EVALUATING THE KNOWLEDGE AND PRACTICE OF THE ABUSE OF PARACETAMOL AMONG UNIVERSITY OF BENIN STUDENTS

BY

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CERTIFICATION

We the undersigned certify that this research work was carried out by **AFEGE AMBROSE EFE** in the Department of Medical Biochemistry, Faculty of Basic Medical Sciences, University of Benin, Benin City.

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DEDICATION

This research is dedicated to God Almighty for his infinite mercy towards me, His divine guideance, provision, love and care towards my academic stay in this great citadel of learning. I also dedicate this project to my family and loved ones and all those who relentless in securimg an academic future.

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CHAPTER ONE

1.0 Introduction

A large number of people, when they fall sick, do not consult the physician. We have noticed that right from popular magazine editors to our domestic servant everyone thinks that he or she is a medical authority, and if we have a fever, cold, cough, constipation or indigestion, our friends or even total strangers volunteer advice on medicines to take like expert physicians. Almost everyone we meet has an excellent remedy for whatever ails we have. In short, this is what is meant be self-medication (Balbuena *et al*., 2009). May be most of the times nothing untoward happens on following such advice, but it can be dangerous. Medicines are important to help us get cured at the right time. But popping medicines on our own, without the doctor's consult can become fatal (Narhi, 2007).

The present youth will be the backbone of future Nigeria. They are carefree never giving a thought for their coming future. They have the ability to learn and acquire knowledge from their surrounding but do not have the intelligence to distinguish between evil and good. Thus, the youth is more prone to habits whether good or bad, but they tend to learn bad habits faster than the good ones as they are easy to follow. Among many bad habits one of the dangerous habits is that of self-medication (Sawair *et al*., 2009; Sawalha, 2008; Zafar *et al*., 2008).

The present survey was aimed to determine the prevalence, attitude, and knowledge of self-medication of Paracetamol among the undergraduate students of the University of Benin and a sustained awareness to the society regarding the risks of self-medication especially paracetamol - an OTC product and its communicability for the future is warranted.

A questionnaire-based survey was conducted to know about the prevalence, attitude and knowledge of Paracetamol a self-medicated drug.

This study aims to gauge the awareness, explore the perceptions and knowledge among educated adults (university students) regarding the most common OTC analgesic 'Acetaminophen' available with a brand name of panadol and paracetamol. University students were selected for this study because the authors wanted to emphasis the fact that even the educated adults of the community have not sufficient information regarding the OTC drugs. Moreover, the authors believe, that lack of knowledge among the community members could be one of the biggest reasons of the misuse of OTC drugs. Our results offer an indirect estimation of likelihood of overuse and misuse among our general population (which is not well educated) via the knowledge level of educated adult users (university students).

CHAPTER TWO

2.0 Literature Review

2.1 Background review

Worldwide, self-medication has been a rising trend and irrational use of the over-the-counter (OTC) drugs is a cause of great concern for public health agencies (Kumar *et al*., 2013; Wazaify, Shields, Hughes, and McElnay, 2005). In modernistic years, innumerable drugs have been available on an over-the-counter basis, inclusive of the drugs that were available merely through prescription in the past (Brass, 2001). Conforming to the previously published studies, an increased confidence is found in general public regarding the self-treatment with OTC medicines over the passage of time. People believe that only safe medicines are legitimate to be sold without prescription and OTC medicines usually do not have serious side effects (Panero and Persico, 2016). One of the major class of medicines distributed via over-the-counter sale is OTC analgesics, including NSAID and paracetamol which are exceptionally popular and extensively used (Wilcox, Cryer, and Triadafilopoulos, 2005 Nov; Wiliński *et al*., 2015). Paracetamol is most widely used as first-line pharmacotherapy for combating pain disorders of different origin and pyrexia (Wiliński *et al*., 2015). Owing to its remarkable analgesic and anti-pyretic properties, paracetamol is considered as safe and effective treatment for several medical conditions (Fontana, 2008). However, OTC analgesics are reported to be taken most inappropriately, with potential health hazards. Moreover, users were found unaware of their possible adverse side effects (Wiliński *et al*., 2015). Unfortunately, paracetamol is a dose-dependent fatal hepatotoxic agent that can cause acute hepatocellular injury leading to centrilobular necrosis (Hinson, Roberts, and James, 2010). Paracetamol overdose is a preeminent cause of hepatotoxicity, which is a substantial problem and contributes significantly to intensive care unit admissions as well as cost of hospitalization (Brass, 2001). Paracetamol has become the most significant cause of ALF (acute liver failure) —a devastating disorder that is triggered by increase in plasma aminotransferase (alanine transaminase/aspartate transaminase) ALT/AST levels (Hinson *et al*., 2010; Jalan *et al*., 2007). Many of such patients develop cardiopulmonary disorders, increased risk of renal complications (up to 2.5 times) and advanced multi-organ failure (Fontana, 2008; Twycross *et al*., 2013), eventually resulting in the death of more than 85% of the patients with poor diagnosis and are deprived of liver transplantation (Wazaify *et al*., 2005).

Paracetamol is the most frequently used OTC drug in deliberate self-poisoning (Hawton *et al*., 1995). Paracetamol poisoning can occur at recommended therapeutic doses and multiple therapeutic or supra therapeutic doses (Lubel *et al*., 2007). An alarming concern in recent years is that, unintentional overdose, rather than intentional overdose have been the main cause of paracetamol induced ALF (acute liver failure) (Jalan *et al*., 2007). In such cases toxic effects are developed through the consumption of smaller amounts of paracetamol but for a very prolonged period of time, usually for pain relief to treat toothache, chronic

backache, or headache (Schiødt *et al*., 1997). One of the most distressing factors accounting for paracetamol toxicity includes scarce knowledge among the users regarding specific symptoms that an overdose might have and the timing of such effects (Hawton *et al*., 1995).

Various studies conducted amidst the Western countries assessing users' knowledge and behaviors towards paracetamol have high lightened poor knowledge, misunderstanding of the API and incomprehension of instructions by them (Boudjemai *et al*., 2013). Paracetamol toxicity is becoming a factual load on health care systems around the globe (Gyamlani and Parikh, 2002) and one the most common cause of ALF in Western countries as well as its prevalence appears to be increasing with time (Fontana, 2008). Among the few eminent developed countries including USA,UK and Australia paracetamol tends to be the second leading cause of toxic drug ingestions (Gyamlani and Parikh, 2002), strong association with high level of diseases, deaths and its toxicity related with alcohol abuse respectively (Schiødt *et al*., 1997).

Various studies done in Developing countries, including Nigeria related to self-medication shows contentment among people in terms of self-medication with paracetamol (Ghumman *et al*., 2013) and high prevalence of self-medication among educated adults (Zafar *et al*., 2008). Majority of the users select paracetamol for self-management of headache (Ghumman *et al*., 2013). A recent study conducted in Developing countries, including Nigeria compared the drug availability, patient preference and knowledge of toxic levels between Non-steroidal anti-inflammatory drugs and paracetamol shows poor awareness of the side effects and high preference of their use without prescription (Zamir and Nadeem, 2016). Unfortunately, there is also lack of published data related to incidences of paracetamol toxicity and other OTC analgesics, which is becoming an alarming situation for public health departments of Developing countries, including Nigeria. Absence of such data deprives us from estimating the knowledge and perception level of our population regarding OTC medicines (Hinson *et al*., 2010; Jalan *et al*., 2007).

2.2 Paracetamol

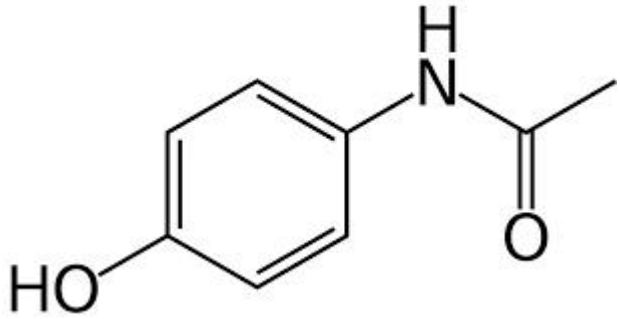

Figure 1. The chemical structure of paracetamol (Alternate Name: acetaminophen)

Figure 2. Paracetamol in its branded pack

Paracetamol, also known as acetaminophen, is a medication used to treat fever and mild to moderate pain. At a standard dose, paracetamol only slightly decreases body temperature; it is inferior to ibuprofen in that respect, and the benefits of its use for fever are unclear. Paracetamol significantly relieves pain in acute migraine but only slightly in episodic tension headache. However, the aspirin/paracetamol/caffeine combination helps with both conditions and is recommended as a first-line treatment for them. Paracetamol is effective for post-surgical pain, but it is inferior to ibuprofen. The paracetamol/ibuprofen combination provides further increase in potency and is superior to either drug alone. The pain relief paracetamol provides in osteoarthritis is small and clinically insignificant. The evidence in its favor for the use in low back pain, cancer pain and neuropathic pain is insufficient (Hinson *et al*., 2010; Jalan *et al*., 2007).

In the short term, common side effects of paracetamol are nausea and abdominal pain, and it seems to have tolerability similar to ibuprofen. Chronic consumption of paracetamol may result in a drop in hemoglobin level indicating possible gastrointestinal bleeding and abnormal liver function tests. There is a consistent association of increased mortality as well as cardiovascular (stroke, myocardial infarction), gastrointestinal (ulcers, bleeding) and renal adverse effects with taking higher dose of paracetamol. The drug may also increase the risk of developing hypertension. Elevated frequency of asthma and developmental and reproductive disorders is observed in the offspring of women with prolonged use of paracetamol during pregnancy, although whether paracetamol is the true cause of this increase is unclear. The evidence for the association between paracetamol during pregnancy and autism spectrum disorder and attention deficit hyperactivity disorder is particularly strong, all this prompting the calls to limit its use in pregnancy to the lowest effective dosage for the shortest possible time (Hinson *et al*., 2010; Jalan *et al*., 2007).

The recommended maximum daily dose for an adult is three to four grams. Higher doses may lead to toxicity, including liver failure. Paracetamol poisoning is the foremost cause of acute liver failure in the Western world, and accounts for most drug overdoses in the United States, the United Kingdom, Australia, and New Zealand (Hinson *et al*., 2010; Jalan *et al*., 2007).

Paracetamol was first made in 1877. It is the most commonly used medication for pain and fever in both the United States and Europe. It is on the World Health Organization's (WHO) List of Essential Medicines. Paracetamol is available as a generic medication, with brand names including Tylenol and Panadol among others. In 2018, it was the twentieth most commonly prescribed medication in the United States, with more than 27 million prescriptions (Hinson *et al*., 2010; Jalan *et al*., 2007).

2.3 Adverse effects

For short-term control of pain, paracetamol is not better tolerated than ibuprofen. Gastrointestinal adverse effects such as nausea and abdominal pain are common, and their frequency is similar to that of ibuprofen. Increase in risk-taking behavior is possible. According to the US Food and Drug Administration, the drug may cause rare and possibly fatal skin reactions such as Stevens–Johnson syndrome and toxic epidermal necrolysis, although an analysis of the French Pharmacovigilance Database indicated no obvious risk of these reactions (Fontana, 2008; Twycross *et al*., 2013).

In clinical trials for osteoarthritis, the number of participants reporting adverse effects were similar for those on paracetamol and on placebo. However, the abnormal liver function tests (meaning there was some inflammation or damage to the liver) were almost four times more likely in those on paracetamol, although the clinical importance of this effect is uncertain. After 13 weeks of paracetamol therapy for knee pain, a drop in hemoglobin level indicating gastrointestinal bleeding was observed in 20% of participants, this rate being similar to ibuprofen group (Fontana, 2008; Twycross *et al*., 2013).

Due to the absence of controlled studies, most of the information about the long-term safety of paracetamol comes from observational studies. These indicate a consistent pattern of increased mortality as well as cardiovascular (stroke, myocardial infarction), gastrointestinal (ulcers, bleeding) and renal adverse effects with increased dose of paracetamol. Use of paracetamol is associated with 1.9-fold higher risk of peptic ulcer. Those who take it regularly at a higher dose (more than 2-3 g daily) are at much higher risk (3.6 - 3.7-fold) of gastrointestinal bleeding and other bleeding events. Meta-analyses suggest that paracetamol may increase the risk of kidney impairment by 23% and kidney cancer by 28%. Paracetamol is particularly dangerous to the liver in overdose, but even without overdose those who take this drug may develop acute liver failure requiring liver transplantation more frequently than the users of nonsteroidal anti-inflammatory drugs. Paracetamol slightly but significantly increases blood pressure and heart rate. The majority of observational studies suggests that, used chronically, it may increase the risk of developing hypertension. The risk is higher with the higher dose (Fontana, 2008; Twycross *et al*., 2013).

The association between paracetamol use and asthma in children has been a matter of controversy. However, the most recent research suggests that there is no association, and that

the frequency of asthma exacerbations in children after paracetamol is the same as after another frequently used pain killer ibuprofen (Fontana, 2008; Twycross *et al*., 2013).

2.3 Overdose (paracetamol poisoning)

Overdoses of paracetamol, that is taking more than the recommended maximum daily dose of paracetamol for healthy adults of three or four grams, can cause potentially fatal liver damage. Paracetamol toxicity is the foremost cause of acute liver failure in the Western world, and accounts for most drug overdoses in the United States, the United Kingdom, Australia, and New Zealand. Paracetamol overdose results in more calls to poison control centers in the US than overdose of any other pharmacological substance. According to the FDA, in the United States, "56,000 emergency room visits, 26,000 hospitalizations, and 458 deaths per year [were] related to acetaminophen-associated overdoses during the 1990s. Within these estimates, unintentional acetaminophen overdose accounted for nearly 25% of the emergency department visits, 10% of the hospitalizations, and 25% of the deaths" (Fontana, 2008; Twycross *et al*., 2013).

Overdoses are frequently related to high-dose recreational use of prescription opioids, as these opioids are most often combined with acetaminophen. The overdose risk may be heightened by frequent consumption of alcohol. Untreated paracetamol overdose results in a lengthy, painful illness. Signs and symptoms of paracetamol toxicity may initially be absent or non-specific symptoms. The first symptoms of overdose usually begin several hours after ingestion, with nausea, vomiting, sweating, and pain as acute liver failure starts. People who take overdoses of paracetamol do not fall asleep or lose consciousness, although most people who attempt suicide with paracetamol wrongly believe that they will be rendered unconscious by the drug. Treatment is aimed at removing the paracetamol from the body and replenishing glutathione. Activated charcoal can be used to decrease absorption of paracetamol if the person comes to the hospital soon after the overdose. While the antidote, acetylcysteine (also called N-acetylcysteine or NAC), acts as a precursor for glutathione, helping the body regenerate enough to prevent or at least decrease the possible damage to the liver; a liver transplant is often required if damage to the liver becomes severe. NAC was usually given following a treatment nomogram (one for people with risk factors, and one for those without), but the use of the nomogram is no longer recommended as evidence to support the use of risk factors was poor and inconsistent, and many of the risk factors are imprecise and difficult to determine with sufficient certainty in clinical practice. Toxicity of paracetamol is due to its quinone metabolite NAPQI and NAC also helps in neutralizing it. Kidney failure is also a possible side effect (Fontana, 2008; Twycross *et al*., 2013).

2.4 Interactions

Prokinetic agents such as metoclopramide accelerate gastric emptying, shorten time (t_{max}) to paracetamol peak blood plasma concentration (C_{max}), and increase C_{max}. Medications slowing

gastric emptying such as propantheline and morphine lengthen t_{max} and decrease C_{max}. The interaction with morphine may result in patients failing to achieve the therapeutic concentration of paracetamol; the clinical significance of interactions with metoclopramide and propantheline is unclear. There have been suspicions that cytochrome inducers may enhance the toxic pathway of paracetamol metabolism to NAPQI. By and large, these suspicions have not been confirmed. Out of the inducers studied, the evidence of potentially increased liver toxicity in paracetamol overdose exists for phenobarbital, primidone, isoniazid, and possibly St John's wort. On the other hand, the anti-tuberculosis drug isoniazid cuts the formation of NAPQI by 70%. Ranitidine increased paracetamol area under the curve (AUC) 1.6-fold. AUC increases are also observed with nizatidine and cisapride. The effect is explained by these drugs inhibiting glucuronidation of paracetamol. Paracetamol raises plasma concentrations of ethinylestradiol by 22% by inhibiting its sulfation. Paracetamol increases INR during warfarin therapy and should be limited to no more than 2 g per week (Fontana, 2008; Twycross *et al*., 2013).

2.5 Pharmacology and pharmacodynamics

Paracetamol appears to exert its effects through two mechanisms: the inhibition of cyclooxygenase and actions of its metabolite AM404. Supporting the first mechanism, pharmacologically and in its side effects, paracetamol is close to classical nonsteroidal anti-inflammatory drugs (NSAIDs) that act by inhibiting COX-1 and COX-2 enzymes and especially similar to selective COX-2 inhibitors. Paracetamol inhibits prostaglandin synthesis by reducing the active form of COX-1 and COX-2 enzymes. This occurs only when the concentration of arachidonic acid and peroxides is low. Under these conditions, COX-2 is the predominant form of cyclooxygenase, which explains the apparent COX-2 selectivity of paracetamol. Under the conditions of inflammation, the concentration of peroxides is high, which counteracts the reducing effect of paracetamol. Accordingly, the anti-inflammatory action of paracetamol is slight. The second mechanism centers on the paracetamol metabolite AM404. This metabolite has been detected in the brains of animals and cerebrospinal fluid of humans taking paracetamol. Apparently, it is formed in the brain from another paracetamol metabolite 4-aminophenol by action of fatty acid amide hydrolase. AM404 is a weak agonist of cannabinoid receptors CB1 and CB2, an inhibitor of endocannabinoid transporter, and a potent activator of TRPV1 receptor. This and other research indicate that cannabinoid system and TRPV1 may play an important role in the analgesic effect of paracetamol (Fontana, 2008; Twycross *et al*., 2013).

2.6 Pharmacokinetics

After being taken by mouth, paracetamol is rapidly absorbed from the small intestine, while absorption from the stomach is negligible. Thus, the rate of absorption depends on stomach emptying. Food slows the stomach emptying and absorption, but the total amount absorbed stays the same. In the same subjects, the peak plasma concentration of paracetamol was reached after 20 minutes when fasting versus 90 minutes when fed. High carbohydrate, but not high protein or high fat, food decreases paracetamol peak plasma concentration four-fold.

Even in the fasting state, the rate of absorption of paracetamol is variable and depends on the formulation, with maximum plasma concentration being reached after 20 minutes to 1.5 hours (Fontana, 2008; Twycross *et al*., 2013). Paracetamol's bioavailability is dose-dependent: it increases from 63% for 500 mg dose to 89% for 1000 mg dose. Its plasma terminal elimination half-life is 1.9-2.5 hours, and volume of distribution is roughly 50 L. Protein binding is negligible, except under the conditions of overdose, when it may reach 15-21%. The concentration in serum after a typical dose of paracetamol usually peaks below 30 μg/ml (200 μmol/L). After 4 hours, the concentration is usually less than 10 μg/ml (66 μmol/L) (Fontana, 2008; Twycross *et al*., 2013).

2.7 Important pathways of paracetamol metabolism.

Paracetamol is metabolized primarily in the liver, mainly by glucuronidation and sulfation, and the products are then eliminated in the urine (see the Scheme on the right). Only 2-5% of the drug are excreted unchanged in the urine. Glucuronidation by UGT1A1 and UGT1A6 accounts for 50-70% of the drug metabolism. Additional 25-35% of paracetamol is converted to sulfate by sulfation enzymes SULT1A1, SULT1A3, and SULT1E1. A minor metabolic pathway (5-15%) of oxidation by cytochrome P450 enzymes, mainly by CYP2E1, forms a toxic metabolite known as NAPQI (*N*-acetyl-*p*-benzoquinone imine). NAPQI is responsible for the liver toxicity of paracetamol. At usual doses of paracetamol, NAPQI is quickly detoxified by conjugation with glutathione. The non-toxic conjugate APAP-GSH is taken up in the bile and further degraded to mercapturic and cysteine conjugates that are excreted in the urine. In overdose, glutathione is depleted by the large amount of formed NAPQI, and NAPQI binds to mitochondria proteins of the liver cells causing oxidative stress and toxicity. Yet another minor but important direction of metabolism is deacetylation of 1-2% of paracetamol to form p-aminophenol. P-Aminophenol is then converted in the brain by fatty acid amide hydrolase into AM404 - a compound that may be partially responsible for the analgesic action of paracetamol (Fontana, 2008; Twycross *et al*., 2013).

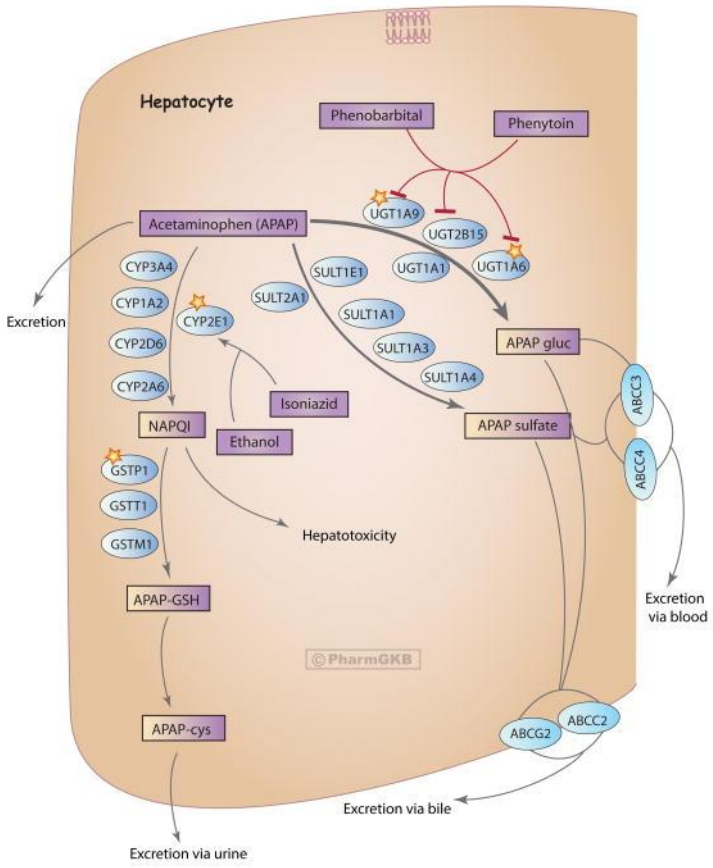

Figure 3. Metabolism and transport of acetaminophen in the liver at therapeutic doses

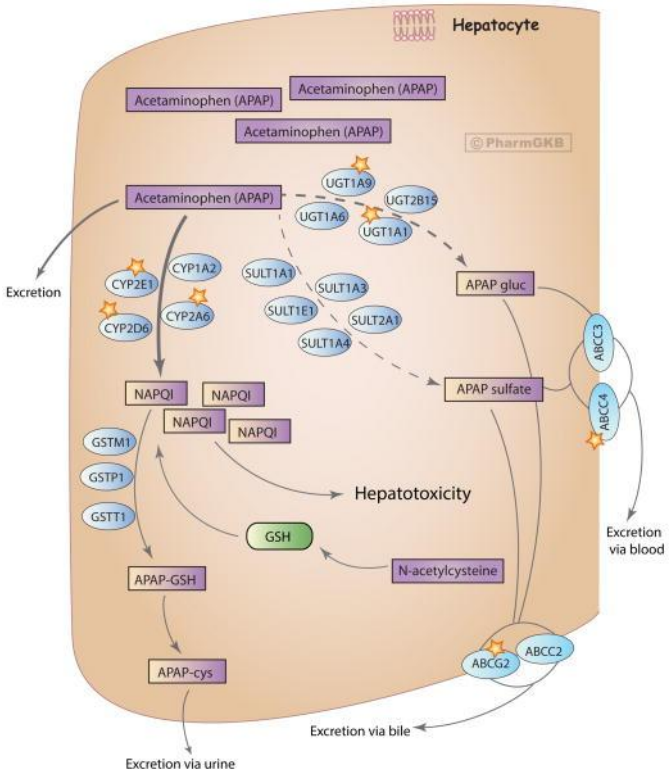

Figure 4. Metabolism and transport of acetaminophen in the liver at toxic doses

CHAPTER THREE

3.0 Materials and Methods

3.1 Inclusion criteria

The respondents were included in the survey on the ground that they were *bona fide* students of the University of Benin, and were enlightened about the essence of the study and filled out consent forms.

3.2 Development of hypothesis

The null hypothesis (H_0) and alternate hypothesis (H_1) were designed for each quarry to accommodate the possibilities of the respondents disagreeing negatively or affirming positively, respectively, with the hypotheses.

3.3 Statistical analysis

Data were entered into the Microsoft excel spread sheet (version 10) prior to descriptive analysis. The data were represented as mean ± SEM. Chi Square analysis (X^2) of the IBM Corp® Statistical Package for Social Sciences, SPSS®, Version 21.0. Histograms and line plots were done using Graph Pad software® Prism 5, Version 5.01 (2007).

CHAPTER FOUR

4.0 Results

Section A: Anthropometric Data

1. Gender of the respondents.

Response	Male	Female
Frequency (f)	73	27
Percentage (%)	73.00	27.00

2. Age of the respondents.

Response	16 – 20 years	21 – 30 years	31 years and above
Frequency (f)	15	85	0
Percentage (%)	15.00	85.00	0.00

3. Marital status of the respondents

Response	Single	Married	Divorced
Frequency (f)	91	9	0
Percentage (%)	91.00	09.00	0.00

4. Weight (Kg) of the respondents.

Response	60 – 70	71 – 79	80 – 90	91 – 100	100 and above
Frequency (f)	54	43	3	0	0
Percentage (%)	54.00	43.00	03.00	0.00	0.00

5. Height (m) of the respondents.

Response	0.400 - 0.490	0.500 – 0.590	0.600 – 0.690
Frequency (f)	45	52	3
Percentage (%)	45.00	52.00	03.00

6. The body mass indices (BMI) of the respondents

Response	16 – 20	21 – 25	26 – 30	31 and above
Frequency (f)	8	73	14	0
Percentage (%)	8.00	73.00	14.00	0.00

Section B: Experience or Studentship

7. Studentship category of the respondents

Response	Full time	Part time
Frequency (f)	100	0
Percentage (%)	100.00	0.00

8. The level of the respondents.

Response	100 level	200 level	300 level	400 level	500 level	600 level
Frequency (f)	7	14	43	31	5	0
Percentage (%)	7.00	14.00	43.00	31.00	5.00	0.00

9. Faculties of the respondents.

Response	Agricultural science	Basic medical sciences	Medicine and Dentistry	Physical sciences	Life sciences	Management sciences	Pharmacy	Arts	Others
Frequency (f)	3	48	21	7	9	3	4	2	3
Percentage (%)	3.00	48.00	21.00	7.00	9.00	3.00	4.00	2.00	3.00

Section C: Knowledge of paracetamol

H_0: The respondents do not have a good knowledge of paracetamol ($p>0.05$).

H_1: The respondents have a good knowledge of paracetamol ($p<0.05$).

Response	True	False	None	Not known
10. It is an off-counter medication	4 (4.00)	87 (87.00)	0 (0.00)	9 (9.00)
11. Can be taken without prescription	39 (39.00)	57 (57.00)	0 (0.00)	4 (4.00)
12. Acetaminophen is its active component	33 (33.00)	44 (44.00)	2 (2.00)	21 (21.00)
13. It is an anti-pyretic	39 (39.00)	38 (38.00)	2 (2.00)	21 (21.00)
14. It is an antimalarial drug	25 (25.00)	52 (52.00)	2 (2.00)	21 (21.00)
15. Its expiry date does not affect its	31 (31.00)	63 (63.00)	0 (0.00)	6 (6.00)

potency				

Df=15; Chi square (X^2) value= 13.65; p>0.05. The, null hypothesis is accepted. The students do not have a good knowledge of paracetamol usage. Data is represented as frequency (percentage).

Section D: Knowledge of dosage

16. A tablet of paracetamol has how many milligrams?

Response	50mg	100mg	500mg	100mg	Total
True	1	15	78	6	100
False	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
None	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Not known	0(0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)

17. How many tablets do you as an adult take per dose?

Response	One tablet	Two tablets	Three tablets	Four tablets	Total
True	12	88	0	0	100
False	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
None	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Not known	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)

18. If symptoms persist after paracetamol consumption, you are supposed to see a

physician after

Response	24hours	48hours	72hours	Total
True	6	41	53	100
False	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
None	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Not known	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)

Section E: Sourcing of paracetamol

H_0: The respondents do not have the appropriate knowledge of where and how to source for paracetamol ($p>0.05$).

H_1: The respondents have the appropriate knowledge of where and how to source for paracetamol ($p<0.05$).

Response	True	False	None	Not known
19. Must be taken with prescription from a medical professional	37 (37.00)	56 (56.00)	0 (0.00)	7 (7.00)
20. Must be obtained from the hospital	19 (19.00)	78 (78.00)	0 (0.00)	3 (3.00)
21. The potency of paracetamol depends on the brand	62 (62.00)	38 (38.00)	0 (0.00)	0 (0.00)
22. There is no	37	19	10	46

known company for the local production of paracetamol in Nigeria	(37.00)	(19.00)	(10.00)	(46.00)

Df=9; Chi square (X^2) value= 21.82; p>0.05. The, null hypothesis is accepted. The respondents do not have the appropriate knowledge of where and how to source for paracetamol. Data is represented as frequency (percentage).

Section F: Pharmaco-toxicology and pharmaco-kinetics of paracetamol

H_0: The respondents do not have a good knowledge of the pharmaco-toxicology and pharmaco-kinetics of paracetamol (p>0.05).

H_1: The respondents have the appropriate knowledge of where and how to source for paracetamol (p<0.05).

Response	True	False	None	Not known
23. Paracetamol cannot be abused irrespective of dose	18 (18.00)	45 (45.00)	0 (0.00)	37 (37.00)
24. Paracetamol must be consumed based of body weight	34 (34.00)	16 (16.00)	0 (0.00)	50 (50.00)
25. Paracetamol metabolism starts from the stomach	14 (14.00)	27 (27.00)	0 (0.00)	59 (59.00)
26. The potency of paracetamol is enhanced by the liver	37 (37.00)	19 (19.00)	10 (10.00)	46 (46.00)

27. Paracetamol can be poisonous	31 (31.00)	63 (63.00)	0 (0.00)	6 (6.00)
28. Consumption of food along-side paracetamol has no effect on its potency	34 (34.00)	15 (15.00)	0 (0.00)	51 (51.00)

Df=15; Chi square (X^2) value= 21.06; p>0.05. The, null hypothesis is accepted. The respondents do not have a good knowledge of the pharmaco-toxicology and pharmaco-kinetics of paracetamol. Data is represented as frequency (percentage).

Section G: Reason for taking paracetamol

H_0: The respondents do not take paracetamol the appropriate reasons (p>0.05).

H_1: The respondents take paracetamol for the appropriate reasons (p<0.05).

Response	True	False	None	Not known
29. For pain amelioration	100 (100.00)	0 (0.00)	0 (0.00)	0 (0.00)
30. As an anti-depressant	0 (0.00)	28 (28.00)	0 (0.00)	72 (72.00)
31. As a psycho-active drug	0 (0.00)	27 (27.00)	0 (0.00)	59 (59.00)
32. High blood pressure amelioration	0 (0.00)	100 (100.00)	0 (0.00)	0 (0.00)
33. For the amelioration of	47	31	0	22

menstrual pain	(47.00)	(31.00)	(0.00)	(22.00)
34. For the amelioration of the pain of post-surgical operation	11 (11.00)	63 (63.00)	0 (0.00)	26 (26.00)

Df=15; Chi square (X^2) value= 18.06; p>0.05. The alternate hypothesis is accepted. The respondents take paracetamol for the appropriate reasons. Data is represented as frequency (percentage).

CHAPTER FIVE

5.0 Discussion and Conclusion

5.1 Discussion

Worldwide, self-medication has been a rising trend and irrational use of the over-the-counter (OTC) drugs is a cause of great concern for public health agencies (Kumar *et al*., 2013; Wazaify, Shields, Hughes, and McElnay, 2005). In modernistic years, innumerable drugs have been available on an over-the-counter basis, inclusive of the drugs that were available merely through prescription in the past (Brass, 2001).

Paracetamol is the most frequently used OTC drug in deliberate self-poisoning (Hawton *et al*., 1995). Paracetamol poisoning can occur at recommended therapeutic doses and multiple therapeutic or supra therapeutic doses (Lubel *et al*., 2007). An alarming concern in recent years is that, unintentional overdose, rather than intentional overdose have been the main cause of paracetamol induced ALF (acute liver failure) (Jalan *et al*., 2007).

This study was carried out ascertain the awareness, explore the perceptions and knowledge among educated adults (university students) regarding the most common OTC analgesic 'Acetaminophen' available with a brand name of panadol and paracetamol. University students were selected for this study because the authors wanted to emphasis the fact that even the educated adults of the community have not sufficient information regarding the OTC drugs. Moreover, the authors believe, that lack of knowledge among the community members could be one of the biggest reasons of the misuse of OTC drugs. Our results offer an indirect estimation of likelihood of overuse and misuse among our general population (which is not well educated) via the knowledge level of educated adult users (university students).

In this research, the views of hundred (100) University of Benin students were sampled to evaluate their knowledge and practice of the abuse of paracetamol, through the distribution of informed questionnaires. Their responses were analyzed using the Chy square (X^2), and

descriptive tables where necessary. The population were all full time students (learners), which included 73% male, 27% female (table 1). Fifteen percent of the population were within the 16 to 24 years of age, with eighty five percent within the age bracket of 21 to 30 years (table 2). Ninety one percent of the sampled population said they single and nine percent were married (table 3). Eight percent of the population had BMI between the range of 16 to 20 Kg/m^2; seventy three percent had BMI between 21 and 25 Kg/m^2; and fourteen percent had BMI between 26 and 30 Kg/m^2.

In the section B, the experience or studentship of the respondents was also assessed, with more of the students in 300 level (43%), followed by 400 level (31%) and then, 200 level (14%). Forty eight percent of the respondents were in the school of basic medical sciences; twenty one percent were in schools of medicine and dentistry, and nine percent in faculty of life sciences.

In section C, the knowledge of paracetamol of the respondents was assessed, and it was observed that, the students do not have a good knowledge of paracetamol usage (i.e., the null hypothesis was accepted; $p>0.05$, Chi square (X^2) value= 13.65). Eighty seven percent said it was not true that paracetamol is an off-counter medication; fifty seven percent said paracetamol cannot be taken without prescription; forty four percent said it was not true that acetaminophen is the active component of paracetamol; while thirty nine percent claimed that paracetamol is an anti-pyretic medication, thirty eight percent said it was not; surprisingly, fifty two percent claimed that paracetamol is an ant-malarial drug, with sixty three percent alleging that the expiry date of the drug does not affect its potency. This observation agrees with the findings of Fontana (2008).

In section D, the knowledge of the dosage of paracetamol was assessed; seventy eight percent said that a tablet of paracetamol has 500mg of acetaminophen (table 16); eighty eight percent claimed that two tablets of paracetamol make a single dose; and fifty three percent of the respondents said that, if symptoms persist after 72 hours of paracetamol consumption, you are supposed to see a physician after, as against, forty one that said forty eight hours. This was previously reported in the findings of Ghumman *et al.* (2013).

In section E, the respondents were questioned about how they source for paracetamol; it was observed that the respondents do not have the appropriate knowledge of where and how to source for paracetamol (X^2 value = 21.82; $p>0.05$, the, null hypothesis was accepted). Fifty six percent of the respondents do not believe that paracetamol must be taken with prescription from a medical practitioner; seventy eight percent said paracetamol must be obtained from the hospital; thirty eight percent said the potency of paracetamol depends on the brand (as against sixty two that said it does not); forty six percent of the respondents claimed that were not aware of any local company that produces paracetamol in Nigeria.

In section F, the knowledge of the pharmaco-toxicology and pharmaco-kinetics of paracetamol was assessed, and it was observed that the respondents do not have a good knowledge of the pharmaco-toxicology and pharmaco-kinetics of paracetamol (X^2 value = 21.06; $p>0.05$, null hypothesis is accepted); ironically, forty five percent claimed that paracetamol cannot be abused irrespective of dose, while thirty seven percent claimed that they were not aware of the health implications of paracetamol dosage; thirty four said it was true that paracetamol must be consumed based of body weight; fifty nine percent said they

were not aware of the part of the gut were paracetamol metabolism starts from, while forty six percent said were not aware whether the liver affects the potency of paracetamol during its metabolism; sixty three percent of the respondents said they were not aware that paracetamol could be poisonous to the body at very high intolerable doses; fifty one percent said that they were not aware if food could affect the potency of paracetamol if consumed together. This has previously been reported by Helena *et al.* (2009).

In section G, the reasons why the respondents take paracetamol was assessed, to ascertain if they were in line with the knowledge of the medical conditions that should involve the administration of paracetamol. However, it was observed that the respondents actually take paracetamol for the appropriate reasons (X^2 value = 18.06; $p>0.05$, the alternate hypothesis was accepted); hundred percent of the respondents said they would take paracetamol for the amelioration of pain; twenty eight percent said paracetamol was not an anti-depressant (seventy two had claimed that they were not aware); twenty seven percent said it was not a psycho-active drug (fifty nine percent has claimed that they were not aware); hundred percent said paracetamol was not a drug that could be administered to ameliorate high blood pressure (HBP); forty seven percent said that they could take paracetamol to ameliorate the pains associated with menstrual cramps; and sixty three percent said that paracetamol could not be used for the amelioration of the pain of post-surgical operation (eleven percent claimed that it could be used). Kumar et al. (2013) reported this observation earlier in their research.

5.2. Conclusion

Based on the reports from this assessment, there is a serious information gap regarding the usage of paracetamol, sources of where to obtain paracetamol, as well as, the pharmaco-toxicology and pharmaco-kinetics of paracetamol. It is quite possible that the field of studies of the students could also have impacted the assessment and judgement of the students. These three key points of knowledge deficiency amongst the assessed students, on paracetamol utilization, *viz*, usage, source and metabolism, should not be disregarded as urgent steps needs to be taken to educate university students on paracetamol usage. This could also be extended to other possible drugs that are abused by these students, noting that they may not be aware of the implications of consuming such drugs.

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