Ahmadu Bello University, Zaria

OVER-THE-COUNTER PAIN KILLERS: RELIEF OR BURDEN?

AN INAUGURAL LECTURE

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PREAMBLE

I have the honour to stand before you today to share my experiences over years as pharmacologist, specifically in my chosen area of specialization, Toxicology and Pharmacokinetics. Pharmacology is the study of effects of drugs and chemicals on the living system. It is broadly divided into pharmacodynamics and pharmacokinetics. While pharmacodynamics is the study of what drugs do to the body, pharmacokinetics is what body does to the drugs in relation to absorption, distribution, metabolism and excretion. Toxicology is study of adverse effects of drugs and chemicals on the living system.

This inaugural lecture is the fifth in the Faculty of Pharmaceutical Sciences, third in the Department of Pharmacology and Therapeutics and first in the present administration of the University, I thank the Vice Chancellor, Prof Ahmad Adamu for this great opportunity.

This topic of today's lecture is **Over-the-Counter Pain Killers: Relief or Burden** is timely looking at the enormous precipitating factors leading to occurrences of pains and associated misuse of painkillers in our society. This is a public health problem the topic seeks to address, which has clinical application with pharmacological basis.

I pray to Almighty Allah to guide me through the lecture and may the knowledge the lecture encompasses benefits humanity.

SECTION ONE

The Beginning of a Great Journey

Introduction

I started my Professional Practice as a Community Pharmacist at Gboko in Benue State in the year 1992 after my NYSC. The period marked the beginning of a new professional exposure since my internship and NYSC were conducted in the hospital setting. Among the various encounters with the patients; the phenomenal episode which etched into my memory was when patients walked into the Pharmacy in many occasions and said, "Give me mix." For the first time I paused and enquired further; only to realize that they meant I should mix various painkiller (analgesic) tablets for them. These observations continued as a community pharmacist, and in fact it became the beginning of what converged to become my research interest. In such a "mix", usually not less than five different painkiller tablets were combined and folded in different papers as a unit dose, taken once, twice or three times daily. Pain killers that are involved are the over-the-counter analgesics acting mostly peripherally and not through the central nervous system. This practice constitutes what is referred to as analgesic misuse.

Drug misuse

Drug misuse is when drugs are taken for a purpose or in a manner that does not follow legal or medical guidelines. This includes:

1. Taking the drug in wrong dose

2. Wrong time of taking drug

3. Incorrect duration of taking a drug

4. Taking the drug for wrong purpose

5. Polypharmacy that does not follow legal and medical guidelines, (NIDA,2024a).

Drug abuse

This refers to misuse of illicit or any psychoactive substances in order to feel high and are associated with altered thinking, behavior and body functions, (NIDA,2024b).

Over-the-counter (OTC) medicines

Over-the-counter (OTC) medicines are medicines that could be bought without a prescription against those prescription drugs that can only be obtained with a prescription. The classification of registered drugs as OTC may differ from country to country depending on the existing regulatory and legal provisions as well as on the organization of the healthcare system. In some developed countries, like Germany for instance, OTC medicines can be purchased only in pharmacies where professional consultation of a pharmacist can be readily available and access to the needed information is given. In many less-developed countries, where OTC drugs are also sold in drug shops or even in ordinary shops, professional advice and information may not be available. This can pose

serious problems when a high proportion of users is illiterate and unable to understand the information in the package inserts. Decisions concerning the classification of OTC and prescription medicines should be primarily based on scientific criteria (efficacy, safety, quality) and health considerations (health needs, healthcare system factor). The development of an OTC formulary can be of significant help in dealing with this problem (Budiono, 2001). Examples of over-the-counter pain killers are paracetamol, aspirin, ibuprofen and diclofenac. They are sometimes combined with caffeine.

Paracetamol

Paracetamol is the commonest OTC used by patients. It is used for mild to moderate pain. It is tolerable with minimum side effects. Unlike non-steroidal anti-inflammatory drugs such as aspirin, diclofenac, it has minimum effect on the gastrointestinal tract. It can be used in both adults and children.

Diclofenac

Diclofenac is one of the Non-steroidal anti-inflammatory drugs used for pain, fever and inflammation. It is some time co-formulated with paracetamol.

Aspirin

Aspirin belongs to the group of salicylates and effective as analgesic, anti-inflammatory and antipyretic drug. Also used for acute (and prophylactic) treatment of migraine and tension type headache. It has pronounced effects on causing gastrointestinal side effects than the other over-the-counter pain killers.

Ibuprofen

Ibuprofen offers advantages over aspirin for many patients since it is better tolerated. It is effective analgesic, anti-inflammatory and antipyretic drug. Ibuprofen used for treatment of dysmenorrhea, migraine, gout, osteoarthritis, and systemic lupus erythematosus.

Caffeine

Caffeine is mild stimulant used as psychoactive drug. It is present in soft drinks, coffee, tea, cocoa, chocolate and numerous prescriptions and over –the-counter drugs. It increases nor-epinephrine secretion and enhances neural activity in numerous brain areas. Caffeine is absorbed from the digestive tract; it is rapidly distributed throughout all tissues and easily crosses the placental barrier. Caffeine is thought to act by competitive antagonism at adenosine receptor. Adenosine is a neuromodulator that affects many functions in the CNS. It is thought to increase absorption of many over-the-counter pain killers.

Pain

Pain is an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage, (Raja, *et al.*, 2020). About 20-33% of adults live with chronic pain, (Zhu *et al.*, 2025). It could be mild, moderate or severe. It could also be acute or chronic. Pain is often symptom of disease and one of the most common reasons for an individual to seek medical attention. It can be classified as nociceptive, inflammatory or neuropathic. Pain if not adequately

managed can cause significant suffering, affects individuals' ability to carry out daily activities and brings about diminished quality of life. Pain, especially if it becomes chronic is an important clinical, societal and economic problem. Globally low back pain attributable to occupational factor alone brought about 216.1billion US Dollar economic losses in 2019 (Chen *et al*., 2023). For these reasons it becomes paramount to effectively manage pain, but not to the extent of being over zealous to the point of misuse.

Non-pharmacological management of pain

The objectives of non-pharmacological management of pain are to reduce inflammation, improve function and reduce stress that intensifies pain. The following are non-pharmacological options:

1. Physica and movement-based (exercise therapy, physiotherapy etc.)
2. Psychological and behavioural (cognitive behavioural therapy, biofeedback etc.)
3. Interventional physical modalities (Acupuncture, acupressure etc.)
4. Lifestyle and self-management (sleep hygiene, weight management)
5. Others (hydrotherapy, virtual reality etc.), (Zhang *et el.*, 2024).

Over-the-counter pain killers' relief

These pain killers bring about relief by inhibiting either cyclooxygenase I or II enzyme or both. When tissue is injured or inflamed, cyclooxygenase (COX) enzymes convert arachidonic acid into prostaglandins. These prostaglandins mediate pain, fever, inflammation, and other effects. These pain killers block production of prostaglandins and are used to relief pain, fever, inflammation, and other effects.

Clinical uses

Analgesia (pain reduction)

They are effective for mild to moderate pain, acute injuries and post-surgical pain with opioids. Common ones used: ibuprofen, diclofenac, naproxen, ketorolac, paracetamol.

Antipyretic (Fever reduction)

They are effective in fever due to infections, post-vaccination and other causes. Ibuprofen and naproxen are common in adults while paracetamol is preferred in children due to lower gastrointestinal risk.

Anti-inflammatory*: (less swelling, redness, heat)*

They are effective in the following conditions:

1. Arthritis such as rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, gout, psoriatic arthritis

2. Soft tissue inflammation such as tendonitis, bursitis, synovitis

3. Other: Pericarditis, bursitis, some inflammatory eye conditions

   Naproxen and indomethacin are often preferred for gout arthritis.

Antiplatelet: Block platelets aggregation (low doses), aspirin is commonly used.

Over-the-counter pain killers' burden

The burden put on us are the adverse effects of these drugs. They include gastrointestinal tract effects. Paracetamol overdose can lead to liver damage. Salicylism is caused by aspirin. There is epigastric pain, nausea, heartburn with ibuprofen, Hepatic disorder with diclofenac.

On the kidney there is acute renal failure, sodium retention due to inhibition of prostaglandin synthesis. There are also analgesic nephropathy and papillary necrosis..

End Stage Renal Disease -ESRD

Reports have shown that rampant abuse of analgesics and analgesic combinations may lead to renal damage severe enough to cause end stage renal disease -ESRD- (Linton, 1980; Waddington *et al*., 2015; Ozer *et al*., 2017) or even the development of urogenital cancer (Mohoney, 1977). In United States, the cost of treating ESRD by either

dialysis or organ transplantation was $6.6 Billion in 1991 (Inglehart, 1993). In 2020, the estimate stood at $50.8B (USRDS,2020). It has been estimated that patients on therapy for ESRD due to analgesic abuse represent about 3% of cases in Queensland, Australia (Buckalew, 1986). For the period of 2002-2015 in the U.S about 200 cases per year was recorded (USRDS, 2020). In Nigeria such figures are scarcely available for the consumption of the public and regulatory bodies. However, a case of one 55-year old business man with analgesic nephropathy was reported by Okafor and his colleagues in 2012, (Okafor *et al.,* 2012). In Nigeria the following costs have been reported: hemodialysis (HD)~$42,785, peritoneal dialysis (PD) ~$47,971/year, (Okafor and Kankam,2012).

How it all started

The idea that came to my mind when I joined the services of Ahmadu Bello University was to pursue my research in the area of analgesics (pain killers). I started by looking at effects of storage condition on the pharmacokinetics of paracetamol in Zaria in human volunteers. Stability of a pharmaceutical product is critical to its effectiveness which can be affected by its storage conditions. Samples of paracetamol from different premises and drug stores in Zaria were evaluated.

Pharmacokinetics

Pharmacokinetics is the study of drug absorption, distribution, metabolism and excretion over time. In other words, it is the study of how the body handles drugs. It is the journey by the drug as it enters and leaves the body.

Absorption, distribution, metabolism and excretion are stations describing the pattern of the journey.

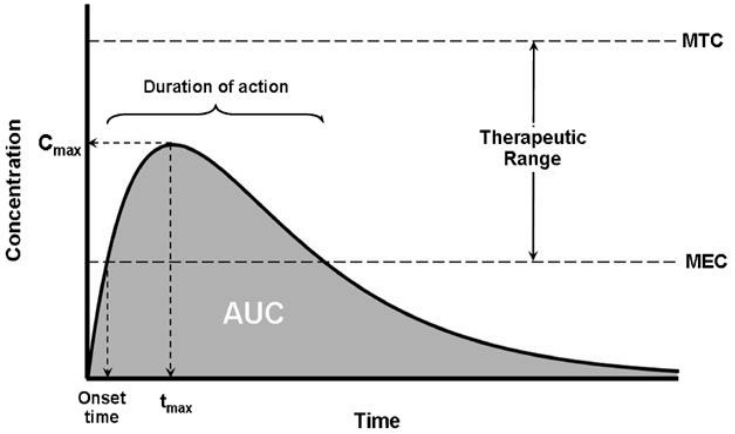

Figure 1: Concentration - time curve of drug

Keys: Cmax = Maximum concentration, Tmax = time taken to achieve maximum concentration,MTC = minimum toxic concentration, MEC = minimum effective concentration, AUC = Area under the curve

Absorption

Absorption is the movement of a drug from its site of administration into the blood referred to as central compartment and the extent to which this happens. Solid dosage forms they first require dissolution of the tablet or capsule. This liberates the drug which is subsequently absorbed into systemic circulation.

Distribution

Drug distribution is the conveyance of drug from the systemic circulation to tissues. After absorption or direct administration into the bloodstream, a drug distributes into the tissues depending on the particular physicochemical properties of the drug. Liver, kidney, brain, and other well-perfused organs receive majority of the drug first. The second stage involves movement of drugs to muscle, most viscera, skin, and fat which is at slower rate.

Factors influencing drug distribution are cardiac output, regional blood flow, capillary permeability, tissue volume, regional differences in pH, transport mechanisms available, the permeability characteristics of specific tissue membranes, extent of plasma protein and specific organ binding.

Metabolism

Drug metabolism is a process whereby a drug is rendered inactive in most cases. Sometimes the drug can still remain active or more active after metabolism. Drug metabolism brings about changes in the chemical structure of a drug to produce inactive drug metabolite. Metabolism also renders the drug compound more water soluble and therefore more easily excreted. Metabolism, sometimes results in bioactivation of a drug. Inactive drugs that undergo metabolism to an active drug are called prodrugs and the process is referred to as bioactivation. Example is the antitumor drug cyclophosphamide which

is bioactivated to an electrophilic cell-killing derivative, phosphoramide mustard.

Excretion

Excretion is a process whereby drugs are conveyed from the internal to the external environment of the body. The principal organs involved in this activity are the kidneys, lungs, biliary system, and intestines. Kidney is the primary organ of removal for most drugs especially for those that are water soluble and not volatile. The three principal processes that determine the urinary excretion of a drug are glomerular filtration, tubular secretion, and tubular reabsorption.

Pharmacokinetic parameters

Pharmacokinetic parameters are used to describe drug absorption, distribution, metabolism and excretion. They are the markers used to describe what happens at each station. They include bioavailability, Tmax, Cmax, absorption rate constant, half-life, clearance, elimination rate constant, area under the curve (AUC) and lag time.

Degradation of pharmaceutical products

There are many factors that could affect such journey which include the way the drug is stored, as poor storage condition could lead to degradation of the drug. Degradation of pharmaceutical products are classified as due to chemical, physical and biological mechanisms. Degradation may be due to one or more of these mechanisms.

Possible results of pharmaceutical product instability could be one or more of the followings.

1. Loss of active drug e.g. aspirin hydrolysis, oxidation of adrenaline

2. Loss of vehicle e.g. evaporation of alcohol from alcoholic mixtures, evaporation of water from oil-in-water creams

3. Loss of content uniformity e.g. impaction of suspensions, creaming of emulsions

4. Reduction in bioavailability e.g. ageing of tablets resulting in a change in dissolution profile

5. Loss of pharmaceutical elegance e.g. fading of coloured solutions or tablets

6. Production of potentially toxic materials e.g. breakdown products from drug degradation. All these could affect how drug travels in the body.

In order to maintain the stability of a drug formulation, it should be suitably packaged and stored. There should be no damage to the drug due to high temperature or exposure to sunlight. All drugs have expiring date but factors such as contact with water, changes in temperature, exposure to air or light could affect expiring date.

Drug interactions

Drug interactions involve drug-drug and drug-food interactions that may affect drug effect when drugs or

drugs with foods are given together. It could be pharmacokinetic drug interaction affecting absorption, distribution, metabolism and excretion which may increase or decrease concentration. It could be pharmacodynamic drug interaction acting through the mode of actions of the drugs. Usually, they may either increase the activity of other drugs leading to enhanced therapeutic outcome and sometimes toxicity or decrease activity leading to therapeutic failure.

1. **Effects of storage condition on the pharmacokinetics of paracetamol in Zaria in human volunteers.**

We started our studies by looking at effects of storage condition on the pharmacokinetics of paracetamol in Zaria in human volunteers. In this study**,** samples of paracetamol from different premises and drug stores in Zaria were collected and evaluated in healthy human volunteers. The plasma concentrations were used to determines the pharmacokinetic parameters. The plasma concentrations were not affected and time taken to attain maximum concentration was also not affected. Area under the curve from zero to infinity, AUCo-infinity, was statistically affected in two sites. There was bioequivalence from all the sites as differences in their relative bioavailability was not more than 25%. In that study we were able to conclude that the tested storage conditions did not affect the pharmacokinetics of paracetamol tablets significantly, (Zezi *et al.*, 2003).

2. Alteration of saliva pharmacokinetics of oral paracetamol by diclofenac on co-administration in healthy human volunteers.

Subsequently, we conducted pharmacokinetic drug interaction to determine how one drug could affect the drug's journey in the body if they are combined. We then looked at alteration of saliva pharmacokinetics of oral paracetamol by diclofenac on co-administration in healthy human volunteers. This study was an example of drug-drug pharmacokinetic interaction.

In our study, the effect of 50 mg diclofenac on the pharmacokinetics of 1000 mg of paracetamol co-administered orally, in healthy human subjects was examined. The drug saliva level of paracetamol was determined using ultraviolet spectrophotometric method. Higher concentrations of paracetamol were observed on co-administration compared with administration of paracetamol tablets alone. There was statistically significant increase in bioavailability parameters, AUC and C_{max} (maximum concentration) between paracetamol alone and co-administration. There was statistically significant reduction in volume of distribution and clearance between paracetamol alone and co-administration. There was no statistically significant change in the other absorption and elimination pharmacokinetic parameters between paracetamol alone and co-administration. There was also insignificant difference in the time maximum (T_{max}) between paracetamol alone and co-administration. The study showed that diclofenac when concurrently administered with paracetamol affects pharmacokinetics of

paracetamol. This work was published in Nigerian Journal of Pharmaceutical Sciences (Yunusa *et al.,* 2019).

3. **Effects of vitamins A And E supplementation on alteration of levels of some liver enzymes and kidney electrolytes caused by aspirin in Wistar rats.**

Here we determined effects of vitamins A and E supplementation on the alteration of levels of some liver enzymes and kidney electrolytes caused by aspirin in Wistar rats. Supplementation of vitamins A or E reduced levels of alkaline phosphatase and aspartate transaminase elevated by 50 and 100 mg/kg aspirin. Serum concentrations of sodium ion were restored to near control values after 50 mg/kg aspirin and vitamins A and E administration (Mahdi *et al*., 2018).

4. **Effect of environmental exposure on the pharmacokinetics of ciprofloxacin tablets marketed in Gombe State using healthy human volunteers.**

In this study we concluded that it is in Gombe south that environmental exposure affected the pharmacokinetic profile of ciprofloxacin particularly absorption and elimination rate constants of ciprofloxacin, (Buba, 2016). This was attributed to the fact that dissolution and assay parameters of this drug after exposure in Gome south did not meet BPC 2002 specifications. This may have serious clinical implications, (Usman *et al.*, 2017).

5. **Effect of *Cola acuminata* (P. BEAUV.) Schott & endl (malvaceae) on the pharmacokinetics and toxicokinetics of ciprofloxacin in Wistar rats,**

In this study, we went further to examine pharmacokinetics of ciprofloxacin under the context of drug toxicity (toxicokinetics) in addition to kinetics in therapeutic doses (pharmacokinetics), (Yunusa, 2025)**.**

SECTION TWO

Some Pharmacological Studies of Paracetamol and Paracetamol Co-Formulated with either Aspirin, Caffeine, Diclofenac or Ibuprofen

In this research work, paracetamol and its selected combinations were evaluated for their efficacy and renal toxicity. Firstly, the survey of common painkiller combinations was carried out and some of them were selected and tested for their efficacy, Table I. For their toxicity, renal system was selected because of serious end stage renal disease associated with the use of over the counter pain killers as reported in literature.

The combinations drugs we studied were paracetamol +caffeine (PC), paracetamol +aspirin +caffeine (PAC), paracetamol + ibuprofen + caffeine (PIC) where their efficacy and toxicity were compared to paracetamol alone after ten days and three months treatment. The findings of the work concluded that paracetamol-diclofenac combination exhibited highest efficacy with minimal renal toxicity, and we were able to publish many journal articles and conference papers. Summary of the results of the study are shown below: Figure 1-4, Plate I and II (Zezi *et al*., 2005; Zezi *et al*, 2006; Zezi *et al* 2007a; Zezi *et al.*, 2007b; Zezi *et al.*, 2007c; Zezi *et al.,* 2011).

Table I. Commonly available co-formulated analgesics in solid forms

S/N	Co-formulation	Trade names
1.	Aspirin 375mg + caffeine 25mg tablet	Cafenol® phensic
2.	Aspirin 760mg + caffeine 60mg power	Alabukun
3.	Aspirin 250mg +caffeine 50mg +paracetamol 250mg tablet	Apc plus
4.	Aspirin 420mg + caffeine 30mg tablet	Drastin plus
5.	Aspirin 450mg + paracetamol 275mg +caffeine 50mg powder.	After 5
6.	Paracetamol 500mg + caffeine 30mg tablet/caplet	Panadol® extra, parakaf extra, sakura extra, sudrex®
7.	Paracetamol 600mg + caffeine 30mg tablet	Sagadon®
8.	Paracetamol 600mg + caffeine 60mg tablet	Toracap extra
9.	Paracetamol 650mg +caffeine 65mg tablet	Boska® extra, Exadon®
10.	Paracetamol 500mg + caffeine 25mg caplet	Pentax
11.	Paracetamol 250mg + acetosal powder	Laila
12.	Propyphenazone 175mg + caffeine 25mg tablet	Optalidon
13.	Paracetamol 325mg +ibuprofen 200mg + caffeine 40mg capsule	Ibucap, Ibulmol; Rex,Ibusec
14.	Paracetamol 325mg +ibuprofen 200mg +caffeine 30mg capsule	Ibex® Ibucin, mobumol, Brupanax
15.	Paracetamol 500mg + diclofenac sodium 50mg caplet	Clofen forte, Diclofen forte.

Zezi, 2006

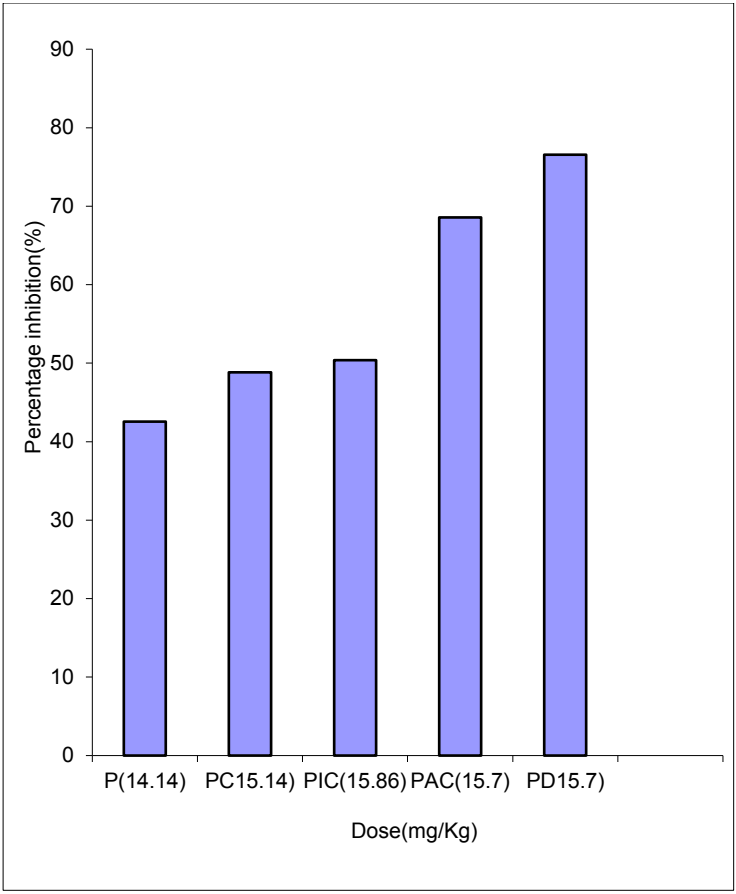

Fig 2: Percentage inhibition of acetic acid – induced writhing in mice produced by treatment with oral P, PC, PIC, PAC and PD at doses equivalent to doses in adult human being after 30 min.

Keys: P = Paracetamol, PC = Paracetamol + Caffeine, PIC = Paracetamol + Ibuprofen + Caffeine, PAC = Paracetamol + Aspirin + Caffeine, PD = Paracetamol + Diclofenac, n = 6,

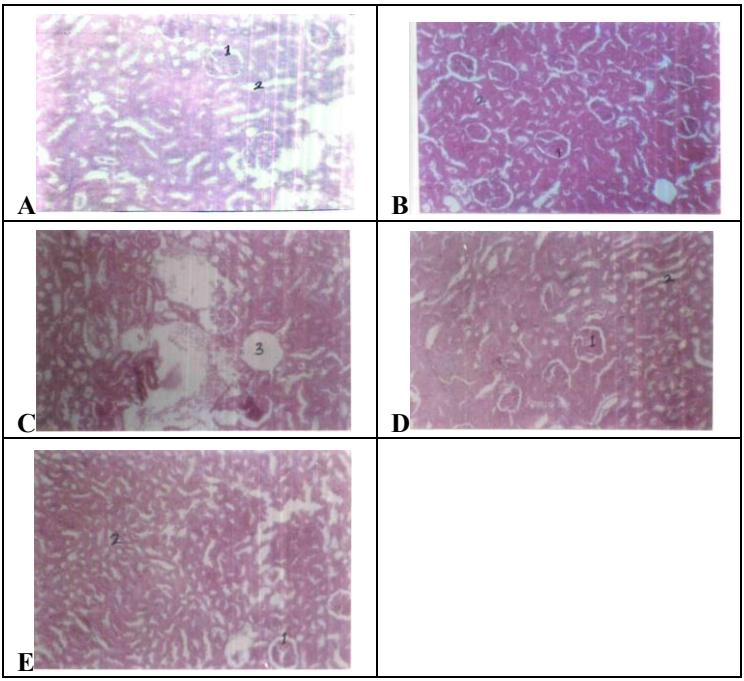

***PLATE I**: Representatives rat kidney histopathology after ten days treatment (H& E stain, original magnification 10x2.5).*

1. Glomerulus, 2. Tubules, 3. drop out

A= Section from control rat that did not receive any drug. Note the normal areas of glomeruli and tubules. B= Section from rat that received paracetamol – caffeine combination (15.14mg/kg) ten days treatment. Note the glomerular atrophy. C= Section from rat that received paracetamol – caffeine combination (15.14mg/kg) ten days treatment. Note the glomerular drop out. D= Section from rat that received paracetamol – aspirin – caffeine combination (15.7mg/kg) ten days treatment. Note the mild glomerular and tubular atrophy. E= Section from rat

that received paracetamol – ibuprofen - caffeine combination (15.86 mg/kg) after ten days treatment. Note the mild glomerular and tubular atrophy.

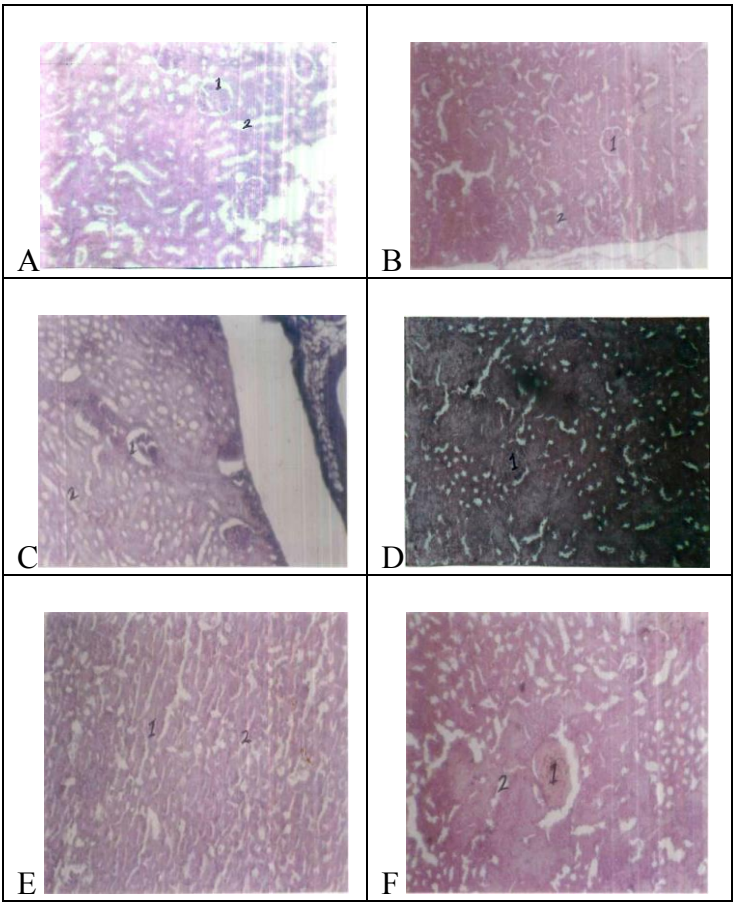

***PLATE II**: Representatives rat kidney after three months treatment (H& E stain, original magnification 10x2.5).*

1. Glomerulus 2. Tubules

A= Section from control rat that did not receive any drug. Note the normal areas of glomeruli and tubules. B= Section from rat that received paracetamol (14.14mg/kg) three months treatment. Note the mild glomerular atrophy. C= Section from rat that received paracetamol-diclofenac combination (15.7mg/kg) three months treatment. Note the moderate glomerular and mild tubular atrophy. D =Section from rat that received paracetamol-caffeine combination (15.14mg/kg) three months treatment. Note the moderate glomerular atrophy. E= Section from rat that received paracetamol-aspirin-caffeine combination (15.7mg/kg) 3 months treatment. Note the mild to moderate glomerular and tubular atrophy.

F= Section from rat that received paracetamol-ibuprofen-caffeine combination (15.86mg/kg) three months treatment. Note the mild glomerular and tubular atrophy.

SECTION THREE

As the Journey Continued

During my literature search, I found out that we are endowed with a lot of natural resources with medicinal values. Plants with analgesic potentials reported in the literature were then screened for their efficacy and toxicities. About 15 plants were screened for this purpose, see table II. Some of them are briefly discussed below:

1. ***Rothmannia longiflora*** **Salisb**

Traditionally *Rothmannia longiflora* salisb leaves concoction is used in the management of pain. Analgesic and anti-inflammatory studies have been reported, (Mallam, 2011). Here, its effect on rat kidney, an organ affected by some orthodox analgesics was investigated. The chronic administration of all the test doses of methanol leaf extract of *Rothman longiflora* showed no significant difference ($P > 0.05$) between the test and control groups for serum sodium, potassium, chloride, urea and creatinine concentrations. On the kidney histology, the glomeruli and tubules were normal both in test and control groups. This study therefore suggested renal safety of the extract on chronic administration to rats. This work was presented at World Congress of Basic and Clinical Pharmacology (WCP) in Cape town, South Africa in 2014, (Zezi *et al.*, 2014).

2. ***Dalbergia saxatilis*** **(Hook. F)**

Dalbegia saxatilis leaves decoction is used in Traditional Medicine for several ailments such as cough, small pox,

skin lesions, bronchial ailments and toothache. In this study, the analgesic, anti-inflflammatory and antipyretic activities of the methanol leaf extract of *Dalbergia saxatilis* Hook. F in rats and mice were investigated. The outcome indicated potential analgesic, anti-inflflammatory and antipyretic effects of the methanol leaf extract of *D. saxatilis* at the tested doses. These support the claim for the traditional use of the plant in treatment of pain, inflflammation and pyresis, (Hassan *et al.,*2015).

3. Olax subscorpioidea Oliv

Olax subscorpioidea in different forms has been used traditionally for the management of pains, inflammatory diseases, yellow fever, cancer and rheumatism. The analgesic activity of its leaf extract was reported. In this present study, elucidation of the possible mechanism of analgesic actions of butanol leaf extract of *Olax subscorpioidea* in mice using acetic acid induce-writhes method was conducted. The outcome of this study revealed the involvement of opioidergic, serotonergic and nitric oxide-l-arginine pathways in the analgesic effect of butanol leaf fraction of *Olax subscorpioidea,* (Odoma *et al.,* 2017).

4. *Eriosema psoraloides* (Lam.)

The analgesic and anti-inflammtory activities of *Eriosema psoraloides* were evaluated. The results of the study suggested that the methanol root extract of *Eriosema psoraloides* possesses analgesic and anti-inflammatory activity, thus supporting the

ethnomedicinal claims of the plant for the management of pain and inflammation, (Bamikunle, *et al.,* 2021).

Table II: Work on plants with analgesic effects

S/N	Plant	Title of the work	Publication
1	*Adenodolichos paniculatus* (HUA)	Evaluation of Analgesic and Anti-inflammatory Activities of the methanolic leaf Extract of *Adenodolichos paniculatus* (HUA) Famaily-leguminosae : papilionoideae.	Sani *et al.*, 2010a
2	*Adenodolichos paniculatus* (HUA)	Effects of the methanolic Leaf Extract of *Adenodolichos paniculatus* (leguminosae) on rat Liver Function(s)	Sani *et al.*, 2010b
3	*Ziziphus mucoronata*	Effect of aqueous Stem Bark extract of *Ziziphus mucoronata* on rat kidney function status after ten Days Daily Treatment	Zezi *et al.*, 2012
4	*Khaya senegalensis*	*Khaya senegalensis* augments the antinociceptive actions of piroxicam in murine models of hyperalgesia	Olurishe *et al*., 2013
5	*Khaya senegalensis*	Khaya senegalensis inhibits piroxicam mediated gastro-toxicity in Wistar rats,	Ishaq, *et al.*, 2014
6	*Borreria verticillata* Linn	Preliminary evaluation of ethanol leaf extract of *Borreria verticillata* Linn(Rubiaceae) for analgesic and anti-inflammatory effects,	Abdullahi-Gero *et al*., 2014
7	*Dalbergia saxatilis* Hook.	Effect of methanol leaf extract of *Dalbergia saxatilis* Hook.f (fabaceae) on renal function.	Hassan., *et al*. 2015

8	*Laggera aurita* Linn	Saponin and flavonoid-riched fractions of *Laggera aurita* Linn F. produce central analgesia in murine models of analgesia.	Shehu *et al.,* 2016
9	*Laggera aurita* Linn	Acute Toxicological, Analgesic and Anti-Inflammatory Effects of Methanol Extract of *Laggera aurita* Linn F (Compositae) in Mice and Rats	Shehu *et al.,* 2016
10	*Rothmannia longiflora Salisb*	Analgesic and Anti-Inflammatory activities of *Rothmannia Longiflora Salisb* in Mice and Rats	Mallam *et al.,* 2016
11	*Olax subscorpioidea* Oliv	Effects of Aqueous and Butanol Leaf Fractions of *Olax subscorpioidea* Oliv. on Inflammatory Cytokines in Wistar Rats	Odoma *et al.,* 2020
12	*Olax subscorpioidea* Oliv	Preliminary Evaluation of the Acute and Sub-Acute Anti-Inflammatory Activities of Aqueous and Butanol Leaf Fractions of *Olax subscorpioidea* Oliv. (Olacaceae)	Odoma *et al.,* 2020
13	*Nymphaea lotus* Linn	Anti-nociceptive, anti-inflammatory and possible mechanism of antinociceptive action of methanol leaf extract of *Nymphaea lotus* Linn	Rege *et al.,* 2021
14	*Eriosema psoraleoides*	Effect of methanol root extract of *Eriosema psoraleoides* on biochemical and haematological parameters and cyclooxygenase levels in rats,	Bamikunle *et al*., 2022
15	*Nymphaea lotus* Linn	Sub-Acute Toxicological Evaluation of Methanol Leaf Extract of *Nymphaea lotus* Linn (Nymphaeceae) in Wistar Rats,	Rege *et al.,* 2023

SECTION FOUR

Along the Line

In 2003 when I became the Coordinator of the then new Department of Clinical Pharmacy and Pharmacy Practice, I added new research focus towards clinical. Details of some of the works are as follow:

1. Effect of Counselling and Reminder Text Messages Follow-Up on Adherence to Antiretroviral Therapy in Hajiya Gambo Sawaba General Hospital, Zaria, Nigeria

The study revealed that patients who received reminder text messages in addition to counselling had significantly higher mean percentage increase in CD4 count (36.7%) compared to the control group (19.12%), which received counselling only (p=0.007). There was no statistical significant difference in the level of adherence between intervention group and control group using self-report form. The study concluded that regular counselling and reminder text messages have significant role in improving adherence to antiretroviral therapy, (Alpha *et al.*, 2016).

2. Evaluation of Pattern of Antihypertensive Prescriptions and Adherence to JNC-7 Guideline in National Hospital Abuja-Nigeria

Calcium channel blockers were the mostly prescribed antihypertensive drugs. Alpha-2 adrenergic receptor agonist had the lowest cost utilization per year. Those patients whose prescription followed JNC-7 guideline had better blood pressure control, (Yusuf *et al*., 2019).

3. Evaluation of Analgesic use Among Athletes in Ahmadu Bello University, Samaru, Zaria, Nigeria

Many athletes require analgesics frequently because they have a higher risk of developing physical injuries or pain. This study was designed to carry out a cross-sectional survey of analgesic use among athletes of Ahmadu Bello University, Zaria in December, 2014.

A total of 192 athletes were studied out of 223 recruited from different sporting inclinations. A semi-structured questionnaire pilot tested was used. A reliability of 0.820 and significant alpha value of 0.05 were obtained. The questionnaire containing 27 questions in 3 sections were then administered to the consenting athletes. Analysis of the data was conducted using SPSS version 17 and descriptive statistics used to report the results obtained. There was evidence of analgesic use among the athletes, and Paracetamol was the most common analgesic used with minimal incidence of side effects being reported by the respondents. However, caution need to be taken since there are increasing evidence of unperceived side effects such as reduced anabolic response to acute exercise bouts and attenuated long-term gains in muscle mass and strength in young healthy individuals as reported by other studies. (Sadiq *et al.,* 2021).

4. Other clinical works carried out included the following:

i. Prevalence and Prognosis of Cerebrovascular Accident in Zaria, Kaduna State (Danjuma *et al.*, 2005).

ii. Identification of Pharmaceutical Care Standards in Zaria-Kaduna Metropolis, Northern Nigeria (Giwa, *et al*., 2010).

iii. Retrospective Study of the Use of Cytotoxic and Molecular-Targeted Drugs in the Treatment of Cancer, (Mahdi *et al.,* 2014).

iv. Rational use of drugs in hypertensive out patients of public hospitals in Kano State, Nigeria, (Umar *et al.*, 2019).

v. Impact of Therapeutic Drug Monitoring of Metformin in Diabetic Patients with Renal Impairment in a Nigerian Healthcare Facility, (Aliyu *et al*., 2019).

vi. Drug Therapy outcome among HIV-infected adults receiving care in Federal Teaching Hospital Gombe, Gombe state, Nigeria, (Bakari, 2024).

SECTION FIVE

Collaborations and Other Contributions to Knowledge

Table III: Collaborations and Other Contributions to Knowledge

S/N	Title	Department/Reference
1	The Relationship between Alkaloid Content and Larvicidal Activity of Tobacco (*Nicotiana tobaccum*), Book of Abstracts, West Africa Society for Pharmacology, International Conferences Abuja, pp. 16.	Pharmacognosy and Drug Dev. Abubakar, *et al.,* 1996
2	Phytochemcial and Some Biological Studies on the Bark of *Mitragyna inermis* (Willd) O. Kuntze (Rubiaceae),	Pharm. and Med. Chem., Ahmadu, *et al.,*2002:
3	Evaluation of Five Medicinal Plants used in Diarrhoea Treatment in Nigeria.	Pharrmacognosy Agunu *et al.,* 2005
4	Pharmacoeconomic Evaluation of Tuberculosis Chemotherapy at ABUTH, Zaria	Pharmacology Danjuma *et al*., 2007
5	Anti-diarrheal Activity of the Leaf Extracts of *Daniellia oliveri* HUTCH and DALZ (fabaceae) and *Ficus syncomonus* MIQ(moraceae),	Pharm. and Med. Chem., Ahmadu *et al*., 2007
6	Preliminary Antidiarrhoeal Activity of Methanolic Extract of *Securinega virosa* (euphorbiaceae).	Pharmacology, Magaji *et al.,* 2007
7	Behavioural Effects of Hydroalcoholic Stem Bark Extract of *Randia nilotica* stapf. in mice	Phamacology Danjuma *et al*., 2008.
8	Central Nervous System Depressant Effect of Hydroalcoholic Leaves, Stem and Root Bark Extract of *Randia nilotica* stapf.(Rubiaceae)	Pharmacology, Danjuma *et al*., 2009a
9	Residual Aqueous Fraction of Stem bark Extract of *Xeromphis nilotica* and Behavioural Effects in Mice	Pharmacology, Danjuma *et al*., 2009b

10	Evaluation of Anticonvulsant Activity of the Hydroalcoholic Stem Bark Extract of *Randia Nicolitica* Stapf. In Mice and Chicks	Pharmacology, Danjuman *et al.*, 2009c
11	Anticonvulsant Properties of the Methanolic Stem Bark Extract of *Acacia albida* del	Pharmacology, Danjuma *et al.*, 2010
12	Acute toxicity and *In vivo* Effects of Lreaf Extracts of *Byrsocarpus coccineeus* Shum and Thonn in Pregnant Rat Uterus	Pharmacology, UNIMAID Wazis *et al.*, 2012
13	Isolation and characterization of stigma-5-en-o-b-glucoside from ethylacetate leaf extract of *Byrsocarpus coccineeus* shum and Thonn	Pharmacology, UNIMAID Wazis *et al.*, 2013a
14	Effect of administration of carbamazepine and/or phenytoin on haematological parameters on Wistar rats	Vet. Pharmacology, Aliyu *et al.*, 2013
15	Biochemical and histopathological changes in liver of albino rats exposed to 1% dichlorvos pesticide at sub-acute period	Pharmacology, UNIMAID Uthman *et al.*, 2013
16	Preliminary Phytochemical Screening and *In vitro* Effects of Leaf Extracts of *Byrsocarpus Coccineus* Shum &Thonn on Pregnant Rat Uterus	Pharmacology. UNIMAID Wazis *et al.*, 2013b.
17	Metformin-Cefixime Co-administration affects Glucose Regulation and Reno-Pancreatic Histology in Alloxan-induced Hyperglycemic Rats	Pharmacology, Olurishe *et al.*, 2013
18	An evaluation of the management of Breast cancer at Ahmadu Bello University Teaching Hospital Shika, Zaria	Pharmacology, Olorukooba *et al*., 2013
19	Flavonoid mixture ameliorates increase in erythrocyte Osmotic fragility and malondialdehyde concentration induced by *Trypanosoma brucci bruccci* infection in Wistar rats	Vet. Pharmacology, Kobo *et al.,* 2014
20	Effect of garlic (*Allium sativum*) and ginger(*Zingiber officinale*) extract on haemato-biochemical parameters and liver enzyme activities in Wistar rats	Human Physiology, Tende *et al.*, 2014

21	Blood Pressure lowering and cardio- protective effects of garlic (*Allium sativum*) and ginger (*Zingiber officinale*) extracts in some laboratory animals	Human Physiology Tende *et al.,* 2014.
22	Evaluation of antioxidant activity of leave extract of *Borreria verticillata* Linn(Rubiaceae),	Pharmacology, AbdullahiGero *et al.*, 2014
23	*In vitro* effects of Stigma-5-En-O-B glucoside isolated from ethylacetate leaf extact of *Byrsocarpus cocineus* shum and Thonn on pregnant rat uterus	Pharmacology, UNIMAID Wazis *et al.*, 2014
24	Effect of ambient temperature on methylenedioxymethamphetamine (MDMA) - induced changes in body temperature and spatial memory in rodents	Human Physiology, Alhassan, *et al.*, 2015
25	Phytochemical Screening and Hypoglycaemic Effect of Methanol Extract of *Solanum anomalum* Thonn. Fruits in Alloxan induced Hyperglycaemic and Normal Wistar Rats	Pharmacology, Abubakar *et al.*, 2016
26	Anti-histaminic and bronchodilatory activities of aqueous and methanol extracts of *Calotropis procera* (Ait) R.Br. root bark on allergic asthma in rodents	Pharmacology Aliyu *et al.*, 2017
27	Comparative Effect of Environmental Exposure on the Quality Control Assessment of Ciprofloxacin Tablet Marketed in Gombe South, Nigeria	Pharm. and Med. Chem., Usman *et al.,* 2017
28	Immune-mediated Anti-inflammatory Activity of Root Bark Extracts of *Calotropis procera* (Ait)R.Br. in Rodents	Pharmacology, Aliyu *et al.,* 2017
29	Methanol Leaf Extract of *Diospyros mespiliformis* Hochst. offers Protection against Some Chemoconvulsants	Pharmacology, Muhammad *et al.*, 2017
30	Sitagliptin-*Moringa oleifera* coadministration did not delay the progression nor ameliorated functional and morphological anomalies in alloxan-induced diabetic nephropathy	Pharmacology, Olurishe *et al.*, 2017).

31	Evaluation of antidiarrhoeal activity of methanol extract of *Combretum hypopilinum* Diels (Combretaceae) leaves in mice	Pharmacology, Ahmad *et al.,* 2020
32	Antioxidant and Hepatoprotective Potentials of Methanol Extract of *Ficus platyphylla* StemBark (Moraceae) in Wistar Rats	Pharmacology Sheidu *et al*., 2020.
33	Antimicrobial and wound healing properties of the methanol extract of *Ficus platyphylla* Del. (Moraceae) stem bark,	Pharmacology, Sheidu *et al.,* 2020).
34	Paradoxical effect of a formulated Nigerian-made modified atkin diet in acute seizure models of mice	Pharmacology, Salaudeen *et al.*, 2020.
35	Uterotonic Evaluation of *Sida Corymbosa* Aqueous Leaf Extract on Non-pregnant Wistar Rat Uterine Tissue	Pharmacology, Bakut, *et al.*, 2020
36	Ethnobotanical survey of medicinal plants commonly used in snakebites in North Western Nigeria	Pharmacology, Maigandi *et al.*, 2020
37	Preliminary Toxicity Studies of Methanol Stem Bark Extract of *Lannea acida* A. Rich (Anacardiaceae) in Wistar Rats	Pharmacology, Ovosi *et al*., 2022
38	Chemical constituents and effect of methanol leaf extract of *Hibiscus articulatus* Hochst. Ex A. Rich (malvaceae) glucose- and streoptozotocin-induced hyperglycaemia using Wistar rats	Pharmacology Abbas *et al.*, 2022
39	Modified Atkins Diet Delayed the Onset of Epileptogenesis, Improved Motor Coordination and Enhanced Learning Memory in Mice	Pharmacology, Salaudeen *et al.,* 2023:
40	Antitumor Activity of a Quinoline-Substituted Chalcone Epoxide	Pharmacology, Muhammad *et al.,* 2023
41	Synthesis and antitumor activity of a 2-hydroxy substituted chalcone	Pharmacology, Muhammad *et al.,* 2023

SECTION SIX

Current and Future Research Focus

Our research thrust is divided into the following:

1. **Pharmacokinetic Studies**

    I. Drug - drug interaction

    II. Drug - food interaction

    III. Effect of the environment on drug pharmacokinetics

    IV. Drug level monitoring

    V. Toxicokinetics

2. **Analgesic drug evaluation**

    I. Elucidation of mechanism of action of analgesics from natural products

    II. Toxicological studies of analgesics

Conclusion

From what has been said so far it is obvious that over the counter pain killers exhibit both relief and burden.

Recommendation

The take home message is contained in this recommendation. For a patient to benefit from the relief of over-the-counter pain killers, he or she must practice:

RESPONSIBLE SELF-MEDICATION

This entails the following:

i. Not to practice mixing of pain killers

ii. Using pain killers when the need arises only

iii. Understanding the beneficial and harmful effects of the pain killers

iv. Using a pain killer at the appropriate dose

v. Not to use a pain killer over a long period of time and to understands when to seek professional advice

vi. Acknowledging that herbal pain killers can cause toxicity

SECTION SEVEN

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