# ABUSE OF NON-OPIOID ANALGESICS IN LAGOS STATE

# AINA, B. A'; ENIOJUKAN J. F., NWAOCHA, N., AND OLADIMEJI, O. O.

Department of Clinical Pharmacy and Biopharmacy and Department of Pharmaceutics and Pharmaceutical Technology, College of Medicine, University of Lagos, Idi-Araba, Lagos, Nigeria.

\*Correspondence

#### ABSTRACT

Due to enormous availability of the non-opioid analgesics in the Nigeria market and as a lot of people engage in self medication, the question of abuse is no more There is this fear of a long-term analgesic nephropathy and other side effects of non-opioid analgesics a majority of which are long term. This, thus led to the need to determine the pattern of abuse as well as determine the extent to which people are realising that indiscriminate use and abuse of drugs could be of serious damage to their health

The study was carried out and it was discovered that a lot of people do not know the relationship between the generic and the branded drug products and as such stand a chance of using two or more similar drugs but with different names in a bid to relieve all sorts of pain. Also a lot of people cannot say for sure which drug they actually reacted to and as such making it even more difficult to carry out studies on side effects of drugs on patients.

#### INTRODUCTION

The non-opioid analgesics such as aspirin, acetaminophen, dipyrone and the non-steroid anti-inflammatory drugs (NSAIDS) constitute a heterogenous group of compounds differing in chemical structure and showing certain pharmacological and therapeutic actions'.

Non-opioid analgesics are used alone or in combination with opioid analgesics or analgesic adjuvants for enhanced effect. The basic rule is to use the most effective drug or combination of drugs for relief of specific pain site that produces the least serious or distressful effects. As a group, the drugs are commonly administered orally although some are now available as suppositories and also for parenteral administration. Unlike opioid analgesics, tolerance or physical dependence does not develop with use of non-opioid analgesics.

effect in that increasing the dose beyond a abuse even though they do not meet certain level does not produce additional effect 2.

When we hear the words "misuse or abuse of drugs", it is easy to think only in terms of heroin addiction and similar phenomena that make frightening news We may forget that opioid dependence is only one extreme of a whole range of drug taking behaviour and that the social uses of alcohol, tobacco and caffeinecontaining beverages and drugs are merely other points in the same continuum3.

Drug abuse (or misuse) can be defined as the administration of any drug usually by self-administration in a manner that deviates from the approved medical or social patterns within a given culture4. What constitutes "drug abuse" will vary with time and place and is not simply a question of the substance involved. In Western society, a person who drinks an excessive amount of alcohol on one occasion would probably not be thought of as misusing the drug but a chronic alcoholic would, and both would be considered drug abusers by a devout Christian or Moslem<sup>4</sup>.

Further, the term 'drug abuse' conveys the notion of social disapproval, and it is not necessarily descriptive of any particular pattern of drug use or its potential adverse consequences. It is not surprising that for any particular drug, there is a great variation in what is considered drug abuse not only from culture to culture but also from time to time and from one situation to another within the same culture. For example, the use of prescribed opioid analgesics for the relief of pain is quite proper, however, the self administration of the same drug in the same dosages, from relief of depression or tension or to induce euphoria is considered drug Occasional use of apioids or marijuana is considered drug abuse but that of alcohol or tobacco is not, by Government agencies<sup>5</sup> Patterns of drug use that do lead to

Non-opioid analgesics have a ceiling adverse effects may be referred to as drug established criteria for drug dependence

> We live in a drug consuming society. For many people a visit to the doctor is not complete without issue of a prescription and the first sign of a cold has them reaching for analgesics and decongestants.

> Statistics have been presented on the abuse of prescription drugs like methadone, cocaine, heroin and dipinanone.

> The problems of analgesic abuse have been extensively documented and many cases of nephropathy and renal failure have been reported in chronic abusers. These persons invariably have a history of regular ingestion of substantial doses over a period of years. For example, six or more tablets per day of a combined analgesic formulation containing phenacetin for 3 years or more?.

In mild cases the nephropathy is reversible if analgesics are discontinued. In more severe cases renal function may continue to deteriorate despite the withdrawal of analgesics. Other features associated with analgesic abuse include peptic ulceration, gastrointestinal bleeding, anaemia, urinary tract infection, hypertension and psychiatric disturbances. An abnormally high incidence of transitional cell carcinoma of the renal pelvis and bladder tumors have been reported in patients with analgesic nephropathy. Phenacetin has usually been considered to be the causative agent of nephropathy but others like NSAIDS, aspirin and paracetamol have been implicated. Kidney damage has also been reported in patients abusing compound analgesic preparations without phenacetin and less often, in patients taking large quantities of single analgesic 8.5.15

Survey studies in the early 1970's found that 9% of the British population used minor analgesic (aspirin, paracetamol, etc) weekly and nearly 3% used them everyday; self-medication being consistently reported to be most prevalent among younger women

In Canada the incidence of analgesic abuse seemed to be about the same as for narcotic dependence. Addicted persons were generally female and over 40; they took from 25 to more than 100 tablets of aspirin per day, usually for headache<sup>12</sup>.

Excessive use of non-opioid analgesics may be related to the mood elevating effects of the caffeine contained in some preparations or to certain misconceptions about the capacity of such mixtures to relieve tension and increase users ability to concentrate on tedious tasks5.

Much mis-prescribing of pain killers seems to occur. One study of 500 patients with headache in Italy found that the treatments prescribed by doctors varied widely, seemed not to be closely correlated with the sub-type of headache (e.g. migraine, muscle contraction), and seemed not to reflect the recommendations given in controlled studies in the scientific literature. A very large number of drugs were used often in combinations and some had scanty or no rationale for use for the indication of headache<sup>13</sup>. One doctor points out that most of the analgesics on the market are simply "alternatives of fashion or convenience, appreciating this helps prevent "kangarooing" from analgesic to analgesic in a desperate search for some drug that suit the patient better "14.

Although nephropathy is uncommonly associated with the long-term use of individual aspirin-like drugs, the abuse of analgesic mixtures has been linked to the development of renal injury including papillary necrosis and chronic interstitial nephritis15. This may progress to irreversible renal insufficiency if misuse of analgesic continues.

Despite numerous clinical observations and experimental studies in animals and man, crucial details of the problem remains unclear. It is thus possible that chronic abuse of any aspirin-like drug or analgesic mixtures may cause renal injury in the susceptible individual16.

### **OBJECTIVES OF THE STUDY**

This study was designed to determine:

- analgesic
- the different pattern of abuse
- the prescribing pattern of the Pattern of Prescribing/Usage prescribers
- result of abuse.

#### METHOD

- Questionnaires were designed and used as the data collection instruments to obtain information from the following:
- doctors, nurses, pharmacists, dentists.
- non-medical personnel which are members of the public.
- Personal interviews were conducted among the respondents.

These groups of people were chosen randomly all over Lagos State. The medical personnel were from government owned hospitals (State and Federal) as well as privately owned hospitals and community pharmacies.

Non-medical personnel were met in the offices, residences, markets, shops, mechanic workshops and even patients in the hospitals. All data collected were analyzed manually. The listed analgesics in the questionnaire were Paracetamol, Panadol<sup>8</sup>, Alabukun<sup>®</sup>, Aspirin, Daga<sup>®</sup>, and Phensic<sup>®</sup>.

#### RESULTS

150 questionnaires were distributed to each group (i.e. medical and non-medical personnel).

# MEDICAL PERSONNEL Nature of Respondents

The response rate was 71.33%. About 52% of the respondents were females and about 62% were between 21 30 years and those above 50 years were about 5%. 36% of the respondents were doctors, 32% pharmacists, 16% dentists, 13% nurses and others 3%. About 22% of all respondents have 5 10 years audification experience. About 23% of the respondents were and Gynaecology, 16% in Clinical Pharmacy, sleeplessness in some patients.

the most commonly abused non-opioid 4% in Hospital pharmacy, and 32% in other fields which included Internal medicine. Haematology and Paediatrics.

The most commonly prescribed of the the different approaches that can be listed non-opioid analgesics was paracetamol used in educating the general public as to the (Table 4). About 96% of the respondents appropriate use of non-opioid analgesics, prescribed paracetamol, 24% prescribed thus reducing the incidence of nephropathy aspirin and about 18% prescribed others and other disease conditions arising as a comprising of piroxicam, ibuprofen. cataflam, etc. About 40% of the respondents prescribed in generic, 10% in brand name and 50% prescribed both in generic and brand names. About 44% of the respondents prescribed the analgesic singly while 47% prescribed the analgesic in combination with medical personnel which include other drugs, the remaining 9% either way. 10% of the combination were with the listed analgesics. The remaining combination was either with chloroquine (91%), Tetracycline (34%), Ampicillin (56%), Phenylbutazone (13%) and others (13%) (Table 1). The drugs were mainly prescribed in combination due to a co-existing disease state such as malaria infection or any other disease condition with accompanying pain or fever while others prescribe in combination on request of the patients.

The respondents prescribed the listed non-opioid analogsics for pain (81%). headache (68%), fever (53%), malaria (52%) and other conditions including arthritis, somatic pain and infections (6%). Prescribing in the tablet form seems to be the first line of choice as 100% of the respondents prescribed the tablet dosage form. About 16% prescribed capsule, 21% syrup, 13% injection and about 14% suppository dosage forms.

# Side Effects

There were only about 28% of reported side effects/problems of the listed nonopioid analgesics. The reported side effects/problems included stomach pain/problem (50%), sleeplessness (7%) and itching/rashes (43%) (Table 3). Aspirin and Phensic accounted for most of the complaints of stomach pain/problem. Itching/rashes was noticed mainly in patients taking chloroquine in combination with the non-opioid analgesics. Phensic<sup>®</sup> and specialists in their field with 20% in Obstetrics Alabukun were reported to cause

# Mode of Use

75% of the respondents prescribed paracetamol after food, 22% before food and 3% either way. About 65% prescribed Aspirin after food and 35% before food. About 80% prescribed Phensic<sup>R</sup> after food and 20% before food. Alabukun\* was prescribed after food while Daga<sup>2</sup> was prescribed before food.

Majority of the prescribers prescribed 2 tablets at once with 22% prescribing 1 tablet of Aspirin and about 3% prescribing 3 tablets of paracetamol, one sachet of Alabukun<sup>®</sup> was prescribed at once. About 56% of respondents prescribed the analgesics for use occasionally, 27% for use three times daily, 5.6% two times daily, 7.5% four times daily and about 2% four times weekly.

# NON-MEDICAL PERSONNEL Nature of Respondents

The response rate was 94%. About 50% of the respondents were females. 51% of the respondents were between ages 21 30 years and those above 50 years accounted for about 6%. About 42% of the respondents attained secondary school level, 21% attained university level, 16% polytechnic and 6% primary school level. Others which accounted for about 14% ranged from those that attained college of education, standard II, advanced level, NCE, correspondence college, commercial school to those that did not go to school at all.

#### **Awareness**

Majority of the respondents were aware of the listed non-opioid analgesics and even those that were not listed. 99% were aware of paracetamol, 96% aspirin and phensic\*, 90% Alabukun\*, 92% Daga\*, and 97% were aware of Panadol®. About 55% of the respondents were aware of other forms of non-opioid analgesics not listed and these include Panadol extra\*, Novalgin\*, Cataflam<sup>®</sup>, Dolviran<sup>®</sup>, Pengo<sup>®</sup>, Indomethacin, Laila<sup>R</sup>, Feldene<sup>R</sup>, Saridon P<sup>R</sup>, Ibuprofen, Optialidon and a host of others.

#### Usage

A great percentage of the respondents that were aware of the non-opioid analgesics actually used them (Table 4). 97% have used paracetamol, 62% Aspirin, 64% Daga\*,

55% Alabukun<sup>®</sup>, 96% Panadol<sup>®</sup>, 78% Phensic<sup>®</sup> and 49% have used other forms of non-opioid analgesics not listed. There was statistically significant difference in the response obtained for the type of analgesic prescribed by the medical personnel and the type used by the non medical personnel for example 29% of the medical personnel prescribed Panadol<sup>k</sup> while 96% of non medical personnel used Panadol\*.

The non-opioid analgesics were used by different persons for different ailments. 84% used the analgesics for pains, 83% for headache, 18% malaria, 0.7% for diarrhoea, 45% for fever and about 3% for other types of ailment such as cold, migraine and stomach upset (Table 2).

About 57% of the respondents used the drug singly, 39% used the analgesics in combination while 4% used them either way (Table 1). Amongst those that used the drugs in combination, about 74% used the listed analgesics in combination with other drugs while the rest used combination of the listed analgesics. The other drugs used in combination include chloroquine (73%), Ampicillin (18%), Tetracycline (16%) and multivitamin and blood supplements. About 46% of the respondents used the drugs in combination as recommended to them and 21% used the drugs in combination to make the analgesics more effective.

#### On Whose Recommendation

A doctor recommended these analgesics for about 56% of the respondents, a pharmacist for 18%, a nurse for 15%, self recommendation for 27%, a parent for 13% and a friend or relation for 10% of the respondents.

#### Side Effects

Majority of the respondents (over 90%) did not have problem with any of the listed and unlisted non-opioid analgesics except in the case of Aspirin where only about 79% claimed not to have problems. The problems encountered include headache, stomach pain, sleeplessness, diarrhoea and others (which include restlessness, weakness, drowsiness, hunger and nose bleeding) (Table 3).

#### Mode of Use

Majority of the respondents (90%) took 2 tablets of the analgesics at once. About 68% of the respondents took one sachet of Alabukun<sup>®</sup> at once while 32% took two sachets at a time. About 6% of the respondents took three (3) tablets of paracetamol or Panadol<sup>®</sup> at once. About 57% used the non-opioid analgesics occasionally while about 11% used them twice daily, about 6% once daily, 9% on weekly basis or rarely.

# DISCUSSION

Non-prescription drugs including nonopioid analgesics are widely used for selfmedication in both developed countries 17, 18, 19 and developing countries 20, 21, 22. These drugs are invaluable, allowing consumers to manage minor medical problems rapidly, inexpensively and conveniently. Pain and headache are two major medical symptoms that make people seek for medical help or resort to self-medication. Non-prescription or non-opioid analgesics are used/abused to treat these symptoms. These analgesics are readily available as over the counter drugs which the consumer can purchase without a prescription from a physician. attempt should therefore be made to encourage the appropriate use of these nonprescription analgesics and at the same time to guard against unacceptable risks.

This study confirmed that non-opioid analgesics are readily available and accessible in Lagos State and we can use this as an index of availability and accessibility of non-opioid analgesics in the country since Lagos is the nerve centre of commercial activity in the country. Most people have heard and have actually used one or more of these analgesics. Paracetamol seems to be the most popular among them since over 90% of the respondents used this analgesic to treat pain and headache. This is in line with the fact that these two symptoms are two major conditions for which non-opioid analgesics are indicated. This result is not surprising because about 79% of the respondents attained at least minimum of secondary school level, so they can read and write and are likely to be receptive to counseling.

It was observed that those that used the Majority of the respondents (about non-opioid analgesics to treat malaria felt 80%) took the analgesics after food, that they were suffering from malaria before using the drug and got better afterwards. This is because a lot of people attribute a slight fever or headache to malaria attack.

These analgesics were recommended to about 56% of the respondents by doctors while only 18% by pharmacists. One might have expected the pharmacist to be the first or next to doctors as the person recommending these analgesics to the consumers. Many reasons could be responsible for this. One is that the doctors would see more patients in their practices than do the community or retail pharmacists. Also the pharmacist may not be available at the counter where the consumer will purchase these analgesics since they are nonprescription or over the counter drugs and the counter clerk and/or consumer may not see any danger in purchasing or taking a drug like paracetamol on daily basis.

In this study, it was discovered that among the respondents, those that partook in more tedious jobs such as mechanics and carpenters used the drugs more frequently than the others involved in less tedious jobs such as traders and hairdressers. Others used the analgesics due to habits or availability of the drugs.

It is soothing to find that more than half of the respondents (about 57%) used the analgesics singly and occasionally and only about 11% used the analgesics in combination with another analgesic among the listed ones.

The remaining 32% used the analgesic in combination with other drugs like chloroguine, ampicillin, tetracycline and blood/vitamin supplements.

The reason given by those that used combination of the listed analgesics was to make the analgesics more effective. It was also discovered that this group could not differentiate between generic and brand names. This group of respondents need counselling/education as to the disadvantage of such analgesics There is ceiling effect to combination. analgesics use so this combination is a waste of money and a danger to health of the consumer.

Majority of the respondents (about 90%) took two tablets of either paracetamol, Panadol<sup>®</sup>, aspirin and Phensic<sup>®</sup> at once. This tallies with the standard dose for these

analgesics which is two tablets at once for an Alabukun<sup>®</sup> and Panadol extra<sup>3(73)</sup> adult. This is not surprising because of the level of education of most respondents.

The few that took three/four tablets gave the reason that two tablets never worked for them. These ones need to be counselled on the danger of nephropathy with this over dosage after a long period.

The few that took one tablet believed taking that two tablets is two much for them and that one tablet usually work for them. This might be due to idiosyncrasy. About 68% took one sachet of Alabukun which is the standard dose for Alabukun<sup>8</sup>. The others took two sachets and the reason given is that one sachet never worked for them and that the kind of tedious jobs they (carpenters, mechanics and drivers) are doing require that they should take more than the usual dose. These group of people need to be counselled as to the danger of gastrointestinal bleeding and insomnia because of aspirin and caffeine which are the active contents of Alabukun<sup>® (23)</sup>.

About 80% of the respondents took aspirin. Phensic<sup>®</sup> and Alabukun<sup>®</sup> after food while the rest took them before food or either way. Aspirin which is the active constituent of these drugs should be taken after food because of the problem of austrointestinal bleeding. The respondents or the public need to be informed about this<sup>23</sup>

Majority of the respondents (over 90%) did not have problem with the use of the listed and non-listed analgesics except in the case of aspirin where about 79% did not have problems. The problems reported include headache (39%), stomach pain (29%), sleeplessness (19%), diarrhoea (1%) and others including restlessness, weakness, drowsiness, hunger and nose bleeding accounted for about 11%. Though it was not possible to determine which of the drugs actually caused any of these problems because of combination of drugs but some of these problems may be caused by aspirin and other drugs containing aspirin e.g. Phensic<sup>\*</sup> and Alabukun<sup>®</sup> (aspirin + caffeine) and the non-steroidal anti-inflammatory drugs

Headache can be a follow-up of the sleeplessness caused by some of the components of the drugs e.g. caffeine in

In this study, it was also found that the most commonly prescribed of the listed nonopioid analgesic was paracetamol. About 96% of the medical respondents prescribed paracetamol while about 24% prescribed This is not surprising because paracetamol is safer than aspirin in terms of short-term adverse effects and has the same analgesic property as aspirin. Aspirin can cause gastrointestinal bleeding if taken on empty stomach, but this is not a problem with paracetamol. It has even been discovered that it might be better to take paracetamol on empty stomach for patients requiring fast therapeutic effects<sup>24</sup>. Aspirin should also be used with caution in asthmatic and ulcer patients.

About 40% of the respondents would prescribe in generic name while 10% would prescribe brand name and 50% would prescribe in both generic and brand names. This does not tally with the recommendation of WHO that says all prescription (100%) should be written in generic names of the drug<sup>25</sup>.

The analgesics were prescribed either singly or in combination with other drugs. Those prescribed in combination were due to co-existing diseases such as malaria, infection or any other disease condition with an accompanying pain or fever while others were prescribed on the request of the patients.

The use of analgesics in malaria was not necessarily for malaria but due to other accompanying symptoms which include pain, fever and headache. This might not be necessary as the symptoms are mainly due to presence of the plasmodium parasite in the blood an as such will disappear if the blood is cleared of the plasmodium parasites with s suitable blood schizonticide.

The reported cases of side effects include stomach pain/problem, itching/rashes and sleeplessness. itching/rashes was noticed mainly in patients taking chloroquine with the analgesics and such could be due to the chloroquine and not the analgesics since it has been documented that itching is one of the side effects of chloroquine in some individuals. Aspirin and Phensic<sup>®</sup> accounted for most of the complaints of stomach pain/problem and this might be due to the ulcerative effect of aspirin on the gastrointestinal tract. Phensic<sup>®</sup> is a brand of aspirin. Phensic<sup>®</sup> was also reported to cause sleeplessness in some patients.

About 75% of the respondents prescribed paracetamol after food and 25% prescribed it before food or either way. There is no cause for alarm here, since it has been found that it might even be better to take paracetamol on empty stomach for fast therapeutic effects<sup>74</sup> and since it does not cause aastric ulceration.

About 35% of the respondents prescribed aspirin before food. This is out of order because aspirin is a drug widely known to cause gastric ulceration when taken on empty stomach. Phensic<sup>®</sup>, Alabukun<sup>®</sup> and Daga<sup>®</sup> are not commonly prescribed by the respondents (about 7.5%) because these are brand names and the prescribers are expected to prescribe in generic names according to WHO standard<sup>25</sup>.

The few that prescribed them, prescribed Alabukun<sup>®</sup> and Phensic<sup>®</sup> after food while Daga<sup>®</sup> before food. This is fair enough and acceptable because Phensic<sup>®</sup> and Alabukun<sup>®</sup> contain aspirin while Daga<sup>®</sup> contains paracetamol.

Most respondents prescribed two tablets of paracetamol at a time which is the

standard dose for an adult. All the respondents who prescribed Alabukun<sup>k</sup>, prescribed one sachet at a time and those that prescribed Daga<sup>k</sup> and Panadol<sup>k</sup> prescribed two tablets at a time which are the standard doses for these drugs. About 78% of the respondents prescribed two tablets of aspirin and the rest one tablet at a time. This variation might be due to individual patient factors. It has been documented that one quarter to one whole tablet of aspirin can be taken daily for secondary prevention of thrombotic cerebrovascular or cardiovascular disease<sup>26</sup>.

In this study we were not able to confirm the reason for prescribing one tablet at a time. But all said and done, we can say there was rational prescribing of the dose of the analgesics listed.

# RECOMMENDATION

- \* Pharmacists should be available at the counter to counsel consumers on proper
- \* use of analgesics and other over-thecounter druas.
- \* Pharmacists should educate the consumer on the need to use analgesics singly and
- \* not in combination with other analgesics
- \* Pharmacists should educate the consumer on use of the analgesics in relationship to food.
- \* Prescribers should be educated or be made aware of WHO drugs use prescribing

All the indicators.

- \* Pharmacists should educate the consumers on the long-term toxicity effect of pro-longed use of these analgesics.
- \* Pharmacists should educate their counter clerks on proper use and long term toxicity of these analgesics for onward counselling of customers when the pharmacist is not available.

#### CONCLUSION

From the results it can be seen that the listed analgesics - paracetamol, Panadol<sup>®</sup>, Phensic<sup>®</sup>, aspirin, Daga<sup>®</sup> and Alabukun<sup>®</sup> and the other non-listed non-opioid analgesics are indeed readily available for use in Lagos State. Although the population sampled represent a minor percentage of Lagos population, it could be seen that some percentage of people living in this part of the country actually abuse the analgesics.

Most of the more serious problems such as nephrotoxicity or hepatotoxicity with the prolonged use of non-opioid analgesics are usually long term, making it even more serious as the side effect at that stage may be irreversible. As such, more public enlightenment campaign should be embarked upon to create awareness as to the long term effects of use of non-opioid analgesics which are readily available in the Nigerian drug market.

TARIE 1. COMPINATION LISE

	Medical (%) n = 107	Non-Medical (%) n = 141
Listed analgesics	10	74
Chloroquine	91.5	73
Tetracycline	34	16
Ampicillin	60	18
Others (NSAIDS, Tonic, etc)	13	16

**TABLE 2: INDICATION FOR USE** 

INDICATION	MEDICAL (%) n = 107	NON-MEDICAL (%) N = 141
Pain	81	84
Fever	53	45
Headache	68	83
Malaria	52	18
Diarrhoea		<1
Dysentery		and the second state of the second
Others	6	3

TABLE 3: SIDE EFFECTS

,	MEDICAL (%) NON-MEDICA n = 107 n = 14	
Stomach problem	50	29
Sleeplessness	7	19.4
Itching/Rashes	43	
Diarrhoea	-	1.4
Headache		39
Others	-	11

# TABLE 4: PRESCRIBED/USED

	MEDICAL (%) n = 107	NON-MEDICAL (%) n = 141
Paracetamol	96	97
Aspirin	24	62
Phensic <sup>®</sup>	5	78
Alabukun <sup>®</sup>	2	55
Daga®	1	64
Panadoj <sup>R</sup>	29	96
Others	18	49

# REFERENCES

- 1. Flower RJ, Moncada S, Vane JR. (1991) Analgesics antipyretics and the anti-Inflammatory agents and drugs employed in the treatment of gout. In: Gilman A.G. Goodman, L.S., Ran, T.W., Mirad (eds). The pharmacology basis of therapeutics. 8<sup>th</sup> edition, Macmillan, New York, 674-715.
- 2. Kantaur TG. (1984) Peripherally acting analgesics. In: Kular, M, Pastemak, G. (eds). Analgesics Neurochemical Behaviour & Clinical Perspectives. Raven Press, New York, 289-314.
- 3. Maddack DH.(1987) Drug Abuse: A Guide for Pharmacists. The Pharmaceutical Press, London.
- 4. Edward G, Arif A. and Jaffe J. (1983) Drug Use and Misuse: Cultural Perspectives, London. Croom Helm,
- 5. Jerome H Jaffe. (1991) Drug addiction and drug abuse in Goodman & Gilman's The Pharmacological Basis of Therapeutics. 8 Ed. Vol. Pp52-573.
- 6. Home Office (1986). Tackling Drug Misuse: a summary of the government's strategy. 2<sup>rd</sup> edn., London, Hame office.
- 7. Martindale: (1996) The Extra Pharmacopoeia. 31<sup>et</sup> edn., 1-102.
- 8. Perneger T.V. et al. (1994) Risk of kidney failure associated with the use of aceta-minophen, aspirin and non-steroidal anti-inflammatory drugs. N. Engl. J. Med., 331, 1675-9.
- 9. Sandler DP. Et al. (1989) Analgesic use and chronic renal disease. N. Engl. J. Med., 320, 1238-43.
- Dubach U.C. et al. (1991) An epidemiology study of abuse of analgesic drugs: effects of phenacetin and salicylate on mortality and cardiovascular marbidity (1968-1987). New England Journal of Medicine. 324, 155-60.
- 11. Edward G. and Brisch C. (1981). Drug problems in Britain, London. Academic Press.
- 12. Boyd EM, and Hottenroth SMH. (1968) Toxicity and Applied Pharmacology, 13, 80.
- 13. Scarani G, Berghei E. and Tognani G. (1987) Pharmacological treatment of a primary headache. Headache. 27, 345-50.
- 14. Laurence DR and Bennett PN.(1987) Clinical Pharmacology. Edinburgh, Churchill Livingstone. 6th Edition, pg301.
- 15. Kincaid-Smith P. (1986) Effects of non-narcotic analgesics on the kidney. Drugs 33, (Suppl. 4), 109-128.
- 16. Maher JF. (1984) Analgesic nephropathy. American Journal of Medicine, 76, 345-348.
- 17. Haggierty RJ and Ragmann RG. (1972) Non-compliance and self-medication. Two neglected aspects of paediatric pharmacology. Paediatrics Clinics of North America 19, 101-15.
- 18. Chaiton A, Spitzer WO, Roberts RS et al. (1976) Patterns of medical use. A community focus. Canadian Medical Association Journal 114, 33-7.
- 19. Silverman HI. (1983) Opportunities to be expected in the over-the-counter drug market. American Journal of Pharmacy, 155, 33-41.
- Raynal AL. (1985) Use of over-the-counter medications in rural Matebeleland, Zimbabwe: the case for upgrading the dispensing skills of rural store-keepers. Central Africa Journal of Medicine, 31, 92-7.
- 21. Handon A, Van der Geest S. (1987) Hazards of self-medication. WHO Forum 8, 469-71.
- 22. Stein CM, Gora NP, Macheka BM, (1989) Self-medication in urban and roral. Zimbabwean communities. British Journal of Clinical Pharmacology, 27, 741.7.
- 23. British National Formulary (BNF) Number 29 (March 1995), pg. 173 & 182.
- 24. Enjojukan JF and Aina BA. (1998) Effect of food and antacid on Paracetamol Bioavailability. Journal of Pharmaceutical Sciences and Pharmacy practice 4(2), 53-56.
- 25. WHO/DAP (World Health Organization/Action Programme on Essential Drugs). 1993. How to investigate drug use in health facilities. Selected drug use Indicators WHO/DAP/93. 1 Geneva. WHO/DAP.
- 26. BNFOp cit. P.104.