
Residual	4356.0	4130.0	4358.0
Total	5040.0±252.0	5280.0±264.0	4800.0±240.0

Values in tables 2a-2e represent Mean± standard error for three replicates with the exception of the residual fraction which was obtained by difference.

Chemical speciation study

Results of chemical speciation of metals in sediments at the banks of the water bodies are

presented (Tables 2a-e). In almost all the sites, the availability of the three metals decreases in the order: Fe>Cu>Zn, except for S3 where the order is Fe>Zn>Cu.

The bioavailable fraction of Fe, Cu and Zn in all locations was low, averaging 15% of the total metal adsorbed to the sediment (Figure 1.0). Of the bioavailable fraction, the exchangeable and carbonate fractions constitute the lowest percentage (Figure 2) averaging 5 and 1% for Fe, 6 and 2% for Cu and 9 and 1% for Zn for exchangeable and carbonate fractions respectively. For virtually all the sites, the Fe-Mn fraction contains the highest level of the bioavailable fraction.

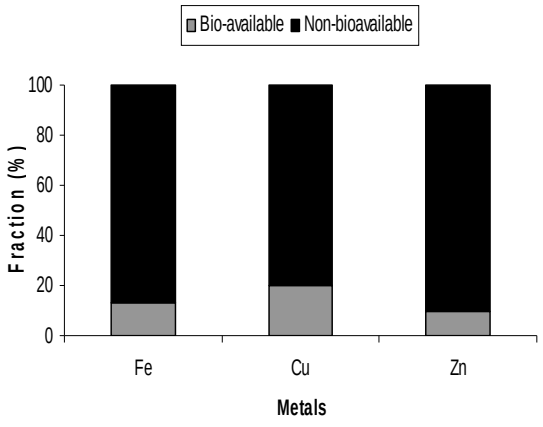

Figure 1.0: Comparison of total bioavailable and non-bioavailable fractions of metals in sediments of water bodies.

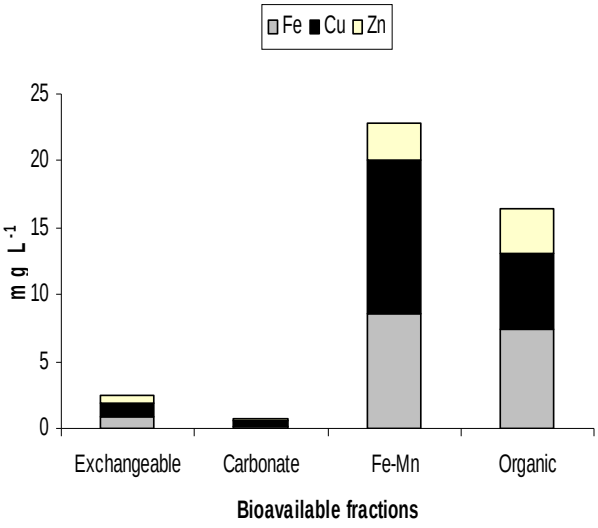

Figure 2: Levels of bioavailable fractions in sediments

DISCUSSION

All water samples investigated were acidic and well below WHO standard of 6.8-6.9 for drinking water as well as the European Union standard of 6.5-8.5 for surface water (Sowa, 1994). This indicates that waters from sites S2 and S3 which are used by the local community for domestic purposes including drinking may have severe health implications on local residents.

Conductivity show similar trend to pH, with S1 the most acidic and having highest conductivity value. The significantly high conductivity for S1 ($p<0.05$) may be attributed to the close proximity to the plant site which is about 100m compared to S2 and S3 which are several hundreds of metres away. At the plant site, stockpiles of gangues from processing operations can be found exposed to air, water and heat which may have easily leached into

S1. In comparison, conductivity values obtained in this study exceeded polluted waters of streams and estuarine water in the neighbourhood of the Kingtom dumpsite in Freetown, Sierra Leone (Barry, 2003) indicating that all water sources are polluted.

Generally, the concentrations of metals obtained in this study are either higher or comparable to reported means of surface waters or rivers in Sierra Leone and elsewhere. The results of Cu obtained in this study (0.04-0.07 mg L^{-1}) is higher than 0.0083 mg L^{-1} for Cu but lower (0.035-0.038 mg L^{-1}) than 0.06 mg L^{-1} for Zn reported by Barry (2003) for streams of the Kingtom dumpsite in Freetown, Western area of Sierra Leone. Okonkwo and Mothiba (2004) reported a much lower concentrations in the range of 1.6-9.3μg L^{-1} for Cd, 2.0-3.0 μg L^{-1} for Cu, 10.5-20.1 μg L^{-1} for Pb and 2.1-2.5μg L^{-1} for Zn in the rivers of Thohandou, South Africa. The relatively high concentrations of metals found in the surface waters of the study area possibly reflect the mining activity as is usually the case for water bodies within the vicinity of mining regions (Nordstrom *et al*., 2000).

For all metals investigated, there was no significant difference ($p>0.05$) in level between locations. However, there was significant difference ($p<0.05$) in levels between the different metals within a given location.The average levels of Ti, Cd and Fe are 3-4 times higher than Pb, Cu and Zn (Table 1). Highest level of metals was found in S1 as in the case for pH and conductivity. In almost all the sites, the availability of the three metals decreases in the order: Fe>Cu>Zn, except for S3 where the order is Fe>Zn>Cu.

The result of bioavailable fraction of metals revealed that Fe, Cu and Zn in all locations was low, averaging 15% of the total metal adsorbed to the sediment (Figure 1.0). Low levels of bioavailable fraction compared to the non-bioavailable (non –labile) fraction of metals in sediments are consistent with literature (Hu, 2002; Abu-Kutaki, 2001), although elsewhere, a much higher level of bioavailable fractions (e.g. 48% Cu, 53% Co and 25% Ni) has been reported (Luo *et al*., 2008). Of the bioavailable fraction, the exchangeable and carbonate fractions constitute the lowest percentage averaging 5 and 1% for Fe, 6 and 2% for Cu and 9 and 1% for Zn for exchangeable and carbonate fractions respectively. Comparable low levels of exchangeable fractions from speciation studies have also been reported (Luo *et al*., 2008). In general, exchangeable and carbonate bound metals can easily be released to the surrounding waters as a result of a change in the ionic composition of the water or a decrease in pH (Sobczyński and Siepak, 2001). Hence, in this study, the low pH of the water bodies and sediments could have resulted in remobilization of the carbonate fraction of the metals. Furthermore, the exchangeable fraction is easily available for leeching into the aquatic environment because the metals are weakly adsorbed via weak electrostatic attraction (Abu-Kutaki, 2001). For virtually all the sites, the Fe-Mn fraction contains the highest level of the bioavailable fraction. This may be due to the fact that metals usually have strong

affinities for iron-manganese oxyhydroxides (Elder, 1988). Despite the relatively low bioavailable fraction (15%) compared to the non-bioavailable fraction (85%) in the present study, the concentration of metals in the bioavailable fraction available to the aquatic systems exceeds the toxicity limit of these metals on algae (Florence *et al*., 1992) implying that the levels of metals present in the water bodies potentially pose a health risk to the local residents in the region.

There was a relatively strong correlation between the level of bioavailable metal found in the sediments to the level of metal present in the water bodies for Fe (R^2 = 0.66 for Fe) but a much weaker correlation for zinc (R^2 = 0.34). No correlation exists for Cu. Similarly, there was also a relatively strong correlation for Fe between the exchangeable fraction in sediment and that present in the water bodies (R^2 = 0.69). Correlation for Cu was however weak (R^2 = 0. 19) whilst no correlation exist for Zn.

CONCLUSIONS

The mining activities carried out in Mogbwemo and its environs by the Sierra Rutile Mining Company have resulted in many streams, dams and lakes to emerge. The quality of water bodies in the surrounding areas has been affected as evident by the low pH, high conductivity and significant levels (ANOVA, $p<0.05$) of heavy metals in the water bodies compared to unpolluted waters. The chemical speciation studies revealed about 1% and 15% for exchangeable and bioavailable fraction respectively of the total metal within the sediment of the water bodies. The Spearman rank correlation revealed a strong correlation between the level of bioavailable metals found in the sediments to the level of metals present in the water bodies for Fe (R^2 = 0.66), a much weaker correlation for zinc (R^2 = 0.34) and no correlation for Cu. The results show that pollutants from the mining activities may possibly have been the primary source of these metals in the water bodies. As this water source is used by local residence of the Mogbwemo community, the findings of this study is of environmental and health significance.

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Evaluation of Antioxidant Activity And Chemical Analysis Of The Leaf Of *Telfairia occidentalis*

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ABSTRACT

The methanol extract of *Telfairia occidentalis* leaf and n-hexane, ethyl acetate, butanol fractions were evaluated for their free radical scavenging activity, with DPPH assay. n-hexane fraction had the highest activity exhibiting an IC_{50} of 78.50µg/ml, comparable to that of the commercial antioxidant BHT. Chromatographic analysis showed the presence of three components in n-hexane fraction ($2H_1$, $2H_3$ and $2H_4$) with Rf values of 0.86, 0.71 and 0.55, respectively. Two components were seperated in ethyl acetate fraction ($2E_1$ and $2E_5$) with Rf values of 0.85 and 0.25, respectively, while the three components of butanol fraction ($2B_1$, $2B_2$, and $2B_3$) have Rf values of 0.90, 0.88 and 0.83 respectively. In addition, total phenolic content of *T. occidentialis* was determined as catechin equivalents. The n-hexane fraction which had the highest DPPH free radical scavenging activity also had the highest total flavonoid contents. The high flavonoid content was responsible for the antioxidant and free radical scavenging activities of *Telfairia occidentalis* leaf.

KEY WORDS: Antioxidants, DPPH, free radical scavenging activity, flavoniods.

INTRODUCTION

Reactive oxygen species (ROS), including free radicals are reported to cause damage of biological system, and to be involved in aging and in the pathogenesis of some diseases such as arthritis, atherosclerosis, diabetes and cancer (Ames, 1983; Feher et al., 1987; Aruoma, 1998). Almost all organisms possess antioxidants and repair systems that evolved to protect them against oxidative damage, these systems are insufficient to prevent them entirely. However, antioxidants may be used to help human body to reduce oxidative damage (Yang et al., 2002). Plants contain different natural products, which have a remarkable role in the traditional medicine in different countries. Nowadays the prevention of many diseases has been associated with the ingestion of different plants rich in natural antioxidants (Johnson, 2001; Virgilli et al., 2001; Adedapo et al., 2008). In recent years, there has been a particular interest in the antioxidant and health benefit of phytochemicals in food and vegetables. This was as a result of their potential effects on human health (Wei and Shiow, 2001). Many researchers especially in the filed of medical science have observed free radical scavenging ability and antioxidant property in *Telfairia*

occidentalis (Oboh and Akindahunsi, 2004; Oboh et al., 2007; Iweala and obidina, 2009, Kayode et al., 2009, kayode et al., 2010). The hypoglyceamic properties of the plant have also been reported (Aderibigbe et al., 1999; Eseyin et al., 2000; Eseyin et al., 2005; Eseyin et al, 2007; Eseyin et al., 2010).

The antioxidant effect is mainly due to compents, such as flavoniods. Antioxidants can interfere with the oxidation process by reacting with free radicals, chelating catalytic metals, acting as oxygen scavengers (Shahidi and Wanasundara, 1992) and preventing lipid auto-oxidation (Brand-Williams et al., 1995; Bondet et al., 1997). Research work had justified the use of the leaf of *Telfairia occidentialis* in Nigeria in the treatment of certain disease in which the participation of reactive oxygen species (ROS) have been implicated. This could be as a result of an antioxidant and free radical scavenging ability (Kayode and Kayode, 2011). Much have been reported on the various medicinal properties of the leaf extract of *Telfairia occidentalis* but little or no report have been published on the active pharmacological constituents isolated from this very important plant. In this research work, attempt were made to isolate some constituents using column and thin layer chromatographic methods.

MATERIALS AND METHODS

Collection of plant materials Plant material

Telfairia occidentalis leaf used for this work was obtained from a local market in Uyo, Akwa Ibom State, Nigeria in March, 2010 and authenticated by Dr. Mrs. Margaret Bassey, a taxonomist in Botany Department, University of Uyo, Uyo, Akwa Ibom State, Nigeria. The leaves were cleaned and dried in the shade, then powered to 40 mesh and stored in an airtight container at 25^{o}c.

Extraction and isolation of the chemical constituents

Air dried powered leaf of *Telfairia occidentalis* (731g) was exhaustively extracted with a total volume of 2.5L of methanol in a soxhlet apparatus using continuous extraction. Evaporation and concentration of the solvent afforded the methanol extract (198.3g). This was further extracted successively with a total volume of 2.5L of the following solvent: n-hexane, ethyl acetate and butanol. Evaporation and concentration of the solvents afforded the n-hexane fraction (HF,93.89g), ethyl acetate fraction (EF, 22.43g) and butanol fraction (BF, 13.23g). ***Phytochemical test was carried out on the crude extract and the fractions.***

The fractions were fractionated on Silica gel (absorbent) (60-120µg mesh) as follows:

n-hexane fraction: Silica gel (148.3g) was used to fractionate 1.0gm of the HF using n-hexane, chloroform, methanol and water as solvent in that order.

Ethyl acetate fraction: Silica gel (93.6g) was used to separate 2.0g of the EAF using benzene, chloroform, ethyl acetate, methanol and water as solvent in that order.

Butanol fraction: Silica gel (114.2g) was used to separate 2.7g of the BF using benzene, ethyl acetate, methanol and water as solvent in that order.

New solvents were introduced gradually in these ratios 80:20; 50:50; 20:80 to prevent cracking. In each chromatographic analysis, 15ml was collected in each test tube and the solvent allowed to evaporate at room temperature. Thin layer (TLC)

chromatographic analysis was carried out on these eluents and the Rf of each eluent was determined. Eluent with identical Rf values were pooled together to obtain the following pooled fractions:

HF: $2H_1$, $2H_3$, $2H_4$ with Rf values 0.86, 0.71 and 0.55, respectively.

EAF: $2E_1$ and $2E_5$ with Rf values 0.85 and 0.25, respectively.

BF, $2B_1$, $2B_2$ and $2B_3$ with Rf values 0.90, 0.88 and 0.83, respectively. The TLC plates of these fractions were sprayed with the following colour reagents:

Conc. sulphuric acid: A light yellow or pale orange colouration confirmed the presence of steroids.

Ferric chloride: A blue colouration confirmed the presence of tannins.

Dragendorff's solution: A reddish-brown colouration confirmed the presence of alkaloids.

Determination of Total Phenolic Content (TPC) of Extract and Fractions

Total phenolics was quantified and expressed as gallic acid equivalent according to a method proposed by Singleton and Rossi (1999). 1ml of Folin-Ciocalteu's reagent, previously diluted (1:20), was added to 1ml of samples (250µg/ml) and mixed thoroughly. To the mixture, 4ml of sodium carbonate (75g/L) and 10ml of distilled water were added and mixed well. The mixture was allowed to stand for 2hr at room temperature. Contents were then centrifuged at 2000g for 5min and the absorbance of the supernatant was taken at 760nm. A standard curve was obtained using various concentrations of gallic acid. Results were expressed as percentage of Gallic Acid Equivalents (GAE) per 100gram of fresh mass.

Determination of Total Flavonoids Contents (TFC) of extract and Fractions

Total flavoniod contents was measured by aluminum chloride colourimetric assay based on the method modified by Marinova, Ribarova and Atanasova (2005). To 0.1ml of extracts in a 10ml volumetric flask, distilled water was added to make the volume to 5ml and 0.3ml 5% $NaNO_3$ was added to this. 3ml of 10% $AlCl_3$ was then added 5minutes later. After 6 minutes, 2ml of 1M NaOH was added and the absorbance measured at 510nm. Cathecol was used as a standard.

DPPH free radical scavenging assay

Free radical scavenging activities was determined using the DPPH free radical method. Various concentrations of the samples were added to 3ml of daily-prepared methanol DPPH solution (0.1nm). The mixture was shaken and left to stand at room temperature in the dark. After 30min, absorbance was measured at 517nm against a blank (containing all reagents except the test samples). Assays were carried out in triplicates. The concentrations of the samples that gave 50% inhibition of DPPH (IC_{50}) were obtained from the graph of 1% (inhibition percentage) versus concentration of the sample in µg/ml. The percentage inhibition of DPPH (1%) was calculated using the equation.

$1\% = (A_{blank} - A_{sample}/A_{blank}) \times 100$

Where A_{blank} is the absorbance of the blank solution

A_{sample} is the absorbance of the test sample.

RESULTS AND DISCUSSION

Results of Phytochemical Analysis of Crude Extract and n-Hexane, Ethyl acetate, Butanol Fractions and Chromatography analysis for steroids, tannins and alkaloids are shown in tables 1 and 2. While the results of total Phenolic Content (TPC) and Total Flavonoid Content (TFC), and DPPH free radical scavenging activity (IC50) for methanol extract and fractions are shown in tables 3 and 4

.

Table 1: Results of Phytochemical analysis of ME, HF, EAF and BF

S/N	Phytochemical test	Crude extract	n-hexane fraction	Ethyl acetate fraction	Butanol fraction
1	Tannin Test with Fe_2Cl_3	Present	Present	Present	Present
2	Saponnin test	Present	Present	Present	Present
3	Alkaloid	Present	Present	Present	Present
4	Test for Steriods Salkowski Test Lieberman-Burchard test	 Present Present	 Present Present	 Present Terpenes Present	 Present Present
5	Flavonoids	Present	Present	Present	Present
6	Glycoside	Present	Present	Present	Present

DISCUSSION

Currently, there is an increasing demand to evaluate the antioxidant properties from plants (Pratt, 1992). In this research work, the methanolic crude extract, fractions and separated constituents were analysed for their antioxidant activity and the phytochemical(s) responsible for this effect. Researchers have observed free radical scavenging ability and antioxidant property in *Telfairia occidentialis (*Oboh and Akindahunsi, 2004; Oboh et al., 2006; Iweala and Obida, 2009; Kayode et al., 2010).

The results of free radical scavenging activity of *Telfairia occidentalis* are shown in table 5. The crude methanolic extract presented a significant free radical scavenging activity, with an IC_{50} of 31.25µg/ml. Comparison of the obtained IC_{50} data (table 5) indicated a potent activity for the HF (IC_{50} = 78.50µg/ml) and a moderate free radical scavenging effect for EAF (IC_{50}=86.30µg/ml) and BF (IC_{50}= 142.40µg/ml). The fractions were purified by column and thin layer chromatography on silica gel to afford the constituents. N-hexane fraction gave three components $2H_1$, $2H_3$ and $2H_4$ with IC_{50} value of 32.5 µg/ml, 70.40 µg/ml and 100.50 µg/ml respectively. Ethyl acetate fraction gave two components $2E_1$ and $2E_5$ with IC_{50} value of 36.50µg/ml and 82.20µg/ml respectively. Butanol fraction gave three components $2B_1$, $2B_2$ and $2B_3$. The DPPH free radical scavenging activity of the constituents from BF were very low.

Table 2: Chromatography analysis for steroids, tannins and alkaloids

Isolated Compounds	Conc. H_2SO_4 (Steroid)	Fe_2Cl_2 (Tannins)	Dragendorff's soln (Alkaloids)
$2H_1$	Present	Present	Present
$2H_3$	Present	Present	Present
$2H_4$	Present	Present	Present
$2E_1$	Present	Present	Present
$2E_5$	Present	Present	Present
$2B_1$	Absent	Present	Absent
$2B_2$	Present	Absent	Present
$2B_3$	Present	Absent	Present
$2B_5$	Present	Present	Present

Table 3: Total Phenolic Content (TPC) and Total Flavonoid Content (TFC) of Extracts and Fractions

Samples	MF	HF	EAF	BF	$2H_1$	$2H_3$	$2H_4$	$2E_1$	$2E_5$	$2B_1$	$2B_2$	$2B_3$
TPC (%)	0.0950	0.0700	0.0720	0.0600	0.0132	0.0124	0.090	0.0720	0.0540	0.0190	0.0740	0.0520
TFC (%)	0.0175	0.0195	0.0135	0.0165	0.0195	0.0110	0.0060	0.0030	0.0015	Very low conc.		

Table 4: DPPH free radical scavenging activity (IC_{50}) for methanol extract and fractions.

Sample	IC50 (μg/ml) (95% confidence limit)
Methanol extract (ME)	31.25(29.50-33.86)
n-Hexane fraction (HF)	78.50(74.59-82.41)
Ethyl acetate fraction (EAF)	86.30(81.93-90.62)
Butanol fraction (BF)	142.40(135.28-149.52)
$2H_1$	32.50(30.87-34.13)
$2H_3$	70.40(66.88-73.92)
$2H_4$	100.50(95.47-105.53)
$2E_1$	82.20(78.09-86.31)
$2E_5$	36.50(34.67-38.33)

The result of total flavonoid content (TFC) is shown in Table 4. The crude methanolic extract had a high TFC (0.0175%). In the fractions: HF had a high TFC (0.019%) followed by BF (0.016%) and EAF (0.013%). In the separated constituents of HF, $2H_1$ had the highest TFC (0.019%) followed by $2H_3$ (0.011%) and $2H_4$ (0.006%). In EAF, $2E_1$ was higher (0.003%) than $2E_5$ (0.0015). Constituents from BF had very low TFC.

The result of total phenolic content (TPC) (table 3) indicated higest TPC in EAF (0.072%)

followed by HF (0.07%) and BF (0.060%). In the separated constituents of HF the TPC was $2H_4$ had the highest (0.090%) then $2H_1$ (0.013%) and $2H_3$ (0.012%). In EAF, $2E_1$ had a higher TPC (0.072%) than $2E_5$ (0.0540%). In BF, $2B_2$ had the highest TPC (0.074%) followed by $2B_3$ (0.052%) and $2B_1$ (0.019%).

Several studies have demonstrated that plants are natural antioxidant sources due mainly to the presence of flavonoids, which act by reducing free radicals (Wilson, 1988; Miller 1996; Pietta, 2000; Geber et al., 2002; Matteo and Esposito, 2003; Behera et al., 2006). The n-hexane fraction (HF) indicated a high DPPH free radical scavenging activity which was contributed by component $2H_1$. The TPC was highest in HF and in the separated constituent $2H_1$. Comparing the BF, though the TPC was high in the separated constituents, it had little or no DPPH free radical activity which inferres that TPC had no effect on the DPPH free radical scavenging activity. It can therefore be inferred from the work that flavonoid contents of the leaves of *Telfairia occidentalis* was responsible for its DPPH free radical scavenging activity.

Researchers have justified the use of the leaf of *Telfairia occidentalis* in Nigeria in the treatment of certain diseases like diabetes, cholesterolaemia, liver problems etc in which the participation of reactive oxygen species have been implicated. This could be as a result of the antioxidant and free radical scavenging ability (Kayode and Kayode, 2011) which might have been attributable to the high flavonoid content of *Telfairia occidentalis* leaf.

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Effects of artemether on the pharmacokinetic parameters of quinine in wistar rats.

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ABSTRACT

The effect of artemether on the pharmacokinetic parameters of Quinine(QN) was carried out in this study. The parameters were investigated using adult Wistar rats. The rats were divided into three groups; A, B and C. Group A served as the control which was administered intramuscularly (i.m) 0.9w/v normal saline while group B was administered QN and artemether (i.m) at a dose of 5.14mg/kgbody weight(b..w). and (0.5mg/kgb.w respectively while Group C was administered QN alone (i.m) at a dose of 5.14mg/kgb.w .Blood samples were collected from each group of animals at 30 min. interval for 8 hr after the injection. The investigation was based on a one-compartment model with first order absorption. Using HPLC method with a limit of detection of 0.5µg/mL, the plasma concentration of quinine was monitored and quantified. The area under the blood concentration –time curve (AUC_∞) of QN was not significantly different ($P \geq 0.05$) when compared QN alone with QN in the presence of artemether being 124 µg/mlhr and 136 µg/mlhr for groups B and C, respectively. The half life ($t_{1/2}$) and T_{max} of QN in the groups B and C were the same being 8hr and 2hr respectively for both while Cmax showed a significant difference ($P \leq 0.05$) being 54.63µg/ml and 90.55µg/ml in the presence and absence of QN, respectively. This work justifies the fact that these drugs can be concomitantly administered since pharmacokinetic parameters like Tmax and the (AUC_∞) of quinine were not significantly affected by artemether.

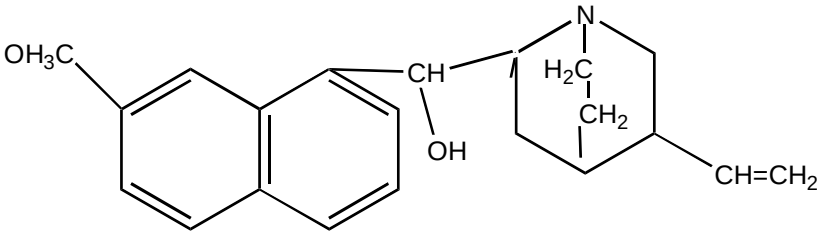
KEYWORDS: Quinine, Artemether, pharmacokinetic parameters.

INTRODUCTION

Artemether and quinine are antimalaria drugs used in the treatment of malaria infections in the tropical countries of the world. Malaria is one of the tropical diseases that is associated with both human and economic loss. Malaria is reported to cause the death of children in Africa, killing nearly one million children each year. Every day approximately 3,000 children die from the disease. According to the Centers for Disease Control and Prevention (CDCP), malaria is also known to be the 5th cause of death from infectious diseases worldwide (after respiratory infections, HIV/AIDS, diarrhea diseases, and tuberculosis). Malaria is the 2nd leading cause of death from infectious diseases in Africa, after HIV/AIDS. (Schild, 1980) Monotherapy was formerly being used for the treatment of malaria but the incidence of resistant strain of Plasmodium species has

led to the introduction of combination therapy

Quinine(QN) is an alkaloid isolated from Cinchona bark in 1820 (Ajibola, 2000). It contains a quinoline and a quinolidine group joined by a secondary alcohol group Fig.1.



Fig, 1. Quinine

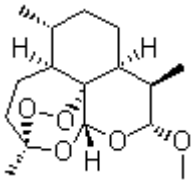


Fig 2. Artemether

QN is laevo-rotatory, but its isomer quinidine is dextro-rotatory. The laevo-rotatory isomer is more efficacious as an antimalaria agent compared to its dextro-rotatory isomer (Schild, 1980; Ajibola, 1998). Artemisinin (qinghaosu) and its derivatives are antimalaria drugs derived from a Chinese plant. Artemisinin derivatives are an important new class of anti-malaria agents. These compounds contain endoperoxide bridges, which are essential for anti-malaria activity (William, 1998 Meshnick, 2002). Artemisinin acts via a two-step mechanism. It is first activated by intraparasitic heme-iron, which catalyzes the cleavage of the endoperoxide . A resulting free radical intermediate may then kill the parasite by alkylating and poisoning one or more essential malaria protein(s) (Meshnick, 2002).

Chemical modifications of Artemisinin (reduction plus etherification) have enabled more potent and more soluble derivatives to be developed. Among these different products is Artemether (Paluther®) (fig. 2), the methyl ether form of dihydroartemisinin ((Luo *et al.*, 1984).

QN is the mainstay for the treatment of multi-drug resistant malaria and in severe malaria in many countries. It is still effective despite reports of reduced sensitivity (Pukrittayakamee *et al.*,1994). The World Health Organization (WHO) has recognized the use of Artemisinin Combination Therapies in the treatment of malaria, as a long-term measure to control spread of the disease under its Roll Back Malaria program (WHO, 2003).

The incidence of resistance to single dosage regimen in malaria treatment has led to combination therapy which has drastically reduced the incidence of resistance. The combinational therapy has led to synergistic

actions of some drugs or in some other cases has led to exacerbations of effects of drugs or reduction in activity. The systemic bioavailability of drugs is an essential process that precedes any pharmacological activity (Rang *et al*, 2003). The objective data of the use of drugs i.e. the relationship between plasma concentration and the intensity of therapeutic/ toxic action , plasma half lives , relative efficacy of different medications etc. are being obtained with the aim of optimizing therapy (Tripathi , 2001). The purpose of this study was to ascertain whether artemether has an effect on pharmacokinetic parameters of quinine in Wistar rats .

MATERIAL AND METHODS

Fifteen adult Wistar rats, weighing between 200-270g were obtained from the animal house of the Department of Veterinary Physiology , University of Ibadan. The rats were kept in standard cages and acclimatized for a period of seven days in the animal house of the Faculty of Pharmacy, Olabisi Onabanjo University , Ogun State , Nigeria . Principles of laboratory animal care" (NIH publication No. 86-23, revised 1985) were duly followed throughout the experimental procedure. The experimental guideline was in conformity with the Faculty of Pharmacy, Olabisi Onabanjo University rules guiding the use of rats for scientific studies. The rats were kept five per cage and fed daily with standard rat diet produced by Bendel's Feed Limited, purchased from Ijokun, Sagamu, Ogun State, Nigeria. All rats were allowed water *ad libitum*. The drugs Artemether (80mg/ml) i.e. 80 mg Artemether preserved in 1ml of 125 x 4mm) column as stationary phase and 0.05% v/v triethylamine in acetonitrile Arachis oil (vehicle) (May and Baker Ltd, Nigeria), QN (600mg/2ml) (Medreich) and normal saline (0.9% w/v) (Unique Ltd, Nigeria) were purchased from Adun-Ade Pharmacy Limited, Sagamu, Ogun State, Nigeria. A 70kg human takes a maximum dose of 160mg Artemether i daily for three days in the treatment regimen for m,alaria while maximum dose of 1800mg per day of QN is given .. Therefore, extrapolating from human doses each adult wistar rat received corresponding doses of 0.5mg/kg/b.w. of Artemether and 5.14mg/kg/b.w. of QN administered intramuscularly. Rats in control Group A received 5.14ml/kg/bodyweight of normal saline. Group B was administered 0.5mg/kg/b.w. of Artemether and 5.14mg/kg/b.w. of QN while Group C was administered 5.14mg/kg/b.w. of QN alone. The tail of each rat was cut at the tip with a sterile scissors and blood was collected at 0 and at 30mins interval for 8 hours into heparinised tubes. The blood samples were then centrifuged within 24 hr at 3000g for 10 mins to obtain plasma

.The plasma was analysed for QN by adapting the method of quinine extraction from biological fluids described by (Babalola, *et al*., 2004). QN was extracted from plasma (1 ml) by addition of 200 µl of perchloric acid to precipitate plasma proteins, followed by addition of 1 ml of 5 M NaOH and 4 ml of diethyl ether for solvent extraction. After mixing using a vortex mixer, the organic layer was aspirated and back extracted into 0.05 M H_2SO_4 . The extracted drug was then chromatographed by HPLC (Buchi Lab. Switzerland) utilizing hypersil BDS C18 (5µm, buffered with Potassium hydrogen phosphate (KH_2PO_4) as the mobile phase.

RESULTS

Pharmacokinetic Analysis.

The mean plasma concentration versus time profiles of QN in the various blood samples after the HPLC analysis are as shown in the graph (fig.3). Each point showing the mean of the plasma concentrations and standard deviation (SD) in Wistar rats at each collection time for each group.

These pharmacokinetic parameters like peak plasma concentration (C_{max}), the time of peak plasma concentration (T_{max}) and the area under the blood concentration time curve (AUC) were calculated from the individual plasma concentrations time curve of the two groups. Half life ($T_{1/2}$) was calculated by using the elimination rate constant (k_e) ($T_{1/2} = 0.693/k_e$) and k_e was determined from the slope of the terminal portion of the log concentration time curve . The area under the curve up to last data point (AUC_t) was calculated by trapezoidal rule method and the area from last data point up to infinity(AUC_∞) was calculated by dividing terminal time drug concentration by k_e. .(Nicholas, 1993) as shown in table 1. The other parameters were calculated using appropriate pharmacokinetic equations. (Ajibola, 2000).

Pharmacokinetic Parameters

Data Analysis: Data are expressed as Mean ± SD. Student's't' test with 95% confidence level was used for statistical analysis of the results.

DISCUSSION

This work seeks to determine the effect of artemether on the pharmacokinetic parameter of QN. The investigation was based on a one-compartment model with first order of absorption (Na-Bangchan, *et al*, 2000). Following i.m administration of artemether, the concentration of QN in the plasma after HPLC analysis differed from those administered with QN alone after 1hr, 1hr 30mins, 2hrs and 8 hrs intervals which were 58.53, 85.34, 90.55, 9.84ng/ml ± SD. respectively. The group A animals were administered 0.9w/v of concentration 90.55ng/ml ± 7 for QN in the absence of artemether in comparison with 54.63ng/ml ± 4 of QN in the presence of artemether. The area under the curve (AUC) depicts the bioavailability of the drug in the systemic circulation and as obtained from concentration versus profile fig. 3, AUC of the two groups vary slightly. The AUC of QN was 136.3 ng/mlhr ± 6 while that of QN in the presence of artemether was 124.8 ng/mlhr ± 11 . The AUC of QN was reduced by 8.4%. in the presence of artemether and this is in agreement with the work of Oliver Burk *et al,* (2005). Artemether has a comparatively high recrudescence rate which has been attributed to the auto induction of CYP2B6- mediated metabolism (Oliver Burk *et al,* 2005). Artemether induces cytochrome P-450 and MDRI expression by activation of Xenosensors Pregnane X receptor and constitive Androstane Receptor which mediate induction of drug metabolizing enzymes and drug transporters (Bertam, 2001, Martin *et al* 2005).

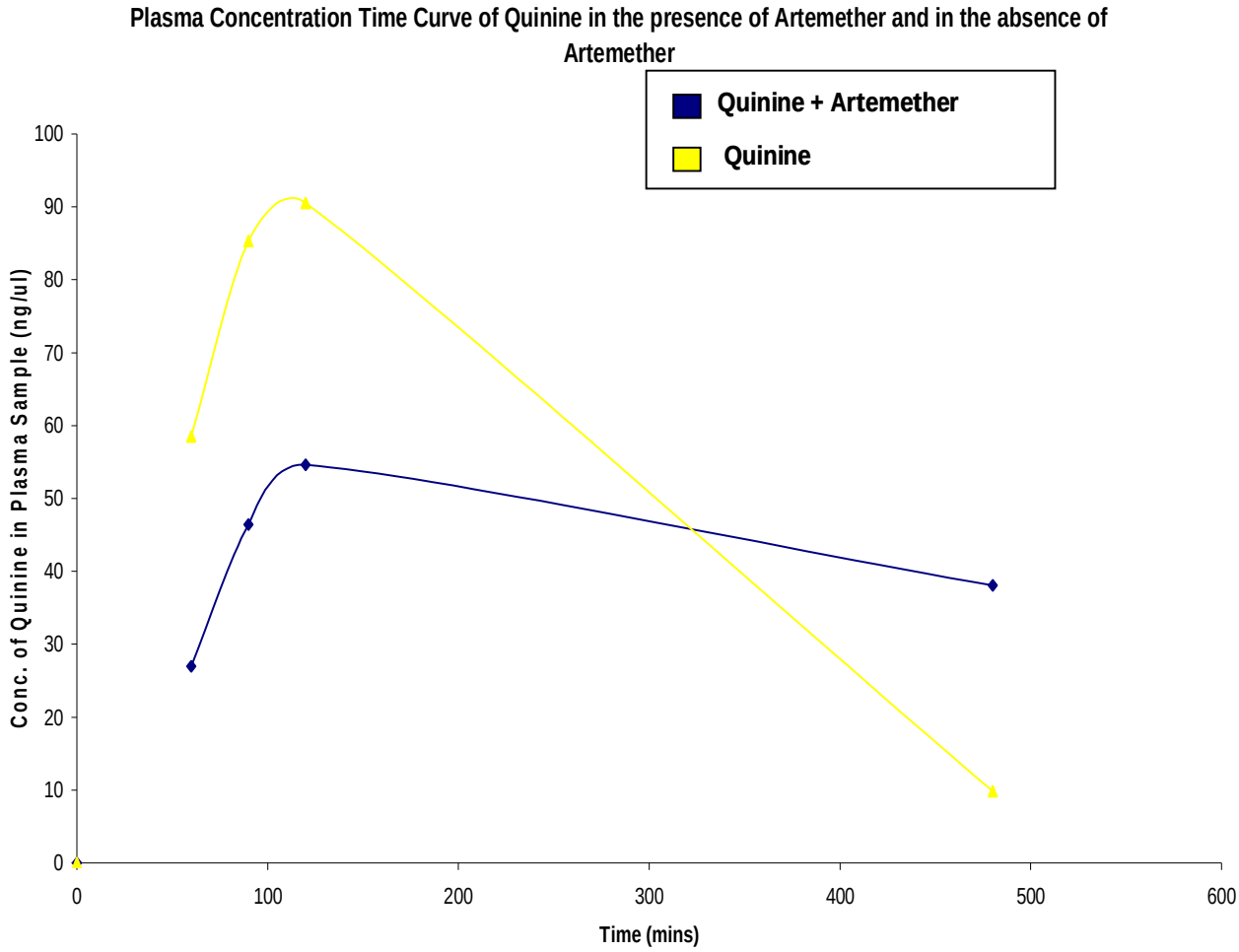


Fig. 3. The mean plasma concentration versus time profiles of QN in the various blood samples of the presence and absence of Artemether. Each point showing the mean of the plasma concentrations and standard deviation (SD)

TABLE 1. Pharmacokinetic parameters obtained from plasma concentration time curve of Quinine plus Artemether and Quinine alone.

Parameters	Quinine plus Artemether	Quinine alone
C_{max} (ng/ml)	54.63µg/ml ± 4.0	90.55µg/ml ±7.0
T_{max} (minutes)	120mins ± 8.0	120mins ± 8.0
$T_{1/2}$ (minutes)	8hrs ± 0.5	8hrs ± 0.5
$AUC_{0-\infty}$ (ng/ml/hr)	124.8 µg/mlhr ± 11.0	136.3 µg/mlhr ± 6.0
K_a	0.3465 hr^{-1}	0.3465 hr^{-1}
K_e	0.085662hr^{-1}	0.085662hr^{-1}
V_d	0.0902L	0.00014L
C_l	4.0x10^2ml/hr	3.7 x10^2ml/hr

The induction of these enzymes increases metabolism of quinine which leads to reduction in the bioavailability of QN in the blood. (Oliver Burk *et al,* 2005). However from the calculations as obtained in the graph fig.3, the peak plasma concentrations (Cmax) were significantly different (P≥0.05) but the lower plasma levels obtained from the two groups are not lower than the therapeutic window for QN, which assures therapeutic efficacy *(Babalola et al, 2004) The* plasma peak concentrations after administration of QN alone and with artemether were 54.63ng/ml and 90.55ng/ml respectively and this is in conformity with the work of Na-Bangchan, *et al*,(2000) and Babalola *et al,*(2004).

The absence of QN in the sample collected at 30minutes interval might be due to minute quantity of QN in the blood sample collected from the animals which was practicably difficult to analyze after centrifugation by HPLC.

CONCLUSION

This work justifies the fact that these drugs can be concomitantly administered since pharmacokinetic parameters like T_{max} and the AUC of quinine were not significantly affected by artemether. Artemether reduces the concentrations of quinine in the blood but this invariably helps in reducing the side effects of quinine significantly. The use of combinations involving artemether and quinine analogues or derivatives is well appreciated and of significance benefit if the therapeutic effects is enhanced or remain the same.

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Cytological And Toxicological Properties Of A Medicinal Mushroom

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ABSTRACT

The cytological and toxicological potentials of an extract of a medicinal mushroom, *Daldinia concentrica,* were evaluated using the *Allium cepa* model. The extract induced macroscopic and microscopic changes causing a concentration-dependent root growth inhibition and chromosomal aberrations in *A. cepa*. Compared to the control, treatment with the extract resulted in significant ($p<0.05$) inhibition of root growth with EC_{50} value of 1%. The onion root cells showed reduced mitotic indices with corresponding increase in concentration of the mushroom extract. The presence of chromosomal aberrations such as fragments, breaks, bridges and sticky chromosomes in significant ($p<0.05$) amounts indicates a high rate of genotoxicity in the mushroom extracts. No chromosomal aberration was observed in the control. These observations call for caution in the indiscriminate consumption of *Daldinia concentria*. Low concentrations and wide spacing of dosage is suggested for the intake of the medicinal mushroom.

KEY WORDS: *Daldinia concentrica*, *Allium cepa*, chromosome aberration, cytotoxicity, medicinal mushroom, genotoxicity

INTRODUCTION

The use of some mushrooms for curing ailments cuts across different geographical domains. Reports on the tradomedical use of some mushrooms in Nigeria and elsewhere is well documented (Oso 1975, 1977, Stamets 2002, Akpaja *et al.* 2003, 2005, Olila *et al.* 2006, Idu *et al.* 2006, 2009).

It is now generally accepted that scientific studies have in recent times begun to confirm what many indigenous societies have known for ages and with this empirical confirmation come the concomitant broadening of the spectrum of the medicinal applications these mushrooms can be used for. According to Stamets (2002), medicinal mushrooms have extraordinarily low toxicity on humans probably because fungi share a more recent common ancestry with animals than with plants, protozoans and bacteria. Fungal medicines are therefore active against many diseases that afflict humans.

The earliest reports on the indigenous use of the mushroom *Daldinia concentric* in Nigeria appears to be that of Akpaja *et al.* (2003, 2005) on the ethnomycology and usage of the mushroom among the Igbo and Bini-speaking people of Southern Nigeria respectively. Subsequent reports on the *in vitro* antimicrobial activity of the mushroom against some human pathogens have been documented (Gbolagade *et al.* 2006). The antimicrobial activity of the mushroom

suggests that the mushroom has active principles that can impair normal cellular division and this impairment may eventually translate into the inability of the target organism(s) to reproduce.

Despite the discovery of about twenty new metabolites including aromatic steroids cytochalasins (Buchanan *et al.*, 1996), daldinones (Qung *et al.,* 2002) from the mushroom, cytological investigations into its effects on pathogenic organism is yet to be deciphered. This is important, more so, as the mushroom has been confirmed to have a novel anti-HIV agent benzofuranlactone named concentricolide (Qin *et al*., 2006). In the light of the anticipated widespread medicinal use of this mushroom, it has become necessary to investigate the effect of the mushroom in a living system to validate its safe usage.

The *Allium cepa* plant assay has undoubtedly proved to be extremely useful and reliable for the evaluation of cytotoxic and anti-mitotic activity of various compounds in aqueous extracts of medical plants (Akinboro and Bakare, 2007, Oloyede *et al*., 2009). The *Allium* test produces similar results to other test systems such as eukaryotes and prokaryotes (Fiskesjö, 1988). In this study, we seek to evaluate the toxicity of aqueous extracts of *Daldinia concentrica* on cell division and chromosomes in a eukaryotic organism like *A. cepa* (onion) with the hope that the results would provide useful information on the genetic safety assessment of the herbal mushroom.

MATERIALS AND METHODS

Plant and preparation of decoction of mushroom

The medicinal mushroom, *Daldinia concentrica*, was collected in December 2009 from some dead logs of wood within the Ugbowo campus of the University of Benin, Benin City situated between latitudes 6^o 06' N, 6^o 30' N and longitudes 5^o 30' E, 5^o 45' E. The decoction was prepared as described by Dede *et al.* (2006). 10g of the mushroom was ground to powder and soaked in 100ml of ambient water in a beaker followed by another 500ml of warm water thereafter for 1h. The extract obtained was filtered with muslin cloth.

Allium cepa Test

Procurement and preparation of onion bulbs

Onion bulbs *(Allium cepa* L., 2n=16*)* bulbs of the purple variety of average size (15-22 mm diameter) were purchased from Lagos Street in Ring Road, Benin City. They were sun-dried for two weeks and those that were not dried, or attacked by fungi, or had started shooting were all discarded at the beginning of the experiment. The outer scales were carefully removed, without tampering with the primordial root ring.

Macroscopic evaluation

For the root growth inhibition evaluation, the *Daldinia concentrica* extract was diluted to obtain 10%, 5%, 2.5% and 1.25%. To account for a number of bulbs in the population that would be naturally slow or poor growing, the bases of seven equally sized bulbs were suspended on the extract samples inside 100 ml beakers and kept in the dark for 72 h (Rank and Nielsen, 1998). Test extracts were changed daily. The negative control was set up with tap water of good quality only (Fiskesjö, 1985). At the end of the exposure period, the lengths of at least 20 best growing roots of roots from each of 5 onion bulbs at each concentration were measured (in cm) with a metre rule. From the

weighted averages for each concentration and the control, the percentage root growth inhibition in relation to the negative control was determined:

$$Over\ all\ mean\ root\ length\ of\ test\ solution = \frac{Total\ length\ of\ roots}{Total\ number\ of\ roots}$$

$$\%\ root\ growth\ of\ control = \frac{Overall\ mean\ root\ length\ of\ test\ solution}{Overall\ mean\ root\ length\ of\ control} \times 100$$

The EC_{50} (the effective concentration at which 50% root growth of control was inhibited) was also calculated by plotting a graph of percentage root growth of control against sample concentrations. The effect of each sample on the morphology of growing roots was also examined.

Microscopic Evaluation

For the evaluation of induction of chromosomal aberration, the onion bulbs were grown on 5%, 1%, 0.1%, 0.01% extract concentrations (v/v) and the control for 48 h at the end of which root tips from these bulbs were cut and fixed in ethanol: glacial acetic acid (3:1, v/v) inside universal bottles and stored at 4°C for 24 h before use. The already fixed root tips were hydrolyzed in 1N HCl at 60°C for 5 min after which they were washed several times with distilled water. Two root tips were squashed on each slide, stained with aceto-orcein for 10 min. Excess stains were removed, and the cover slips carefully lowered on to exclude air bubble. The edges of the cover slips were sealed on the slides with clear fingernail polish as suggested by Grant (1982). Six slides were prepared for each concentration and the control out of which five (at 1000 cells per slide) were analyzed at ×1000 magnification for induction of chromosomal aberration using Nikon Eclipse (E400) light microscope. The mitotic index (MI) and frequency of chromosomal aberrations (CA) were calculated as in previous studies (Olorunfemi *et al*. 2011).

$$Mitotic\ index = \frac{Number\ of\ dividing\ cells}{Total\ number\ of\ cells} \times 100$$

$$\%\ Aberrant\ cells = \frac{Number\ of\ Aberrations}{Total\ number\ of\ cells} \times 100$$

Statistical Analysis

The SPSS 10.0 statistical package was used for this analysis. The means, with 95% confidence limits and the standard errors for each of the quantitative sets of data were calculated. Differences between the control and the individual dosage group of each extract were analyzed by means of the Students' *t*-test of significance at the $P < 0.05$ level.

RESULTS

Table 1 shows the results of the effects of the extract of *Daldinia concentrica* on root growth of *Allium cepa*. Good root growth was achieved in the control. At tested concentrations, root growth was highest at the 1.25% concentration of all the extracts and least at 10%. Inhibition of root growth was concentration dependent and statistically significant ($P < 0.05$) at tested concentrations. The EC_{50} for the decoction of *Daldinia concentrica* was 1% (Fig. 1).

Table 1: Effects of *Daldinia concentrica* extract of on root growth of *Allium cepa*.

Concentration (%)	Mean root length (cm) ±S.E*	Root Growth (%) of control
Control	4.9 ± 0.17	-
1.25	2.0 ± 0.22	40.8
2.5	0.8± 0.09	16.3
5	0.4 ± 0.11	10.2
10	0.2 ± 0.03	4.1

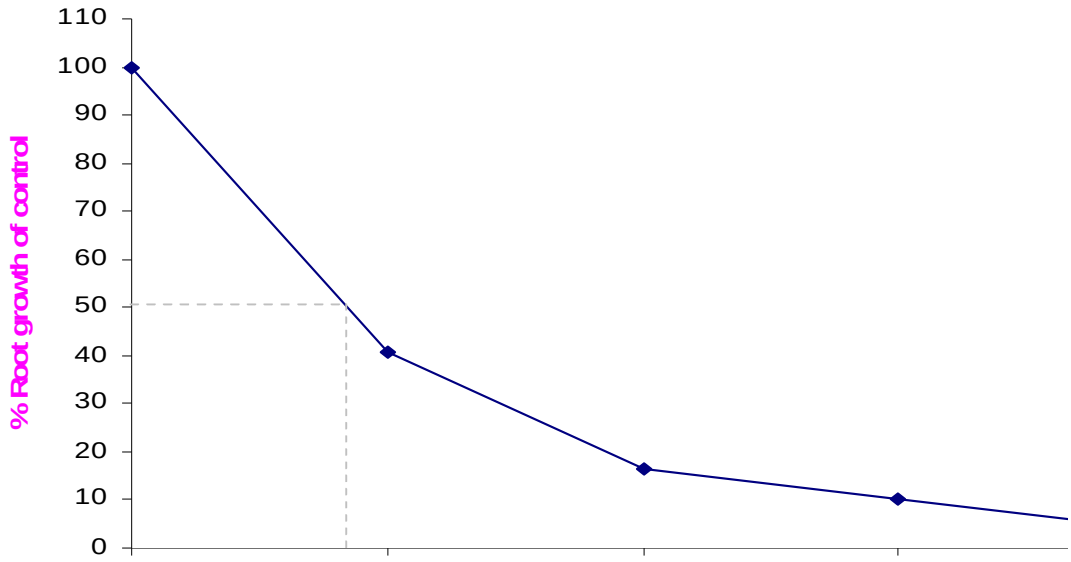


Fig. 1: Growth inhibition curve of Allium cepa roots grown in the mushroom extract

The effect of *Daldinia concentrica* extract on cell division and chromosome behaviour of *Allium cepa* are presented in Table 2. Mitosis was observed to be normal in the cells of the control and had a mitotic index (MI) value of 46. With increasing concentration of the extracts however, there was concentration-dependent decrease in the mitotic index. There were no dividing cells at the 10% concentration of the extracts. The frequency of these aberrations was, however, not concentration dependent. The incidence of aberrant cells was observed to be lowest (4%) in cells of roots treated with 5% of mushroom extract and highest (38%) in cells of roots treated with 0.01% of the extract.

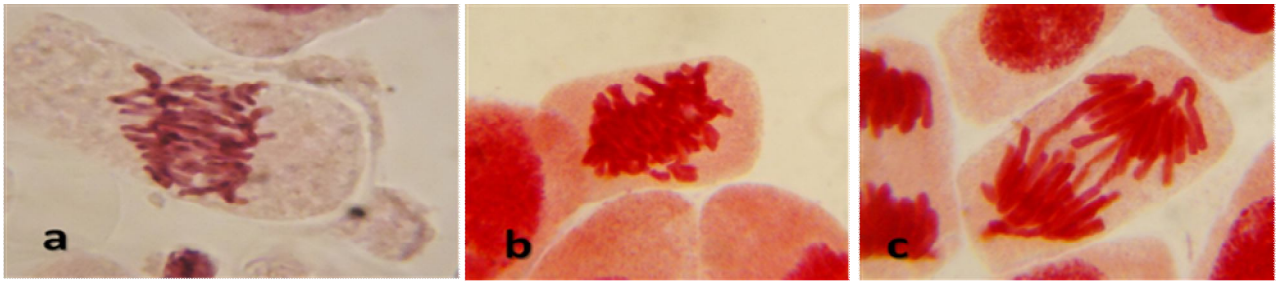
Table 2: Mitotic activities of the root cells of A. cepa treated with Daldinia concentrica extract

Extract concentration (%)	No of dividing cells	Mitotic index	% Aberrant cells	Mitotic inhibition
Control	229	46	-	-
0.01	192	38	0.06	17.39
0.1	146	29	0.12	36.96
1	106	21	0.14	54.35
5	20	4	0.16	91.30

* 5000 cells/per concentration of each extract and the control.

The statistical analyses of the different concentrations of the mushroom extracts showed significant ($p<0.05$) between the treatments and the different values of mitotic indices and chromosomal aberration percentages.

The types of chromosomal aberrations induced in the mushroom extract is presented in Plate 1. The chromosomal aberrations induced by extract at various concentrations were spindle disturbance, fragments, breaks, bridges and sticky chromosomes.



DISCUSSION

The potential cytotoxic and genotoxic effects of aqueous extracts of *Daldinia concentrica* on *Allium cepa* were evaluated. Studies have shown that in *Allium cepa*, (Fiskesjo, 1997, Babatunde and Bakare, 2006, Akinboro and Bakare, 2007) whenever there is root growth inhibition (macroscopic parameter), there is always reduction in the number of dividing cells (microscopic parameter). Results of our study are in agreement with this assertion. The inhibition of root growth in *A. cepa* is in consonance index varied from 46 in control and to 4 in 5% extract. The decreased mitotic index values in the treated onion roots is an indication of the with the assertion of Nielsen and Rank (1994) that the sigmoid curve is a typical dose response for toxic substances whose negative effects is an indication of the cytotoxic effects of the mushroom extract. This observation is consistent with earlier report on the mushroom *Ganoderma lucidum* (Curtis) P. Karst, (Olorunfemi *et al.* 2011).

The mitodepressive ability of the mushroom extract (the ability to block the synthesis of DNA and nucleus proteins) is demonstrated by the reduction in the number of dividing cells at tested concentrations. The mitotic presence of cytotoxic substances in the *D. concentrica* extract, which caused inhibition of mitotic activities, while the observation of

aberrant cells in the treated onion root tip meristems indicates genotoxic effects (Akinboro and Bakare, 2007) of the mushroom extract. The chromosomal aberrations induced by the extract at various concentrations were spindle disturbance, fragments, breaks, bridges and sticky chromosomes which arise from changes in structure of the chromosomal material. Chromosome bridges and fragments are clastogenic effects, both resulting from chromosomal and chromatid breaks (Kovalchuk *et al*. 1998) while stickiness reflects high toxicity of a substance as well as irreversibility of the change (Turkoglu, 2007). Acentric fragments in anaphase is the result of chromosome or chromatids interruptions indicating interference with DNA while bridges probably occur by the interruption and joining chromosomes or chromatids or as a result of chromosome stickiness, or it may be ascribed to unequal translocation or inversion of chromosome segments (Turkoglu, 2007, Gömürgen, 2005).

The presence of alkaloids in the extracts of *Borreria filiformis* and *Vinca rosea (*Ene and Osuala, 1990) and *Azadirachta indica*, *Morinda lucida*, *Cymbopogon citratus*, *Mangifera indica* and *Carica papaya* (Akinboro and Bakare, 2007) have been reported to induce chromosomal aberrations. The spindle disturbances detected in this study might have been due to the presence of alkaloids in the tested extract. As opined by Akinboro and Bakare, (2007), the presence of chemicals with turbagenic potentials may be responsible for the complete arrest of cell division at high concentration of the mushroom extract. These observations may explain the ability of the mushroom extract action as an antimicrobial agent as reported by Gbolagade (2007). Although the present study has not been able to ascertain the actual ingredients responsible for the observed chromosomal aberrations; they are however obviously consumed as part of the diet in the mushroom.

The results suggest that *Daldinia concentrica* extract possess mitodepressive effects on the growth of the meristematic root cells, as well as cell division property of *A. cepa.* The widespread tradomedical use of this mushroom by many cultures in Nigeria (Akpaja, 2003, Idu *et al.,* 2007, Osemwegie *et al.,* 2005) needs to be properly studied. Moreso, increase in the cytotoxicity and genotoxicity as the concentration increase suggests that there is need to succinctly determine the dose at which it would be effective and at the same time, safe. Regulation backed by education and research is needed to improve the quality and quality use of traditional Chinese medicine (Li *et al*. 2003). This assertion also holds true for the Nigerian traditional medicine. While the traditional use of this medicinal mushroom cannot be stopped, it may be possible to conduct studies into the precautionary measures that can be observed in the use of the mushroom for treating the many health problems it is known for having answers to. In conclusion, the results call for caution in the indiscriminate consumption of *Daldinia concentrica*. Low concentrations and wide spacing of dosage is suggested for the intake of the medicinal mushroom.

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Antibacterial Effect of Methanolic Extract of the Root of *Aspilia africana*

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ABSTRACT

The leaf of Aspilia Africana (Pers) C.D. Adams (Asteraceae) is widely used in ethno medicinal practices in Tropical Africa because of its ability to stop bleeding and promote rapid healing of wounds. It is also used in the management of problems related to cardiovascular diseases, lumbago, venereal diseases and parasitic infections. This study was carried out on the root part (which has not been very well exploited in ethno medicinal practices) to determine if it is as potent as the leaf part. The methanolic extract of the root was subjected to preliminary phytochemical screening and it has indicated the presence of saponins, tannins cardiac glycosides, flavonoids, terpenoids and carbohydrates. Acute toxicity test showed that it has LD_{50} of 707.11mg/kg in mice. The in-vitro antibacterial test using agar well diffusion method showed activity against known wound pathogens such as Staphylococcus auerus (clinical isolate), Staphylococcus aureus (ATCC 25922), Staphylococcus aureus (NCTC 8853), Bacillus substiles, Escherichia coli (ATCC 25922), Escherichia coli (NCTC 10418) and Pseudomonas aeruginosa (ATCC 25922). This indicates that the methanolic extract of the root has potentials for use as antibacterial agent in wound care.

KEYWORDS: *Aspilia africana* ; antibacterial; wound pathogens

INTRODUCTION

Aspilia africana is widely used in ethno – medicinal practices in West Tropical and East Africa as a general healing agent, pain killer, sedative, abortifcient, echolic, lactation stimulant and most importantly as a haemostatic agent because of its ability to stop bleeding even from a severed artery. It is also reputed to be used to promote rapid healing of wounds and in the treatment of malaria and eye problems (Dalziel et al., 1960). *Aspilia africana* commonly known as wild sunflower and as hemorrhage plant because of its haemostatic properties is an herb or weed that is grown on land and fallows and widely distributed across tropical Africa. In Nigeria it is grazed by cattle and sheep and is much used in western Nigeria as food for rabbit and hares (Burkill, 1985). The plant belongs to the family Asteraceae. It can grow up to 2 metres in height and is densely cuspid with hairy stem and of perennial woody root stock. The leaves are crowded into capitular heads surrounded by a ring of small green leaves with brilliant yellow star shaped petals. (Akubue, 1983). *Aspilia africana* is known by the Ibibios and Efiks as edemedong, Ibos as orangila, Yorubas as yunyun and Hausa as toozalin- yan- maata. *Aspilia africana* is one of the plants that exhibit a wide range of biological activities including antiviral, fungicide and antibacterial activities (Okwuonu et al., 2008). This work was designed to explore the antibacterial and

antifungal activities of the root part using the extract from methanol.

MATERIALS AND METHODS

Plant Collection and Extraction

Aspilia africana was obtained from Ikot Ntuen village, along Oko Ita – Use Ikot Amama road in Ibiono Ibom Local Government Area of Akwa Ibom State, Nigeria, in November 2010. It was identified and properly authenticated at Department of Pharmacognosy and Drug Development, Faculty of Pharmacy, University of Uyo. The air dried plant material consisting of the root part only was powdered and extracted with methanol by maceration for 72 hours at room temperature. The methanolic extract was concentrated to obtain a reddish brown residue code named 'MER'

Preliminary Phytochemical Screening

The preliminary phytochemical screening was carried out on MER using the methods of chemical analysis reported by Trease and Evans (2009), Harbourne (1984) and Sofowora (1993).

Toxicity Test (LD_{50})

The toxicity test (LD_{50}) was carried out using Lorke's method (Lorke, 1983).

In-vitro antibacterial and antifungal studies using agar well diffusion method

The strains of the micro-organisms used for the tests were obtained from the Pharmaceutical Microbiology laboratory of the Faculty of Pharmacy, University of Uyo. The test organisms were characterized and identified using the methods described by Bradshaw (1986). The organisms were cultivated overnight in a nutrient broth and sabouraud dextrose broth and sustained on agar slants at 4 ^{0}C before use. 0.20ml of this overnight broth culture of each organism was dispensed into 20ml of sterile nutrient broth for bacterial organisms and 20ml of sabouraud dextrose broth for fungal organisms and incubated for 4 hours to standardize the culture to 10^6 cfu/ml. (Lovian, 1980)

Preparation of the Extract

Lower and higher concentrations of MER were prepared. For the lower concentrations, 1.0g of MER was dissolved in 10ml of 99% methanol to obtain a concentration of 100mg/ml for the stock. Two fold dilutions were carried out on the stock to get 50mg/ml, 25mg/ml, and 12.5mg/ml concentrations. For the higher concentrations, 5g of MER was dissolved in 10ml of 99% methanol to obtain a stock of 500mg/ml; appropriate dilutions were made to obtain 400mg/ml, 300mg/ml and 200mg/ml concentrations.

Preparation of Muller Hinton Agar

38g of Muller Hinton Agar was suspended in 1000ml of distilled water and boiled to dissolve. This was sterilized by autoclaving at 121^{0}C for 15 minutes.

Preparation of Plates

0.2ml of the 10^6 cfu/ml concentration of the test micro-organism was introduced into the plates (petri dishes) followed by the sterile Muller Hinton Agar and swirled to mix. The mixture was allowed to solidify in the petri dish on bench. 4.0mm sterile cork borer was used to bore five holes aseptically - four holes at the periphery for the different concentrations of MER and labeled appropriately. One hole was made in the centre for the control. Lastly the different concentrations of MER were transferred into

the labeled holes. Methanol (99%) was used as control. The plates were allowed 30 minutes for diffusion and incubated at 37^0C for 24 hours. Microbial sensitivity was determined in triplicate. After the incubation the diameter of inhibition zone was measured horizontally and vertically for each zone and the mean determined.

RESULTS AND DISCUSSION

The phytochemical screening of MER showed high presence of saponins and tannins while other typical plant chemicals namely cardiac glycosides, flavonoids and carbohydrates (reducing sugars) were moderately present. Terpenoids were observed to be faintly present while alkaloids, phlobatannins and anthraquinones were not detected. (Table 1)

Acute Toxicity and lethality (LD_{50}) on MER in mice gave i.p. LD_{50} of 707.11mg/kg weight. (Table 2)

The result in table 3 shows that MER possesses different degrees of antibacterial activity against some wound pathogens like all strains of *Staphylococcus aureus*, *Pseudomonas aeruginosa* (ATCC 25922) *and Escherichia coli*. It also has activity against *Bacillus substiles* which is also known to cause skin diseases (Trease and Evans, 2009).

The extent of the activity of MER against micro-organisms seems to be directly related to the type and concentration of the bioactive substances present. These bioactive substances are usually responsible for the pharmacological activities of medicinal plants. El Tantaway et al., (1999) have reported of the presence of α-pinene, a terpenoid in the leaves of *A. africana* known to possess anti-inflammatory activity which might have contributed to the wound healing action of the leaves by suppressing inflammatory reactions invoked by injured tissues. Besides, many other workers have reported the presence of alkaloids, saponins, tannins, cardiac glycosides, terpenoids and carbohydrates in the leaf part of the plant (Okoli et al., 2007; Eweka and Eweka, 2009 and Anibijuwon et al., 2010). But our investigations have shown that these secondary metabolites were present in reduced quantities in MER. The presence of saponins and tannins in the leaves is reported to be partly responsible for the haemostatic activity of the leaves in arresting bleeding from damaged or injured vessels by precipitating proteins to form vascular plugs (Okoli et al., 2007). In particular, tannins which are astringent, help to hasten healing of wounds and inflamed mucous membrane, (Okwu and Josiah, 2007), by binding to the proteins of the exposed tissues and precipitating the proteins to form a mild antiseptic protective coat under which regeneration of new tissue takes place leading to rapid healing of wounds (Okoli et al., 2007).

Preliminary phytochemical screening of the root extract revealed that saponins and tannins are also present in high concentrations in the root part of the plant; therefore the root extract may be expected to have some haemostatic effect as the leaves. We also note that an important antimicrobial secondary metabolite – alkaloid is lacking in the root extract while it is significantly present in the leaves. This may be the cause of the differences in the doses that elicit activity between the leaves and the roots. The concentrations of the root extracts lower than 100mg/ml could not give any antibacterial sensitivity, but doses of the leaf extract as low

as 12.5mg/ml recorded significant antimicrobial inhibitions (Adeniyi, 2000).

Flavonoids which are usually implicated as super antioxidants that provide protection against oxidative cell damage, allergies, virus ulcers and inflammations (Saleh et al., 1995; Del-Rio et al., 1997) have also been detected in the root extract. The evaluation of the potentials of MER as an antimicrobial agent which promotes rapid healing of wounds showed that this activity may be very strong against bacteria only, indicating that MER is basically antibacterial.

The effect of the extract on *Pseudomonas aeruginosa* and *Bacillus substiles* is also significant. *Pseudomonas aeruginosa* is known to have a secondary effect on wounds and skin burns by expanding the affected areas (Oyewale et al., 2004). *Bacillus substiles* are also implicated in skin infections; thus the activity of the extract against this organism justifies the use of this plant to treat skin infections in traditional folk medicine. The activities of *Shigella dysenteriae* (clinical isolate), *Salmonella typhii* (NCTC 8571), *Candida albicans* I and II were not inhibited by MER indicating that it is basically not effective against fungi.

Failure of the extract to show antibacterial activity at the lower concentrations cannot be used to conclude that the extract has no activity against the organisms; neither can it be concluded that the plant part does not contain bioactive substances that can exert antibacterial activity because the potency of the extract depends on the method

Table 1: Result of Phytochemical Screening of Methanolic Extract of Roots of Aspilia africana

Phytochemical constituents	Roots of *Aspilia africana*
Alkaloids	_
Anthraquinones	_
Carbohydrates (reducing sugar)	++
Cardiac glycosides	+++
Digitalis Glycosides	++
Flavonoids	++
Phlobatannins	_
Saponins	+++
Tannins	+++
Terpenoids	+

Key: - = absent; + = faintly present;
++ = moderately present; +++ = highly present.

Table 2: Result of Acute Toxicity and Lethality (LD_{50}) Test of Methanolic Extract of Root of A. africana

Concentration of the extract (mg/kg)	No of death per group of the mice
5000	3/3
4000	3/3
3000	3/3
1000	3/3
500	0/3

$LD_{50} = \sqrt{(D_0 \times D_{100})} = \sqrt{(500 \times 1000)} = 707.11 mg/kg$

(D_0 = dose at 0% death; D_{100} = dose at 100% death)

used to obtain the extract (Anibijuwon et al., 2010). It has also been established that the age of the plant when harvested and the season in which the plant is harvested affect the amount of the bioactive ingredients of the plants as these active ingredients vary in quality and quantity from season to season (Sofowora, 1982).

Table 3: Result of Anti Microbial Activity of the crude Methanolic Extract of the Root of A. africana

	MER				Control	MER				Control
Conc. in mg/ml / Test organisms	12.5	25.0	50.0	100.0	99% MeOH	200	300	400	500	99% MeOH
	zones of inhibition in millimetres					zones of inhibition in millimetres				
Staphylococcus auerus(clinical isolate)	–	–	–	–	–	26.33±0.43*	26.67±0.50*	27.33±0.57*	28.00±0.00*	–
Staphylococcus auerus (NCTC 6571)	–	–	–	–	–	21.33±0.44*	21.67±0.65*	23.00±0.00*	23.67±0.55*	–
*Staphylococcus auerus (*ATCC 25923)	–	–	–	–	–	10.67±0.54*	11.33±2.0*	13.00±0.0*	15.00±0.0*	–
Bacillus substiles (NCTC 8853)	–	–	–	–	–	18.00±0.00*	19.67±0.33*	20.00±0.00**	21.00±0.00*	–
Shigella dysenteriae (clinical isolate)	–	–	–	–	–	–	–	–	–	–
Salmonella typhii (NCTC 8571)	–	–	–	–	–	–	–	–	–	–
Pseudomonas aeruginosa (ATCC 25922)	–	–	–	–	–	7.33±0.33*	7.67±0.66*	8.00±0.00*	9.33±0.11*	–
Escherichia coli (NCTC 104418)	–	–	–	–	–	–	–		11.67±0.40*	–
Escherichia coli (ATCC 25922)	–	–	–	–	–	–	–	20.33±0.22*	21.33±0.33*	–
Candida albicans I	–	–	–	–	–	–	–	–	–	–
Candida albicans II	–	–	–	–	–	–	–	–	–	–

*P<0.05 (ANOVA; LSD post hoc); values shown are Mean ± SEM (n = 3).

CONCLUSION

The activity of the methanolic extract of the root of *Aspilia africana* is basically antibacterial and not antifungal as all the strains of the fungi used in this test were not inhibited. This antibacterial activity has confirmed that root part of the plant is potentially useful in the treatment of wound sepsis and mycobacterial infections and can be deployed in wound management because it is able to check the activities of wound contaminants, promote rapid wound healing by eliminating infections and thus allowing the natural tissue repair process to go on unhindered and without side effects as result of toxicity (LD_{50} is high). The study has further provided a rationale for the use of the plant in wound care in ethno-medicinal practices in Africa. This is the first time an antibacterial study has been conducted on the root part of *Aspilia africana.*

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Complementary and alternative medicine (cam) use among cancer patients in selected tertiary health facilities in southwestern nigeria.

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ABSTRACT

Complementary and Alternative Medicine (CAM) is a comprehensive term used to refer to Traditional Medicine (TM) systems such as Traditional Chinese Medicine and to various forms of indigenous medicine. A survey was carried out to ascertain the prevalence of the use of CAM among cancer patients attending tertiary hospitals in Southwestern Nigeria. After obtaining permission from Research Ethics Committee and consent from participants, questionnaires were distributed to one hundred and twenty (120) cancer patients attending cancer treatment facilities. The result showed that out of the 64% of the cancer patients presently on CAM, 39% expected cure from the use of CAM while 3% hoped that use of CAM will lead to suppression of growth of the cancer cells followed this trend: 55% of the patients regularly consumed vegetables, 51% were on daily course of vitamins and other supplements, 38% performed regular exercises, while 20% relied on prayers. Fifteen percent of the patients consulted social workers, 12% used music therapy and 7% used local herbs. The study further revealed that consumption of vegetables, vitamins/ supplements and regular exercise was the most common CAM used by the cancer patients. The uses of vitamins/ supplements, vegetable and exercise have formed a mainstay of prescription in the management of cancer in Nigerian hospitals.

KEY WORDS: Cancer, CAM, Exercise, Supplements, Vegetable, Vitamins.

INTRODUCTION

The definition of alternative medicine involves a variety of behavior techniques like spiritual techniques and relaxation methods, Clinical approaches such as massage, herbal remedies and chiropractic, have not previously been considered as components of alternative medicine. Clinical therapy also includes mind therapy such as mental images, hypnosis, relaxation and body therapy such as acupuncture, chiropractic and herbal treatment. These practices have entered mainstream society and culture but are neither widely taught in medical schools nor generally available in hospitals (Boon *et al*., 2000). These practices complement mainstream medicine by contributing to health and satisfying demands that are not met by conventional practices. They also diversify the conceptual framework of medicine (Burstein, 2000).

The prevalence of CAM use is estimated at 25% among residents of the United Kingdom, 50% among German, French and Australian populations and 42- 69% among residents of the United States (Richardson *et al*., 2000). Some patients believe that access to CAM should be part of standard cancer treatment. As cancer incidence increases and survival time lengthens, the population seeking information about and access to CAM is likely to increase (Richardson *et al*., 2000). While the use of Traditional Medicine (TM) remains widespread in developing countries, use of CAM is also increasing rapidly in developed countries. In many parts of the world, policy-makers, health professionals and the public are wrestling with questions about the safety, efficacy, quality, availability, presentation and further development of this type of healthcare (Burstein *et. al,* 1999). Complementary medicine includes all such practices and ideas which are outside the domain of conventional medicine in several countries and defined by its users as preventing or treating illness or promoting health and well being. Complementary and Alternative Medicine can also be defined as groups of diverse medical and healthcare systems, practices, products that are not currently part of conventional medicine (Burstein *et al*., 1999).

The primary objective of this study is to examine CAM use among cancer patients attending selected tertiary health institutions in Southwestern Nigeria.

MATERIALS AND METHODS

The human subjects used for this research study were cancer patients attending Cancer Centers in two tertiary health institutions in Southwestern Nigeria. The Centers are University College Hospital, Ibadan, (Department of Radiotherapy) and Lagos University Teaching Hospital (Department of Surgery). Ethical approval was obtained from the University of Ibadan/ University College Hospital Health Research Ethics Committee and Lagos University Teaching Hospital. Informed consent and questionnaires were distributed to one hundred and twenty cancer patients. The participants were assisted on completing parts of the questionnaire that seemed difficult for them to complete. The participants were eighteen years old and above and included

both males and females. Only one hundred respondents were received.

QUESTIONNAIRE

CAM therapies were classified into seven major categories: special diets (vegetarian, vega, macrobiotics, gershon diets and others), psychotherapy (with social workers, psychologist or support group), movement and physical therapy (exercise, yoga, taichi or chigong, chiropractic or osteopactic manipulation and massage), mind or body therapy (imagery/ visualization, hypnosis, meditation, biofeedback, energy healing or therapeutic touch, journaling and music therapy), spiritual practices (prayer for self and prayer/ spiritual healing by others), vitamins and herbs (melatonin, essiac, mistletoe, laetrile, shark or bovine cartilage, homeopathy, ayurvedic and folk remedies) and other approaches such as immune-augmentative treatment, 714X cancel, bioelectromagnetic therapy and acupuncture (Lee *et al*., 2000).

After the patients were admitted in the hospital, the purpose of the study and the administered questionnaire were explained to them. Their eligibility was then determined as part of the consent process. The patients were allowed the freedom of withdrawal from the study at any time and that they were at liberty to skip any survey question. To increase accuracy, patients were requested to indicate their responses directly on the questionnaires. Questionnaires were returned to the principal investigator at the clinic. All questionnaires were coded before administration to the participants to ensure confidentiality.

RESULTS

Out of the 64% of the cancer patients still using CAM, 39% expected cure, 3% wanted suppression of cancer growth and 4% were expecting complementary effect with the conventional therapy while 3% expected symptomatic relief only with the use of CAM (Table 1). Fifty-one (51%) of the patients using CAM indicated that there was improvement with the use of CAM while 8% of them said there was no improvement and 18% of them were not sure if there was improvement or not.

Table 2 shows that 55% of the cancer patients from the study population used vegetables, 51% of the cancer patients took vitamins and other supplements, 38% performed routine exercises, 20% used prayer (by themselves), 15% consulted social workers, 12% used music therapy and 7% used local herbs. Twenty-eight percent (28%) of those patients who used CAM claimed that they derived satisfaction while seven (7%) percent did not derive any satisfaction (Fig. 1).

DISCUSSION

The awareness of the use of Complementary and Alternative Medicine (CAM) increases everyday as the number of cancer patients increases (Table 1). This can be related to the incorporation of CAM to treatment plan in the hospitals. CAM treatment employed in the hospitals includes, use of vitamins/ supplements, advising patients to take more vegetable, fruits and perform regular exercise. The high proportion of the study population still affirming that they were using CAM

presently at the time of the research confirmed its inclusion into medical practice. The patients accepted it as part of their treatment plan and complied appropriately. The desire of some of the study population was to obtain cure from the disease from the use of CAM. Some were however concerned about the suppression of growth as well as relieve from its symptoms. More than half of the patients (Table 1) confirmed that there was improvement as they used CAM. For those who failed to recognize any improvement, their providers attributed non-compliance to the use of CAM.

Only few patients in the study population complained about adverse effect of CAM prescribed by their CAM providers. This showed that they were tolerated by most of the patients. The main source of dissemination of the information of CAM used (such as vitamins/ supplements, vegetables, exercise and support from social workers, psychologist and psychiatrists) in the health institution is the health personnel. This justifies its inclusion in medical practice.

Vegetable was the most commonly used CAM among the participants followed by vitamins/ supplements (vitamin C and vitamin E), exercise, prayer by self, social workers intervention and music therapy respectively. This could be attributed to the fact that these CAM were easily available, affordable and no special skill was required for their use. It was believed that the vegetable and vitamins would help to improve certain functions in the body and improve immunity as well (Decker, 2007). The evidence for a protective effect of vegetable and fruit consumption is consistent with previous findings in cancers of the stomach, esophagus, lung, oral cavity and pharynx, endometrium, pancreas and colon (Van *et al*., 2000). The types of vegetable or fruits which mostly appear to be protective against cancer were raw vegetables, followed by allium vegetables, carrots, green vegetables and tomatoes. Substances present in the vegetables that have been found to offer protection against cancer and proliferation of cancer cells are isoflavones, saponins, vitamin C, vitamin E, phytosterols, allium compounds among others (Van *et al*., 2000).

Studies have also shown that overall; exercise had a positive effect on physical and psychological functioning of cancer patients while under treatment. These benefits include: increased functional capacity, increased lean muscle mass, decreased body fat, improved natural defense mechanisms, decreased nausea and fatigue, improved sense of control, improved mood, improved self esteem and improved quality of life. Exercise rehabilitation had a beneficial effect on the physical and psychological well being of patients with breast cancer (ARFA, 1999; Quinn, 2003).

One limitation of the present study is that participants were unable to provide all samples and full information of CAM used except for vitamins, massage and prayer. Furthermore, the study focused on all types of cancer presentation at the two study centers and was not designed to evaluate in quantifiable terms the efficacy and adverse effects the CAM used by the patients.

CONCLUSION

Uses of vitamins/ supplements, vegetable, exercise and involvement of social workers have been included in management of cancer in Nigerian hospitals. Complementary and Alternative Medicine (CAM) has been accepted as part of conventional treatment by cancer patients who expect cure or suppression of cancer growth from the use of CAM.

It is very important that as CAM is on the increase among patients attending health facilities in Nigeria, the clinical evaluation of CAM, drug interactions and its side effects should be undertaken to ascertain their safety and effectiveness.

Table 1: Effectiveness And Adverse Effect Of Cam Use Among Cancer Patients

VARIABLE	FREQUENCY (n)	PERCENTAGE (%)
STILL USING CAM NOW		
Yes	64	64
No	15	15
Not indicated	21	21
Total	100	100
CAM USE EFFECTIVENESS		
Suppress cancer growth	3	3
Cure	39	39
Symptom relief	3	3
Complementary effect	4	4
Suppress cancer growth + cure	1	1
Suppress cancer growth+Cure + symptom relief + Complementary effects	12	12
Suppress cancer growth +Symptom relief	3	3
Cure + Symptom relief	3	3
Suppress cancer growth +Symptom relief + complementary effect	2	2
Cure + Complementary effect	2	2
Suppress cancer growth + cure + symptom relief	4	4
Not Indicated	24	24
Total	100	100

Table 2: Types Of Cam Use Among Cancer Patients.

VARIABLE	FREQUENCY (n)	PERCENTAGE (%)
TYPES		
Vegetable	55	55
Gershon's diet	1	1
Social worker	15	15
Psychologist	4	4
Psychiatrist	1	1
Support group	4	4
Exercise	38	38
Yoga	3	3
Massage	5	5
Imagery/Visualization	6	6
Hypnosis	3	3
Meditation	2	2
Music therapy	12	12
Prayer (by self)	20	20
Prayer by others/ spiritual healing	3	3
Vitamins/supplement	51	51
Folk remedies	1	1
Burton's immune therapy	4	4
Other herbs	7	7
DISCUSSION OF CAM WITH DOCTOR		
YES	60	60
NO	25	25
Undisclosed	15	15
Total	100	100

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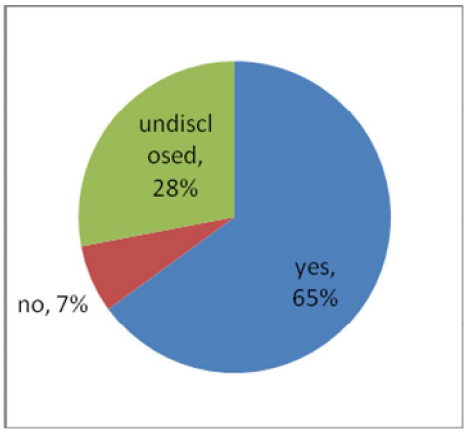

Figure 1: Satisfaction with CAM Treatment by Cancer Patients

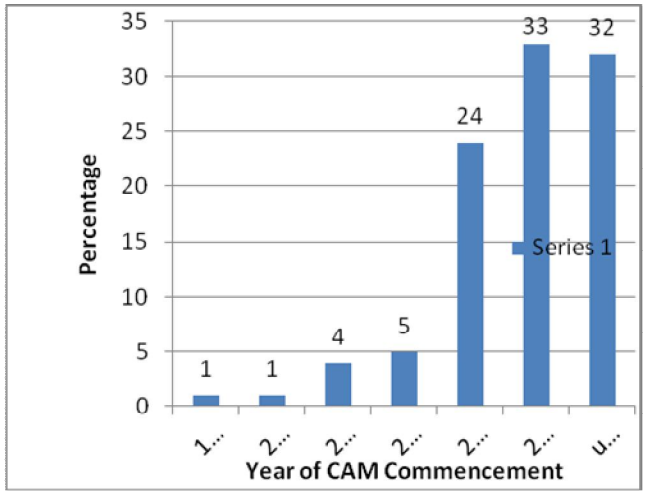

Fig. 2: Year of CAM Commencement by Cancer Patient

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Effects of Artesunate Alone and In Combination with Folic Acid on the Liver and Serum Iron Level of Male Wistar Rats

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ABSTRACT

The effects of oral administration of artesunate alone and with folic acid on the liver and on the serum levels of iron were assessed in eighty-one male wistar rats with a mean weight of 180 g (172-188 g). Thirty-six rats received artesunate of graded doses ; another thirty-six rats received a combination of artesunate and folic acid; while normal saline was administered to the remaining nine rats which served as the negative control group. Comparison of means of results was done with the student's t-test at a 95% level of significance. The results showed that in rats treated with 6.00 mg/kg of artesunate alone, there was a significant decrease in liver weight from 3.25±0.55 to 2.64±0.12g. Necrosis of the hepatocytes as revealed by liver histology also occurred. The serum iron level rose significantly from 784±11.49 μmol/L to 1773±11.32 μmol/L. It was also found that folic acid reversed metabolic and tissue disorder associated with lower doses of artesunate but offered partial relief to the same disorders associated with higher doses of the drug. This is evident by the decrease in serum iron and the the healthy cytoarchitecture of the liver .

KEYWORDS: Artesunate, folic acid, iron, serum, liver

INTRODUCTION

In Nigeria, 80% of the human population are exposed to malaria. At least 60 million people have repeated malaria in a year. The mortality rate has been put at 100,000 persons per annum (Jeremiah *et.al*,2007). In sub-Saharan Africa about 300,000 children die yearly of malaria. In the world, the World Health Organization estimates that 300 to 500 million clinical cases and 1.5 to 2.7 million deaths due to malaria occur each year world wide (Ogunbonna *et.al*,1990) .

Artesunate is the synthetic derivative of Artemisinin, the antimalarial principle isolated from the plant *Artemisia annua (*Woedenbag *et al*,1994). Artesunate is considered an effective alternative drug for *P. falciparum* because clinical findings to date have not revealed any pattern of resistance to it (Kabwang *et al* 1994, Baradell and Fitton *et al*,1995) . Artesunate is commonly administered with folic acid. The objective of this study is to evaluate the effect of artesunate and its concomitant administration with folic acid on the liver and also on the serum iron levels. This study is of clinical significance because artesunate breaks the megaloblast, attacks the cell membrane of the parasite in it and consequently kills the parasite. The Iron in the megaloblast is liberated into the peripheral blood circulation from where they shunt into the serum and plasma resulting in megaloblastic anemia which in turn inhibits DNA synthesis in red blood cell production especially when there is folic acid deficiency. In humans folic acid is reduced to tetrahydro folic acid (THFA) by an enzyme dihydrofolate reductase (DHFR). THFA (the active form of folic acid) is required for the de-novo synthesis of nucleic acids and certain amino acids. This is why artesunate should be administered in conjunction with folic acid. The findings in this study when extrapolated to human will bring succour to malaria patients who takes solace artesunate as drug of therapy. (Reich and Deykin 1978, Udobre *et al* 2009).

Artesunate (NEROS Pharmaceuticals Ltd Lagos), Folic acid (Vitabiotics England) were purchased in Uyo.

MATERIALS AND METHOD

Drug administration and collection of blood

Eighty one male wistar rats were obtained from the National Veterinary Institute, VOM in Jos, Plateau State. The rats were kept in the animal House under standard Laboratory condition in the Department of Pharmacology and Toxicology, Faculty of Pharmacy, University of Uyo and fed on Growers Marsh (Top feeds, Sapele, in Nigeria) and water *ad libitum.* The rats were weighted after three weeks and had a mean weight of 170 g.

The eighty-one (81) male wistar rats were divided into nine groups of 9 rats each and then treated as shown in table 1. Following daily oral administration of the drugs the rats were sacrificed on the 6^{th} day, and blood was collected by passing a needle on syringe through the ventricle of the heart (Reich and Deykin 1978) .

The serum was prepared from the clotted blood by gently decanting the serum from the cells into iron-free centrifuge tubes. The tubes were then spun at 10,000 revolutions per

second for 3 min in a centrifuge machine (MSE, England). The serum was then decanted into another set of clean tubes and stored at -15^{0}C for 24 h.

Analysis of serum

The serum samples obtained from the rats treated with artesunate alone, artesunate and folic acid and then physiological saline (control) respectively were analyzed in an atomic absorption spectrophotometer, (Perkin Elmer 2280) for iron levels at wavelength of 248nm. The results obtained were compared with the control values.

Histological Analysis

The liver tissue samples removed from the experimental rats were fixed in 10% neutral solution for 42 h, and then passed through 70%, 95% and absolute alcohols for 1½ h each. The tissues were then infiltrated through molten paraffin wax in the oven maintained at 60^0 for 1 h and then sectioned at five microns (5 μ) thick for light microscopy.

The haematoxylene and Eosin method of staining was applied. Sections were dewaxed in xylene, cleared in absolute, 95%, 70% alcohol and then in water. The sections were stained in haematoxylene for 15 minutes, differentiated in 1% acidified alcohol by rinsing twice and then counter stained with eosin for 3 minutes and dehydrated in 70%, 95% and absolute alcohol. The sections were cleared in xylene and mounted with DPX mountant for microscopy.

Statistical Analysis.

The student's t-test was used to test whether there existed any significant differences between the means of the treatment groups and those of the corresponding control groups. The data obtained are expressed as mean $\pm$ S.D student's t-test was used for the analysis and $P \leq 0.05$ was taken to be statistically significant.

RESULTS AND DISCUSSION

Tables 2 and 3 show that the concentrations of iron in the serum increases significantly ($P \leq 0.05$) with increase in the dose of artesunate. In rats treated with a mixture of artesunate and folic acid, the folic acid reduced the serum iron concentration. For example, the serum iron concentration was 1068±14.28 when 1.50 mg/kg artesunate was administered but reduced to 803±13.47 when the same dose was coadministered with 1.50 mg/kg folic acid. In the presence of high iron concentrations artesunate releases free radicals which kill the schizonts of malaria parasites. These results indicate that equivalent doses of folic acid can reverse metabolic disorders occasioned by the administration of low doses of artesunate but might interfere with the activity of artesunate against the schizonts of plasmodia (Udobre *et al*, 2009.

At a dose level of 6.00 mg/kg artesunate, the 1.50 mg/kg folic acid administered could not bring down the serum iron concentration. The high dose of the drug might have destroyed the megaloblasts and the iron in them liberated into the peripheral blood circulation from where the iron shunt back into the serum and plasma thus increasing the iron level at the expense of tissues and organs, a condition referred to as megaloblastic anemia (Liy and Wu, 1998)

The results in tables 4 and 5 show that at the dose level of 6.00 mg/kg artesunate the percentage weight of the liver decreased significantly from the control value of 3.25±0.12 to 2.64±0.12 ($P \leq 0.05$). At the dose level of 6.00 mg/kg artesunate co-administered with 1.50mg/kg folic acid, the percentage liver weight increased from 2.64 ±0.12 to 2.92±0.20 ($P \leq 0.05$), but not up to the value for control rats (3.25±0.55). These results support the earlier observation that co-administration of folic acid with artesunate can reverse the metabolic disorders associated with artesunate administration at lower doses of artesunate. This reversal effect may be achieved at higher doses of artesunate if higher doses of folic acid are employed (Edoho *e tal* 2006)

Nuclei stained blue-black in all the sections and cytoplasms shades of pink. In the group that received normal saline liver cells radiate from central vein. The liver cells have a distinct cell outline. The nuclei stain deeply basophilia. The cells cytoplasm stain deeply eosinophilia. Hepatic sinusoids run between two sheets of liver cells. These imply that the hepatocytes of the control group are normal (as seen in fig 1a).
In the group which received high dose of artesunate of 6.00 mg/kg body weight, necrotic areas are seen. The cell outline is not prominent; the liver cell nuclei are pyknotic. The hepatic sinusoids are wider. There is venodilatation with blood clot inside it. These imply that the hepatocytes are destroyed at a dose level of 6.00 mg/kg body weight artesunate (see fig 1b).

In the group which received 6.00 mg/kg body weight artesunate and 1.50 mg/kg body weight folic acid, there is less distortion of the cytoarchitecture; the cells appear less sequestrated; the cell outline is not prominent and the cell nuclei appear pyknotic. The hepatic sinusoids are wider than with artesunate alone and run between the hepatic cells (fig 1c). These results imply that folic acid help to relieve liver disorder associated with artesunate administration.

CONCLUSION

This study shows that administration of a high dose of artesunate up to 6.00 mg/kg to male wistar rats caused necrosis of the hepatocytes, significant decrease in liver weight and significant increase in serum iron level. The doses of folic acid offered total relief to metabolic disorder associated with lower doses of artesunate but partial relief to the same disorder associated with higher doses of the drug. In this study, it is observed that the combination therapy yielded good result but that the folic acid should not be administered in very high doses to prevent the loss of efficacy of artesunate and not in very low doses so as to preserve its clinical relevance.

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Table 1: table of dosage patttern of drug administration to the rats.

Group	Dose of Drugs/Chemicals in mg/kg body weight
A	0.75 mg/kg artesunate
B	0.75 mg/kg artesunate + 0.75 mg/kg folic acid
C	1.50 mg/kg artesunate
D	1.50 mg/kg artesunate + 1.50 mg/kg folic acid
E	3.00 mg/kg artesunate
F	3.00 mg/kg artesunate + 1.50 mg/kg folic acid
G	6.00 mg/kg artesunate
H	6.00 mg/kg artesunate + 1.50 mg/kg folic acid
I	Physiological Saline (Control)

Table 2: Effect Of Artesunate Alone And With Folic Acid Administration On Serum Iron Level

Group	Treatment Group	Mean Serum Iron (μM)
A	0.75mg/kg artesunate	804±15.45
B	0.75 mg/kg artesunate + 0.75 mg/kg folic acid	790±14.18
C	1.50 mg/kg artesunate only	1068±14.28*
D	1.50 mg/kg artesunate + 1.50 mg/kg folic acid	803 ±13.47*
E	3.00 mg/kg artesunate	1130±15.33*
F	3.00 mg/kg artesunate + 1.50 mg/kg folic acid	978±13.08*
G	6.00 mg/kg artesunate only	1773±11.32*
H	6.00 mg/kg artesunate + 1.50mg/kg folic acid	1661±14.23*
I	Physiological Saline (Control)	784±11.49

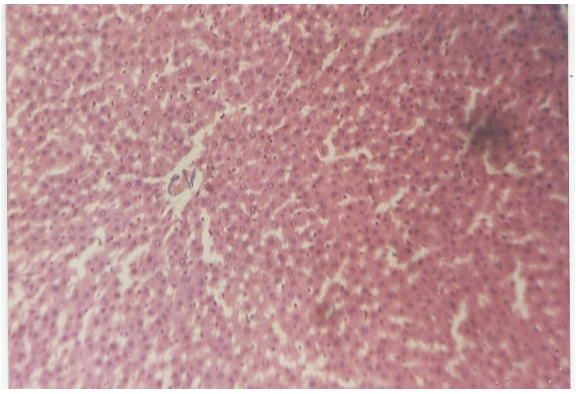
The results are expressed as mean ± standard deviation * significant ($p < 0.05$)

Table 3: Liver Weight Results

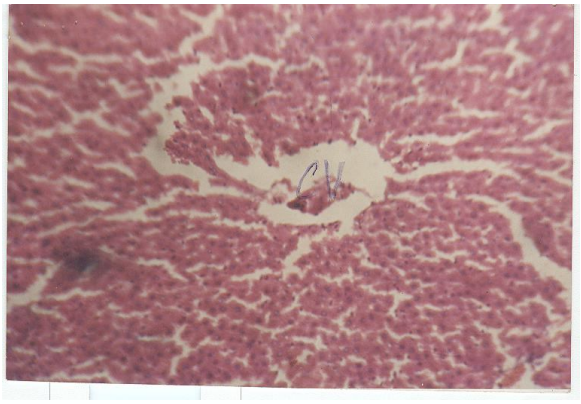
Group	Treatment Group	Liver weight (g)
A	0.75 mg/kg artesunate	3.10±0.24
B	0.75 mg/kg artesunate + 0.75 mg folic acid	3.17±0.21
C	1.50 mg/kg artesunate	3.24±0.39
D	1.50 mg/kg artesunate + 1.50 mg folic acid	3.27±0.58
E	3.00 mg/kg artesunate	2.99 ± 0.46
F	3.00 mg/kg artesunate + 1.50 mg folic acid	3.06 ± 0.50
G	6.00 mg/kg artesunate	2.64 ± 0.12*
H	6.00 mg/kg artesunate + 1.50 mg folic acid	2.92 ± 0.20*
I	Physiological Saline (Control)	3.25 ± 0.55

The results are expressed as percentage liver weight ratio, which is liver weight/body weight x100

(a) Magnification × 2500



(b) Magnification × 2500



(c) Magnification × 2500

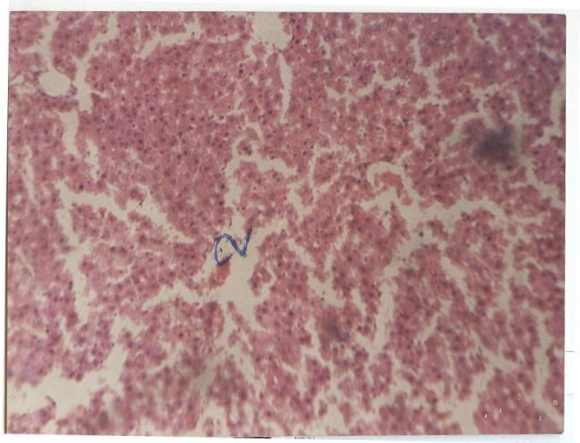


Fig. 1: Liver sections from rats treated with (a) physiologic saline (b) Artesunate alone (c) Artesunate and folic acid.

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The Place of Specialized Pharmaceutical Services in Hospital Pharmacy Practice

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ABSTRACT

Professions exist to serve society. The mission of our profession must therefore, address the needs of society and individual patients. In this regard, the pharmacy profession has a responsibility to identify new opportunities for pharmacy practice in a changing health sector context, to assess and to test them, and to demonstrate the ability to implement them successfully. In addition, in the traditional relationship between the doctor as prescriber and the pharmacist as dispenser, the prescriber was accountable for the results of pharmacotherapy. This situation has changed in rapidly evolving health systems worldwide. The practice of pharmaceutical care now assumes the pharmacist to be responsible for patients under their care, and society will not only accept that assumption but hold the profession for it. These have informed the choice of the subject under review.

INTRODUCTION

The separation of pharmacy from medicine first took place in the early charity institutions engaged in caring for the sick and the injured. History records the fact that pharmacies were important segments of hospital activities as far as the 4th century. In this era, hospitals were part of monasteries. However, it was after the plague in the 14th century, that pharmacy separated from medicine and hospitals of that era and were reported to have had well equipped pharmaceutical service centres. The first hospital pharmacist in America is believed to have been Jonathan Roberts, a pharmacist of the Pennsylvania Hospital in Philadelphia in 1752 (Piecoro and Chudzik, 1972). Back here in Nigeria, formal pharmacy education started in early 1900's. It was in 1902 that the first pharmacist has his name entered into the register of Pharmacists (Brown and Ogun, 1998). From then until the 1960's pharmacy curricula were dominated by compounding and dispensing. As a result of multiplicity of drugs and complexity in clinical uses, subjects like pharmacology, toxicology and pharmaceutical microbiology were incorporated into pharmacy curricula. Clinical pharmacy involving patient drug monitoring later came into focus for better patient drug management. In 1989, the National universities commission (NUC) approved minimum standards of five year training curriculum for pharmacy. Consequently, in order to meet with challenges of development in pharmacy, faculties of pharmacy in Nigeria sporadically introduced some form of clinical pharmacy orientation in their curricula. In 1990, the NUC gave directive

for the introduction of uniform clinical pharmacy training in pharmacy schools and clinical pharmacy became a component of the basic undergraduate (B. Pharm) training. In 1992, selected Deans of Pharmacy schools and the then registrar of the then Pharmacists Board of Nigeria were sponsored to a trip overseas to understudy clinical pharmacy practice in two pharmacy schools in the UK (University of London and University of Strathclyde schools of pharmacy) and two pharmacy schools in the USA (Howard University and Philadelphia schools of pharmacy).

Contemporary Hospital Pharmacy Practice

The provision of pharmaceutical services in hospitals has emerged as one of the most dynamic and challenging areas within the profession of pharmacy. Hospital pharmacy practice traditionally involves supplying of medications for in-patients and out-patients use, the preparing of sterile medications, bulk compounding pre-packaging, drug formulation, research and serving as focal point in the dissemination of information relating to drug therapy to the entire hospital staff. In addition to these traditional roles, the pharmacist is now beginning to utilize his professional judgment and expertise not only within his department, but also in previously unexplored areas such as the nursing station, the medical laboratory and at the patient's bedside. As experts in medicines, pharmacists are, perhaps, the most accessible and trusted source of advice and treatment in any well organized Hospital setting. Today, their contribution to health care is developing in new ways to support patients in their use of medicines and as a part of clinical decision-making across the range of specifications. These emerging new roles as a vital member of the healthcare team not only allow the pharmacist to utilize his knowledge of drugs to the highest degree, but also make clear the importance of sound pharmacy service to the total care of the patient.

The Backbone Of Modern Hospital Pharmacy Practice

The current trend in Hospital pharmacy practice is dominated by patient oriented rather than product oriented pharmaceutical services. Clinical pharmacy is a new stress area in Hospital pharmacy practice in Nigeria. What is clinical pharmacy? The term clinical pharmacy was coined to describe the work of pharmacists whose primary job is to interact with the health care team, interview and assess patients, make specific therapeutic recommendations, monitor patients' responses to drug therapy and provide medicines information. Clinical pharmacists work primarily in hospitals and acute care settings and provide patient rather than product oriented services. Practice of clinical pharmacy requires an expert knowledge of therapeutics, a good understanding of disease processes and knowledge of pharmaceutical products. In addition, it requires strong communication skills, with solid knowledge of medical terminology, drug monitoring skills, provision of medicine information, therapeutic planning skills and the ability to assess and interpret physical and laboratory findings (Society of Critical Care Medicine and the American college of Clinical Pharmacy; 2000).

The world is said to be a global village. The impacts of globalization are now being felt in all facets of life and in all professions. While trying to keep pace with global development in pharmacy practice, the historical and developmental stages in our society should be our guiding principles in the adaptation of new changes and challenges in pharmacy practice. It is now an axiom that over-emphasis on patient oriented pharmacy practice in places like the USA has led to depreciation in the other vital segments of the pharmacy profession. The consequence of this is that graduates of Chemistry, Biochemistry, and Microbiology are now assuming the roles of formulation scientist, roles which are exclusive to the pharmacy profession. In Nigeria, only very few pharmaceutical manufacturing companies have their quality control personnel as pharmacist. This area has been taken over by graduates of Chemistry, Biochemistry and Microbiology. One of the laws of survival is law of self preservation. In our opinion, while we lay emphasis on clinical pharmacy and patient oriented pharmaceutical care and services, the core ingredients of the profession of pharmacy should not be abandoned. In this regard, we strongly recommend the adaptation of our new Pharm. D curriculum to the realities of our professional practice and experience.

Emergence Of Specialized Pharmaceutical Services In Hospital Pharmacy Practice

In the last seventeen years, clinical pharmacy became increasingly specialized and a developed specialty for better patient care in Hospital and institutional setting.

The need for specialized pharmacy practice in a Hospital setting arose as a result of:
accelerating trend towards specialization in the health professions , the unmanageable scope of knowledge necessary to discuss clinical pharmacy in general terms that apply to all clinical services and patient populations, and
the unique nature of certain patients, and disease conditions. (Piecoro and Chudzik, 1972)
In addition, in collaboration with other members of the patient care team, pharmacists share the responsibility for patient care outcomes, not just by providing basic dispensing functions and drug information services, but by solving patient and drug related problems and by making decisions regarding drug prescribing, monitoring and drug regimen adjustment. Specialized pharmaceutical services now operate in many Hospitals in the USA and specialization is now attained through Residence programmes.

It is generally referred to as specialized pharmacy Residencies. A specialized pharmacy residency is designed to build those competences developed by a residency pharmacy practice. All accredited residencies in the USA are full time commitments that require at least one year to complete. Some specialized residences may be offered in combination with other programmes, such as a fellowship, which may require additional years to complete. Specialized pharmacy sections in Hospitals serve as an avenue by which pharmacy professionals from diverse practice environments may obtain and utilize support, guidance and professional development. It serves pharmacists with interests in providing pharmaceutical care or any of its components

beyond traditional institutional and community drug distribution. To qualify for residence a first degree in pharmacy is required in the USA and in some states such as New Mexico; the applicant must possess a Pharm. D degree from accredited college of pharmacy or school of pharmacy and must be eligible for licensure as a pharmacist in the state of New *Mexico* (A document of American society of Health-system Pharmacists.).

American society of Hospital pharmacy (ASHP) recognizes specialized residencies in an ever expanding number of areas such as:

Cardiology

This involves six months of clinical services in the cardiovascular intensive care unit and telemetry units, with the remaining six months devoted to research and clinical service electives of the resident's choice. The resident is normally integrated into comprehensive clinical pharmacy services and is involved in teaching and research activities.

Clinical Pharmacokinetics

This residency provides exponential training in the application of clinical pharmacokinetics skills to develop and monitor a patient's pharmacotherapy. The resident gains experience in managing therapy for a broad range of patient population with varying medical conditions, including patients with infections disease and those with cardiac, neurological and psychiatric conditions. A pharmacokinetics residency provides extensive involvement in computer-assisted data interpretation, drug analysis methodology, teaching, and research.

Critical Care

A critical care pharmacy practice residency offers training in caring for the special pharmacy needs of critical patients of all ages. Much time is spent in the intensive care units, and experience is gained in areas such as hemodynamic monitoring, shock, burns, infections diseases, analgesia, and drug over dose management. Treatment of critical pathology associated with pulmonary, cardiac, renal, neurological and hepatic organ systems is stressed. A residency in critical care may also provide teaching and research.

Drug Information

This residency provides training in the skills necessary for managing complex drug information services. Residents learn how to effectively use medical information and databases, appropriate method for monitoring, accuracy in patient drug use and safety, and pharmaco-economic principles. Residents acquire scientific writing skills, an understanding of drug policy development, and clinical and marketing research experience. The drug information resident is active in handling and responding to drug information requests, educating patients, health care professionals and students about drug therapy and drug delivery systems, assisting in the development of drug policies, and managing the formulary.

Emergency Medicine

It is designed to develop a clinical practitioner with skills in emergency medicine, critical care and toxicology. Experience is gained by rotation in level 1 trauma centre, toxicology unit, burn intensive care, neurotrauma, cardiology, and

the psychiatric crisis centre. Residents usually complete a research project and participate in nursing and pharmacy students' education.

Geriatrics

A residency in geriatric pharmacy practice emphasizes the management of pharmacotherapy in elderly patient with acute and chronic health conditions. Training involves providing for the special needs of elderly patients through a knowledge of geriatric disease states, ageing, organ function and related drug response alterations, and pharmacokinetics and pharmacodynamic predictions. Other issues such as health maintenance, compliance, patient education, and social issues are also emphasized. Residents are usually involved in clinical research activities and professional education

Pediatrics

Residents gain experience caring for pediatric patients with acute and chronic conditions in such areas as infectious disease, cardiology, pulmonology and rheumatology. Training involves knowledge of pediatric conditions, developmental organ function and related dose-response alterations, and pharmacokinetics and pharmacodynamic predictions. Attaining competence in pediatric service involves psychological adjustment; technical competence; development of judgment in practice situations and the ability to create and maintain service objectives.

This training is best provided through some sort of specialization and residency in pediatric pharmacy.

Infectious Disease and Internal Medicine

Residency training here involves exposure and experience in microbial virulence factors, host defense mechanisms, and epidemiology of infectious diseases, including microbiology research and management.

A residency in internal medicine pharmacy practice in the other hand is designed to develop broad, acute and ambulatory experience in such areas as critical care, cardiology, endocrinology, infectious disease, pulmonary and renal care, and oncology. This type of residency requires a strong foundation of pharmacy practice skills, and emphasizes consultation, clinical and didactic teaching, and quality assurance of care.

Nuclear Pharmacy

The diverse and unique practice of nuclear pharmacy encompasses product formulation, the radio-pharmaceutical distribution system and the clinical, developmental and support services offered to nuclear medicine and radiology. Current approaches to nuclear pharmacy management, radiation protection and technology, and quality assurance activities are emphasized. Sound knowledge of radioactive decay, biological half-life and dosage calculations is essential in this area of specialty.

Oncology

In an oncology pharmacy practice residency, the resident will plan appropriate therapy, oversee anti-cancer drug preparation, and expertly manage the therapy and associated adverse effects in patients receiving anti-cancer and supportive care therapies. The resident is

exposed to the management of cancer related problems such as pain, nutrition disorders, nausea and vomiting and infectious diseases. Although the focus of the residency is primarily on clinical practice and patient care, opportunities for teaching and clinical research-including new and investigational drug research are emphasized.

Nutrition Support

Residents participate in managing the nutrition support service through assessing and diagnosing nutritional status, and designing and monitoring nutritional and electrolyte treatment plans. Experience is gained as residents are required to work with a broad spectrum of patients, including trauma and surgical patients, patients having endocrine abnormalities and renal and hepatic compromised patients. The resident learns about various infusion techniques and systems for administering nutritional agents.

Psychiatric

The resident gains experience in treating diverse psychiatric and behavioural problems, including schizophrenia, depression, mania, bipolar disease, phobic states, substance abuse, personality disorders and related behavioural problems, and neurological disorders in adolescents and adults. Patient communication and assessment skills are emphasized, along with research activities, drug information and education.

Pharmacotherapy

Residency programme in this area prepares the resident to ensure safe, appropriate, and economical use of drugs in patients. Among the specialized functions of this residency are to collect and interpret data, to design, recommend, implement, monitor, and modify patient specific pharmacotherapy, interpret, generate, and disseminate drug therapy knowledge and design, recommend, implement monitor and modify system-specific policies and procedures in collaboration with other professionals to optimize health care.

Primary Care

Primary care pharmacy residency emphasizes communication and assessment skills, chronic disease management and preventive care, acute care and emergency care, and therapy modifications for special patient groups. Other skills developed include drug literature analysis, and the development of new clinical services in a variety of ambulatory care settings. Opportunities for further refinement in drug information, pharmacokinetics consults, and maintaining patient records and statistical data for continuity of care and research are available. (Specialized residences: A document of American Society of Health-system Pharmacists and University of New Mexico, Residency Programme Guidelines).

Pharmacy Practice Management

In pharmacy practice management residency, emphasis/focus is on operational, fiscal and health care related issues which influence pharmaceutical care. Leadership skills such as effective communication, negotiation, and departmental management are emphasized. Appropriate skills necessary to conceptualize, implement and evaluate innovative pharmacy services are also stressed.

Management care pharmacy systems

A residency in management care pharmacy practice prepares the resident to manage populations, outcomes and systems. The resident builds the knowledge, skills and abilities needed to assume administrative or managerial roles and responsibilities in any managed care setting, including pharmacy benefit management companies and health maintenance organizations.

Other emerging areas of specialization/residency include: High risk obstetric services; HIV-AIDS services; Rehabilitation services; Trauma Intensive service; Ambulatory Care Service; In-patient Anticoagulation Service.

All these specialized pharmacy service residencies are twelve month programmes designed to prepare a practitioner to lead in conceptualizing, planning, developing and demonstrating specialized pharmacy services (University of New Mexico, Residency programme guidelines).

The Place And Benefits Of Specialized Pharmaceutical Services In Hospital Pharmacy Practice

In rapidly developing profession of Pharmacy the place of specialization in Hospital pharmacy practice can not be over emphasized. The benefits derivable from these specialization are enormous. Specialization in any field results in increased competence and improved services. The rapidly evolving clinical oriented pharmacy practice in the hospitals has been hampered in Nigeria, largely because of conflict of interest, inter-professional rivalries and the present structure of our Health centres. Presently, Hospital pharmacists are still largely confined to the traditional role of dispensing of drugs to the patients. The impact of the pharmacist as a patient counselor and as a monitor of drug therapy and its outcome on the patient and in the hospitals is yet to be felt. It is important to state here that the extensive academic background of pharmacists and their traditional role in preparing and providing medicines and informing patients about their use position them to assume responsibility for the management of drug therapy. In an increasing complex health care environment, it has become difficult to compare the effectiveness of different treatments. Health care interventions can no longer be based on opinion or individual experience alone. Scientific evidence build up from good quality research should be used as a guide, and should be adapted to each individual patient's circumstances. While it is true that the undergraduate training in our medical schools and faculties of pharmacy are somewhat general in nature, competence in the varied areas of the medical field requires specialization in these fields. For pharmacist to make meaningful contributions in the area of patient oriented clinical services and for them to be fully integrated into the patients care processes, specialization in various areas of practice is critically important. A position paper on critical care pharmacy services, prepared jointly by the Society of Critical Care Medicine and the American college of Clinical Pharmacy highlighted derived benefits from specialized pharmaceutical services in Hospital pharmacy.

Some of these benefits are:

Better management of drug costs and therapy

Illustration: A patient having spinal TB was placed on streptomycin injection for the first few weeks. The condition did not show any signs of improvement. Input by a Pharmacist specialized in pharmacotherapy, for instance would not only have saved this patient, but cost of wrong and ineffective therapy would have been avoided and the patient would have been better managed.

Reduction in mortality - Clinical pharmacy services such as clinical research, provision of drug information, drug admission histories and participation on a cardiopulmonary resuscitation team were associated with reduced mortality

Reduction in Adverse drug effect- Prospective controlled trials demonstrated that when pharmacists assume responsibility for pharmacotherapy as part of a multidisciplinary health care team, significant reductions in Adverse Drug Events were achieved.

Reduction/Elimination of prescribing errors. A study involving critical pharmacists showed that preventable Adverse Drug Events was reduced by 66% i.e. from about 10 to 4 per 1000 patients per day.

In conclusion, it must be emphasized that to incorporate specialized pharmaceutical services into Hospital pharmacy practice, a number of issues must be considered.

Existing guidelines and literature for clinical pharmacy practice and drug use process in the hospitals must be reviewed and adapted for each area of specialization

Each pharmacy unit in the Hospitals and practitioners should continually strive for the highest level of service possible

Special practice experiences are essential for specialized pharmaceutical services in Hospitals and these specialized experiences are gained through residencies. Hospital pharmacists and Hospital pharmacy administrator should initiate the establishment of pharmacy specialty residency programmes.

Active and participatory emphasis on clinical oriented pharmacy practice should be strengthened and the scope of activities expanded.

The introduction of specialized pharmaceutical services and/or residencies in our tertiary Hospitals in particular, will attract many more young pharmacists into Hospital pharmacy practice and improve clinical services rendered.

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