ANALYSIS OF CAFFEINE IN PHARMACEUTICAL AND PERSONAL CARE PRODUCTS IN FISH AND WATER SAMPLES FROM UREJE DAM, EKITI STATE, NIGERIA.

By

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DECLARATION

I, **OLUKAYODE, TOYOSI LAWRENCE** hereby declare that the content of this project is a product of my own research effort, under the supervision of **Dr. OKEKE, O. S.** and has not been presented elsewhere for the award of degree. All sources have been duly distinguished appropriately acknowledged.

.... 14-12-2017 ....

OLUKAYODE, TOYOSI LAWRENCE **Date**

CERTIFICATION

I certify that this work was carried out by **Olukayode, Toyosi Lawrence** in the Department of Fisheries and Aquaculture, Faculty of Agriculture, Federal University Oye-Ekiti, Ekiti State.

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DEDICATION

This project work is dedicated to the Almighty God and my wonderful parents Mr. and Mrs. Olukayode Obareke.

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ABSTRACT

Pharmaceuticals and Personal Care Products (PPCPs) are cosmetics, drugs, or other consumer products used to cleanse, beautify, or treat humans or animals; including prescriptions and over the counter drugs, soaps, fragrances, solvents, non-ionic and anionic surfactants, bleaches, dyes, and sunscreen agents. They are termed Contaminants of Emerging Concerns and are Endocrine Disrupting Substances in both aquatic animals and humans. This study therefore seeks to analyze Caffeine in PPCPs that could be present in fish and water samples from Ureje dam, Ado-Ekiti, Ekiti State. Fish and water samples were collected. Questionnaire survey was done using Random sampling method to find out peoples' knowledge, attitudes and practices with regards to PPCPs, their modes of disposal and their effects on the aquatic ecosystem and human health. High Performance Liquid Chromatography was used to analyse for the presence of Caffeine in the samples while Descriptive analyses were used to analyse the questionnaire results and they were presented in pie charts. The fish and water samples from Ureje dam did not show any peak at 8.87minutes retention time for Caffeine indicating that the samples do not contain detectable levels of Caffeine and so are safe for human consumption, human use and domestic purposes. Of the respondents, 37% had heard about PPCPs; 34% know what they are; 34% use PPCPs; 54% are not sure these PPCPs have effects on waterbodies and aquatic life. Also, throwing in trash cans and then to garbage collection points rated highest (43%) among modes of disposing contents and containers of PPCPs and 57% think that their mode of disposing these contents and containers is appropriate. Furthermore, 83% and 26% of the respondents are not aware that PPCPs and the chemicals they are made up of could have negative effects on fish in their environment and on humans respectively. These indicate a low level of knowledge and awareness of PPCPs.

Table of Contents

LIST OF FIGURES

LIST OF TABLES

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND

Pharmaceuticals and Personal Care Products (PPCPs) are cosmetics, drugs, or other consumer products used to cleanse, beautify, or treat humans or animals (Nutrition Center for Food Safety and Applied Food and Drug Administration, 2015). Examples include prescriptions and over the counter drugs, soaps, fragrances, solvents, non-ionic and anionic surfactants, bleaches, dyes, and sunscreen agents (Caldwell, 2015).

Pharmaceuticals and Personal Care Products include a wide range of medicines (both over-the-counter and prescription), illicit drugs, and byproducts from everyday items. The substances are referred to as either synthetic or non-synthetic (natural) (United States Department of Agriculture, 2011). In recent years, environmental concerns and research on Emerging Pollutants (EPs, chemicals which are not normally monitored in the environment, while having the possibilities to enter into the environment and lead to potential adverse effects to both ecological systems and human health) have increased (Geissen *et al.,* 2015). Pharmaceuticals and Personal Care Products (PPCPs) are one of a number of types of emerging pollutants, whose bioactive compounds and metabolites have been found in groundwater, surface water, drinking water and agricultural lands (Daughton and Ternes, 1999; Zhou *et al.,* 2013), and which have become an important focus (Boxall *et al.*, 2012; Stuart *et al.*, 2012; Richardson and Ternes, 2014).

In the past few years, anthropogenic intensification and eutrophication have caused a decline in the water quality resulting in milfoil invasions, algal blooms, hypoxia, and fish kills (Liang and Guillory, 2015). Recently, researchers around the world have also begun to explore pharmaceuticals and personal care products (PPCPs) as another category of contaminant concern for freshwater ecosystems. In order to achieve their desired effects, PPCPs contain chemical compounds that are specially designed to interact with physiological systems (Boxall *et al.*, 2012). These reactive components have been shown to persist in sediments, soils, and surface waters (Adolfsson-Erici *et al.,* 2002; Benotti *et al.*, 2009; Banerjee *et al.*, 2016). Also, most literature focus on the presence of certain compounds in sewage effluent, medical waste effluent, groundwater, drinking water, landfills, and surface waters. Large data gaps exist documenting the occurrence, fate, or activity of PPCPs or their metabolites in any of these types of water (Kümmerer, 2009). Recently, researchers have also begun to study psychoactive and illicit drugs in the environment. Recent technological advances, including solid phase extraction followed by liquid chromatography-mass spectrometry, have allowed for detection of PPCPs in the ng/L range in aquatic samples (Lam *et al*., 2004). Given the widespread use of PPCPs, it is important to consider how we dispose of them and the possible effects on both the environment and human health (Daughton and Ternes, 1999; Enick and Moore, 2007; Schirmer and Schirmer, 2008; Caldwell, 2015).

As a result of the fact that PPCPs have a way of leaching out slowly into the waterbody as a result of harmful chemicals from the drugs, cosmetics, fragrances, detergents etc. mostly chemicals are slowly released into the aquatic ecosystem. Furthermore, PPCPs released can find their way into the aquatic ecosystem and cause detrimental effects on the fisheries resources. Flushing of PPCPs and dumping refuse materials near the water body also contribute to high level of pollutants in the aquatic ecosystem. The impact and effect of these chemicals on the aquatic ecosystem and organisms therein cannot be over emphasized (Bowles, 2010).

This study therefore seeks to analyze Caffeine in pharmaceuticals and personal care products that could be present in fish and water bodies in Ekiti State using Ureje dam as a case study. Furthermore, levels of found chemical would be ascertained.

1.2 Justification

PPCPs are Contaminants of Emerging Concerns and are Endocrine Disrupting Substances in both aquatic animals and humans (Geissen *et al.*, 2015, Fairbairn *et al.*, 2016).

There is need to establish the presence or absence of PPCP chemicals and their particular potential sources in Ureje dam Ado-Ekiti, Ekiti State.

Individuals need to understand the effects of these chemicals on fish and humans to encourage and ensure proper disposal of contents and containers.

1.3 Objectives

The main objective of this study is to analyze Caffeine present in pharmaceutical and personal care products respectively in Ureje dam in Ekiti State.

Specifically, this study seeks to

I. To evaluate level of found chemical (caffeine) in urban (Ureje) dam and identify plausible causes.

II. To find out what individuals know about pharmaceuticals and personal care products, their modes of disposing their contents and containers and possible consequences of such actions.

1.4 Hypotheses

The hypotheses of this work are as follows

1. Chemical (caffeine) present in PPCPs cannot be found in some waterbodies in Ekiti State.
2. Individuals are not aware of the implications of improper disposal of contents and containers of PPCPs.

CHAPTER TWO

LITERATURE REVIEW

2.1 Pharmaceuticals and Personal Care Products (PPCPs)

Pharmaceuticals and Personal Care Products (PPCPs) as environmental pollutants, was first investigated in Europe in 1980s. With the advent of monitoring and research in the United States, literature has grown exponentially since 2000.

PPCPs are not truly "emerging" pollutants. It is the understanding of the significance of their occurrence in the environment that is beginning to develop. Since the 1970s, the impact of chemical pollution has focused almost exclusively on conventional "priority pollutants", especially on those collectively referred to as "persistent, bio-accumulative, toxic" (PBT) pollutants, "persistent organic pollutants" (POPs), or "bio-accumulative chemicals of concern" (BCCs).

The vast majority of all "emerging" pollutants are not new to the environment. According to Daughton *et al.,* 2001, there are two major sources for pollutants that are truly "new" to the environment:

- Chemicals newly introduced to commerce (e.g., new drugs or pesticides).
- New anthropogenic processes (e.g. gallium arsenide quantum dots).

PPCPs in the environment are raising concerns of:

- Aquatic species: Feminized male fish, river otters and frogs are being found in rivers and lakes due to the presence of synthetic estrogen hormones from birth control pills.
- Increase of bacteria due to resistance to antibiotics: antibiotics including penicillin and triclosan, the active ingredient found in antibacterial soaps, deodorants, and household cleaners, are being dumped into the water supply and killing natural bacteria, both good and bad. This may lead to an environment where bad bacteria can thrive (Hirsch *et al.,* 1999). Some evidence has been found surrounding the same hormone problem in fish occurring in human males. Males that live in rural areas that were exposed to certain pesticides as well as European males exposed to estrogen in the environment experienced lower sperm counts. A rise in the numbers of breast

and uterine cancers, early puberty and birth defects of the genitals have been linked to environmental exposure to estrogenic compounds.(McBride *et al.*, 2002).

2.2 Caffeine

Caffeine is one of the most widely consumed drugs in the world, present in coffee, tea, cocoa, and many pharmaceutical drugs e.g. Anacin, Aspirin, Acetaminophen, BC-Powder, Orphenadrine, Vivarin, e.t.c. for its stimulant and analgesic (pain-relieving) effects (Bruton *et al.*, 2010a). Agricultural runoff and landfill leachate may also be important inputs (Hollingsworth *et al.*, 2003, Buszka *et al.*, 2009, Bruton *et al.*, 2010a). In humans, only a small fraction of caffeine is excreted as the unchanged molecule. Most is excreted as Paraxanthine (1, 7-dimethylxanthine) (Vanderveen *et al.*, 2001). In a report of 50 randomly selected Minnesota lakes and rivers, Ferrey (2015) found a maximum caffeine concentration of 0.067μg/L in some lakes. Caffeine has also been shown to impact aquatic ecosystems on a microbial level (Shaw *et al.*, 2015). Gibson *et al.*, (2009) performed aquarium experiments looking at the effects of caffeine on *Pseudomonas*, a bacterium commonly found in aquatic habitats. In response to caffeine, they observed increased growth, bacterial colony count, and the development of a bio-film like sheen on the glass of the experimental aquarium. Gibson *et al.*, 2009 also observed that increased ammonia concentrations correlated with the metabolic activity of the bacteria, which is highly toxic to fish. Shaw *et al.*, (2015) found that caffeine stimulated gross primary production by 39% in algal biomass after 21 days.

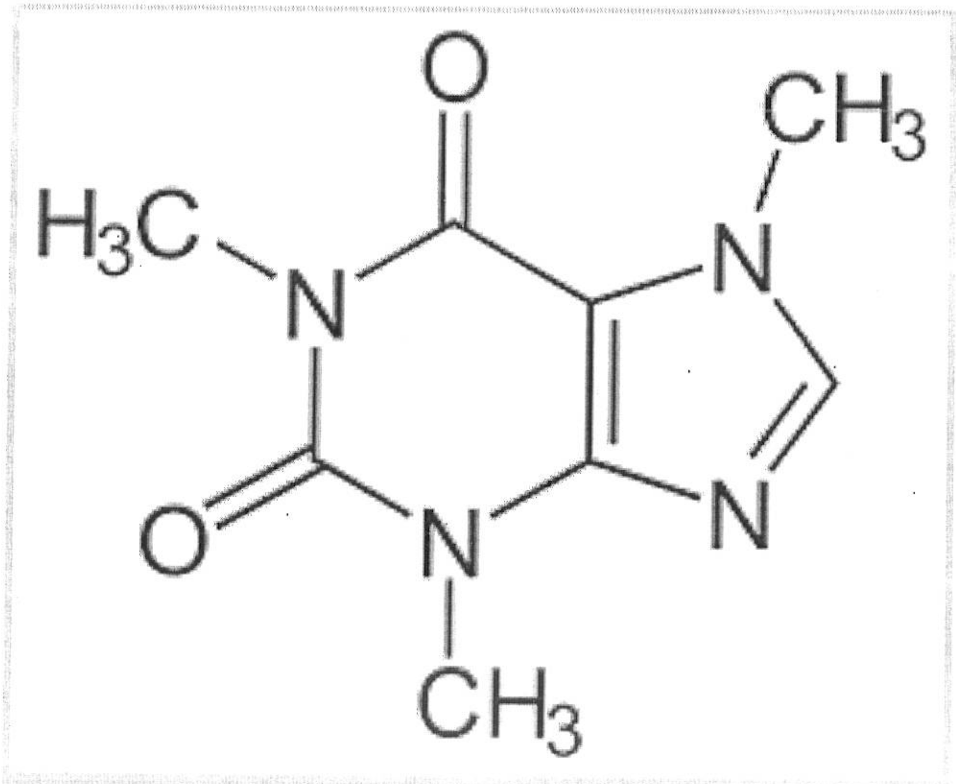

Fig 1: Structure of Caffeine (Wikipedia)

2.3 Sources of PPCPs

The majority of PPCPs found in aquatic systems are the result of consumer use, excretion, disposal of unused products flushed down toilets, or from wastewater treatment facilities (*Caldwell, 2015*). Wastewater treatment facilities treat water, typically from homes, manufacturing sites, or runoff, by removing suspended particles and pollutants (*Perlman, 2016*). Since neither municipal wastewater treatment plants, nor onsite wastewater treatment systems (including septic systems) can effectively treat the complex mixture of PPCPs present in sewage, PPCPs are often released directly into the environment (Jones *et al.*, 2004, Vieno *et al.*, 2005, Carrera *et al.*, 2008, Benotti *et al.*, 2009, Schaider *et al.*, 2013, Papageorgiou *et al.*, 2016, Banerjee *et al.*, 2016). Other sources include aquaculture facilities and releases to soils and subsequently groundwater from biosolids and manure application (Boxall *et al.*, 2012). In aquatic ecosystems, sewage effluent is often cited as the primary influence on detection frequencies and concentrations of PPCPs (Fairbairn *et al.*, 2016).

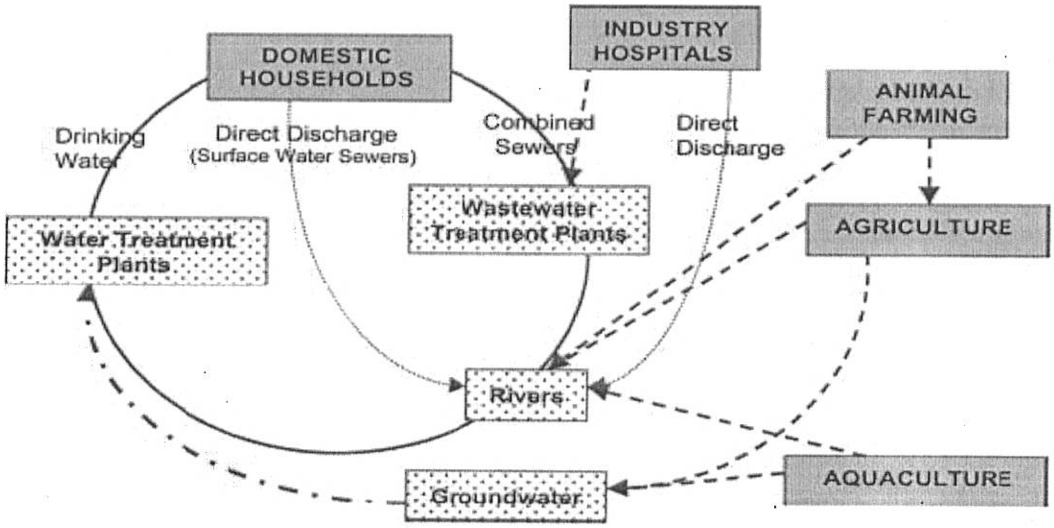

Fig 2: Sources and pathways of the urban PPCP (Ellis, 2006).

2.4 Problems and Effects of PPCPs

2.4.1 Problems and Effects on fish and other Aquatic organisms

PPCPs can have a variety of effects on biological processes in aquatic environments. Some contain anti-bacterial or anti-fungal properties which are helpful in treating certain infections and illnesses in humans or livestock, but can have dire consequences for aquatic organisms, even those at high taxonomic levels, such as fish (Kümmerer, 2004, Sumpter *et al.*, 2006). Synthetic estrogen from birth control pills, antihistamines from allergy medication, pain relievers like ibuprofen and acetaminophen, anti-depressants, triclosan (an antimicrobial agent), caffeine, bisphenol (found in durable plastics), and illicit drugs, have been shown to have a wide range of biological impacts, including lethal toxicity at very high concentrations, feminization of fish and amphibians, and changes in bacterial communities in aquatic ecosystems (Crain *et al.*, 2007, Drury *et al.*, 2013, Ferrey, 2013, Rosi-Marshall *et al.*, 2015). Most of the literature regarding PPCPs and their impact on aquatic organisms focuses on the impacts of exposure at high concentrations, with a particular emphasis on mortality. However, a number of significant sublethal effects including histological changes, behavioral effects, biochemical responses, and gene regulation can occur at low concentrations (Klaper and Welch, 2011). A study by Boxall *et al.*, 2012 demonstrated the effects of some PPCPs at varying concentrations in fish and vertebrates and found out that the effect level for different organisms varies based on the level of exposure (Boxall *et al.*, 2012).Regarding EDCs, endocrine-related effects on growth and development from environmental exposures have been observed in fish. Some laboratory studies also suggest human health effects, such as those on fetal development, timing of puberty, or disruption of thyroid function (World Health Organization and United Nations Environment Programme, 2013).

PPCPs can also alter the microbial communities of aquatic ecosystems. Microbial communities serve as the basis of aquatic food webs, a resource for higher trophic levels, and the decomposition of organic matter. Any disturbance in this microbial community as a result of PPCP pollution could alter the structure of aquatic ecosystems (Shaw *et al.,* 2015). Diphenhydramine, an antihistamine, has been shown to cause significant increases in *Pseudomonas species* and decreases in *Flavo bacterium species* in stream biofilms (Rosi Marshall *et al.,* 2013, MedlinePlus, 2015).

2.4.2 Problems and effects on Humans

Scientists and health advocates have also drawn attention to the possible human health implications of PPCPs. Persistent organic pollutants, many of which come from PPCPs, are known to bio-accumulate in the food chain (Klaper and Welch, 2011). Widespread exposure to these pollutants through product consumption or use has been linked to impaired neurodevelopment, immune and reproductive function, and endocrine system disruption, causing inflammation, birth defects, and certain cancers. Even low level exposure to endocrine disrupting chemicals can impact fetal, neonatal, and childhood development (Damstra, 2002). Most of the data describing the impacts of PPCPs on humans focuses on consumption or use of the initial PPCP, not environmental exposure. Humans can also be exposed to PPCPs in water via direct contact from recreation or through drinking water sources (Kümmerer, 2004*).* According to Jones *et al.,* 2004), pharmaceuticals from sewage effluent can cause drug-resistant pathogens in the water.

Pharmaceuticals from sewage effluent can cause drug-resistant pathogens in the water. Exposure to these pathogens while recreating polluted bodies of water may have health implications. Studies have shown that PPCPs are also prevalent in drinking water. Loraine and Pettigrove (2006) studied parts of the Colorado River that were severely impacted by septic systems and tested the river water entering and leaving a drinking water treatment facility sourced from the Sacramento-San Joaquin River Basin. The pre-treatment water contained phthalate esters, sunscreens, clofibrate, clofribic acid, ibuprofen, triclosan and diethyltoluamide. The treated water, delivered to humans for consumption, still contained many of these compounds, including benzophenone, ibuprofen, and triclosan, indicating that water treatment facilities are unable to effectively or completely remove these compounds (Loraine and Pettigrove, 2006). In addition to surface water, groundwater is a widespread source for drinking water, and thus, the prevalence of PPCPs in groundwater should also be considered. According to the United States Geological Survey (USGS), PPCPs can move from septic systems into groundwater (Phillips *et al.*, 2015). However, few studies have documented this phenomenon. Exposure to high concentrations or chronic low levels could pose a tremendous threat to human health.

2.5 Possible Solutions to these Problems

Strategies for preventing EDCs and PPCPs from entering water supplies include improved wastewater treatment and other source water protection strategies. Once EDCs and PPCPs have entered a utility's water supply, no single treatment process can remove them all due to their wide range of physicochemical properties. In general, both conventional and advanced water treatment systems have the capability to reduce the concentration of EDCs (State of the Science of Endocrine Disrupting Chemicals, 2012).Ensure Proper Waste Disposal. Wastes are returned to manufacturer. Educate Consumers of Proper Waste Disposal; develop educational information for customer distribution, direct mailing, utility bill stuffers, television commercials, radio spots, direct education (community events Earth Day, senior community centers) and provide Consumers Pharmaceutical Waste Disposal Options. If no collection options exist, or will be provided, consider recommending consumers to remove all personal identification from prescription bottles; mix all unused drugs with coffee grounds, kitty litter, or another undesirable substance, and/or place this mixture in a sealed container before disposing in the trash, on the day of pick-up.

2.5.1 Ubiquity in the Aquatic Environment

PPCPs are frequently detected in freshwater samples from around the world, even in supposedly pristine bodies of water (Vieno *et al.,* 2005, Fairbairn *et al.*, 2016, Banerjee *et al.*, 2016). For example, atrazine was detected in surface waters far from agricultural application in the United States, with a drinking water treatment plant as the only known source of contamination (Benotti *et al.,* 2009). According to Benotti *et al.,* 2009, researchers have detected atrazine in food. Subsequent disposal of this food may be the source of atrazine loading into the surface waters. A national study spanning 139 streams in 30 different states found measureable amounts of one or more medications in 80% of the water samples drawn. Of the types of compounds tested, the most prevalent were steroids and nonprescription drugs. Detergent metabolites had the highest percentage concentration in the locations detected (Kolpin *et al.*, 2002). Fairbairn *et al.,* 2016 found that PPCPs like erythromycin, an antibiotic, reached levels as high as 10 μg/L downstream of wastewater treatment plants. In another study, Ferrey (2013) detected 56 different PPCPs and other chemicals downstream of a wastewater treatment plant. Bodies of water close to intense urbanization or livestock production are especially susceptible to PPCP contamination (Koplin *et al.,* 2004).

2.5.2 Breakdown of PPCPs in Surface Waters

Once in the aquatic environment, PPCPs may be eliminated through processes such as biodegradation, sorption, photodegredation, and sedimentation (Vieno *et al.*, 2005). By studying the persistence of eight different pharmaceuticals in aquatic outdoor field microcosms, Lam *et al.*, 2004 found that half-lives ranged from about 1 day with acetaminophen, a pain reliever, to 82 days with carbamazepine, an anticonvulsant, in sunlit microcosms of exposed pond water and natural autoclaved water. Over the 30 day experiment, Lam *et al.*, (2004) also found that these eight pharmaceuticals did not break down in the dark control microcosms, suggesting that photodegradation, not biodegradation, may be a limiting factor in their persistence.

2.5.3 Fluctuation in PPCP Prevalence

Researchers have also found that PPCP concentrations vary considerably with seasonal or population changes. A study of 23 different stream locations in Iowa showed that organic wastewater contaminants, many of which are also PPCPs, varied with stream flow (Koplin *et al.*, 2004).

Koplin *et al.*, 2004 observed that organic wastewater contaminant concentrations decreased as stream flow increased. Other studies have attributed this phenomenon to reduced dilution, slowing the degradation processes of PPCPs and allowing them to persist longer in aquatic environments (Musolff *et al.*, 2009, Luo *et al.*, 2011, Veach and Bernot, 2011). Koplin *et al.*, 2004 also noted a correlation between the frequent detection of methyl salicylate, a common ingredient in UV sunscreens, and high summer temperatures.

PPCPs in aquatic ecosystems vary based on societal influences such as source proximity and population fluctuations as well as physicochemical and environmental influences. Fairbain *et al.*, 2016 noted that increased PPCP concentrations have been associated with cold, low flow conditions due to reduced degradation and in warm, high flow conditions due to increased wastewater treatment flow, reduced retention time and removal efficiency. They also described the seasonal changes in agricultural herbicides in surface waters, spiking in the early summer, when application rates and precipitation are the highest. While studying the Aura River in Finland, located near a wastewater treatment facility, Vieno *et al.*, 2005 found that PPCP concentrations increased during winter months and decreased during spring and summer months. Another study of the Upper White River watershed in Indiana demonstrated the same seasonal trend with increased PPCP concentrations in the winter and decreased concentrations in the spring and summer months (Veach and Bernot, 2011). A study of seasonal variation of stimulatory drugs in the Llobregat River in Spain near a drinking water plant indicated that nicotine, caffeine, and paraxanthine had the opposite trend, with the highest concentrations detected in the spring and summer (Huerta-Fontela *et al.*, 2008).

2.6 Eighteen Common PPCPs

A number of PPCPs are prevalent in aquatic ecosystems and may have important impacts on the environment and human health. Below is a review of the current literature of each compound, its probable source, prevalence in aquatic ecosystems, and reported effects on the environment and human health.

2.6.1 Stimulants: Paraxanthine (1, 7-Dimethylxanthine), and Cotinine

Paraxanthine (1, 7-dimethylxanthine) is one of the primary breakdown products of caffeine. In humans, paraxanthine has many of the same effects as caffeine including increased systolic blood pressure, plasma epinephrine levels, and free fatty acids (Benowitz *et al.*, 1995). Recent studies using polar organic integrative samplers, a passive diffusion method, have detected concentrations of paraxanthine as high as 0.0234 µg/L15 upstream of a wastewater treatment plant to 0.0019 µg/L downstream in receiving bodies of water including rivers and creeks (Bartlet-Hunt *et al.*, 2009). Driesen (2015) reported concentrations of 1672 µg/L in the wastewater from the Experimental Center of Carrión de los Céspedes in Seville, Spain. Caffeine has been shown to impact a number of freshwater species including water flea intoxication, brine shrimp mortality, and growth changes in the fathead minnow (Bruton *et al.*, 2010a). In lentic biofilms, caffeine can stimulate gross primary production by 39% (Shaw *et al.*, 2015). The impacts of 1, 7-dimethylxanthine are not as well understood. One study reported an LC50 in the Cladocerans order (water fleas), the concentration required to kill 50% of the population, exceeding 100,000 µg/L (Fernández *et al.*, 2010).

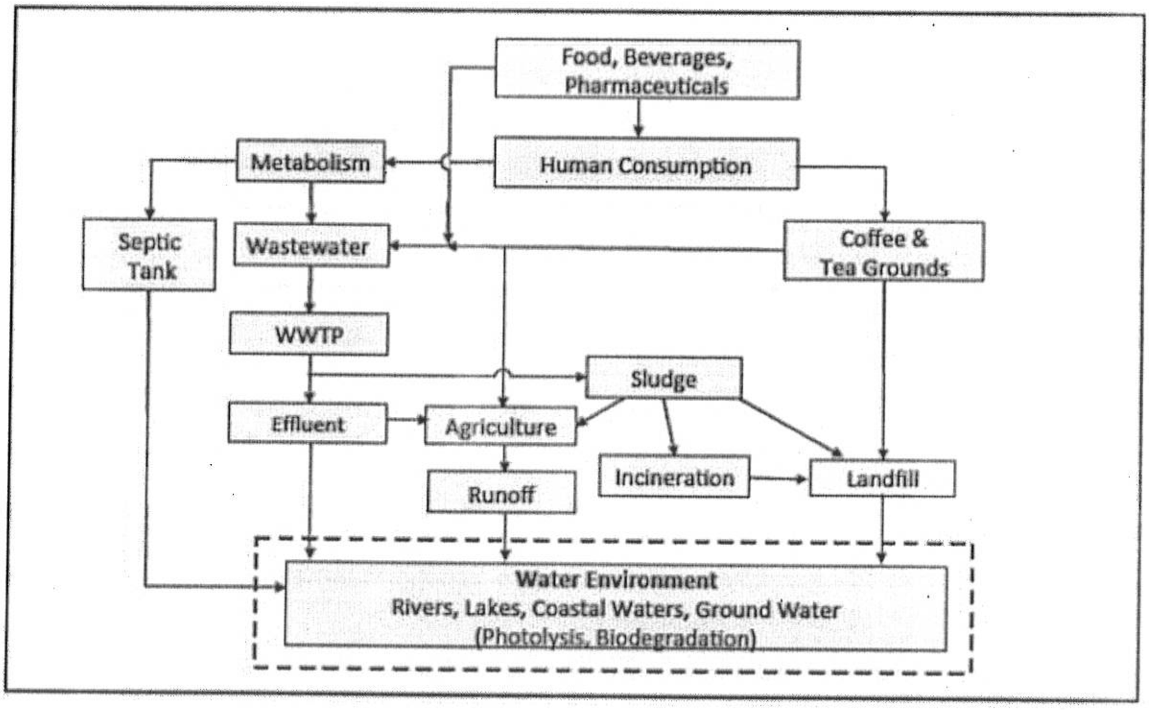

Fig 3: Caffeine routes into the environment (Bruton *et al.*, 2010a).

Cotinine is a breakdown product of nicotine. In humans approximately 70-80% of nicotine is excreted as cotinine. Previous studies have found cotinine concentrations in lake waters as high as 0.0421 µg/L (Benowitz *et al.*, 1995, Ferrey, 2015). The effects of cotinine on aquatic organisms are not well understood. According to Crane *et al.*, 2006, the effects of cotinine should be similar to those of nicotine, which include binding to nicotinic-Ach receptors, facilitating release of Ach, dopamine and glutamate neurotransmitters in the water flea, Daphnia pulex. Other researchers have linked cigarette butts in aquatic ecosystems to mortality in Daphnia species. Slaughter, 2011 found an LC50 of one smoked cigarette butt per liter of water for Atherinopsaffins, marine topsmelt, and Pimephalespromelas, fathead minnow.

2.6.2 Over the Counter Medications: Acetaminophen, Cimetidine, Diphenhydramine, Ibuprofen, and Naproxen

Acetaminophen is typically used for its analgesic and antipyretic (fever reducing) properties. Humans excrete less than 5% of acetaminophen unchanged, the rest is excreted as metabolites (Mazaleuskaya *et al.*, 2015). Bartlet-Hunt *et al.*, 2009found acetaminophen in all river and creek samples except for one site upstream and one site downstream of a wastewater treatment plant. It was detected in all sewage effluent samples except for one. Acetaminophen concentrations downstream of a wastewater treatment plant reached 0.064 μg/L, compared to 0.0044 μg/L upstream (Bartlet-Hunt *et al.*, 2009). At very high concentrations, acetaminophen can be lethal to the zooplankton *Daphnia magna* (Kim *et al.*, 2010). Kim *et al.*, 2010 found that in *Daphnia magna*, the EC50 (the concentration of a drug that elicits a half-maximal response) was 8200 μg/L after 96hours of exposure.

Cimetidine is typically used to treat peptic ulcer disease in patients with renal failure and gastro esophageal reflux disease, a condition in which a backflow of stomach acid causes heartburn and damages the esophagus (MedlinePlus, 2010). In a study of 9 patients with normal renal function after a single intravenous dose of cimetidine, 47.3% was excreted unchanged (Larsson *et al.*, 1982). In surface waters in the Han River in South Korea, cimetidine has been detected at levels as high as 5.38 μg/L (Choi *et al.*, 2008), the highest concentration reported in the world as of 2008. According to Shaw *et al.*, (2015), cimetidine can stimulate gross primary production in lentic biofilms by 46%. For *Daphnia magna*, the predicted no effect level concentration or concentration below which there is no effect, is 35μg/L (Buth *et al.*, 2007).

Diphenhydramine is used as an antihistamine, antiemetic, sleep aid, sedative, and central nervous system depressant. In the human body, diphenhydramine breaks down in gastrointestinal tract to a number of metabolites. Humans only excrete 1.9% of diphenhydramine unchanged (Couper and Logan, 2014). The Minnesota lakes report, published in 2015, tested for different PPCPs in 50 lakes in Minnesota in 2008 and 2013. They found that diphenhydramine reached levels of 0.0357μg/L in 2008 (Ferrey, 2015). In lentic biofilms, exposure to diphenhydramine can decrease primary production by 24% (Shaw *et al.*, 2015). Xie *et al.*, (2016) found that exposure to diphenhydramine at 21.7μg/L caused enhanced swimming and decreased feeding rates in the crustacean *Carassius auratus*.

Ibuprofen is one of the world's most widely consumed pharmaceuticals, used to treat pain, inflammation, and fevers. It is almost completely broken down in the body with little or no unchanged drug found in urine (Paíga *et al.,* 2013, Mazaleuskaya *et al.*, 2014).A study of 42 water samples from Portugal found ibuprofen in landfill leachates, wastewater treatment plant influents and effluents, hospital effluents, and surface waters. In the surface waters of the Lima River, researchers detected concentrations of 0.723µg/L. Paíga *et al.,* 2013 attributed these high concentrations to the widespread consumption of ibuprofen among the Portuguese population, noting how wastewater treatment plants, landfills, and hospitals were importance sources of pollution. They also ran an environmental risk assessment on the concentration of ibuprofen leached from landfills, concluding that it does pose a significant ecotoxicological threat to aquatic organisms including fish, daphnids, and algae (Paíga *et al.,* 2013). In a different study, *Daphnia magna* exposed to levels of ranging from 0.5 µg/L to 50 µg/L of Ibuprofen experienced a decrease in the total amount of eggs produced per female, total number of brood per female, and body length (Wang *et al.,* 2016).

Naproxen is an over the counter medication used to relieve pain, tenderness, swelling, and stiffness caused by several different types of arthritis (MedlinePlus, 2015b). Vree *et al.,* 1993 recovered 50.8% of unchanged naproxen in human urine. Naproxen is stable in water for 14 days and can partially degrade in activated sludge (Qurie *et al.,* 2014). Naproxen can be fatal at high concentrations. The plankton *calyciflorus* has an LC50 (24h), lethal dose at which 50% of the population is killed, of 6248 µg/L. *Daphnia magna* has an EC50 (48h), concentration of half-maximal response, of 1740 µg/L (Ornelas *et al.* 2010).

2.6.3 Prescription medications: Amphetamine, Carbamazepine, Gemfibrozil, Morphine, Phenazone, Sulfamethoxazole and Warfarin

Amphetamine and amphetamine-type stimulants, a larger class of drugs, are psychoactive drugs that stimulate the central nervous system (De la Torre *et al.,* 2004). Physicians prescribe amphetamine for the treatment of Attention Deficit Hyperactivity Disorder (ADHD), narcolepsy, and as an appetite suppressant. Adverse effects include anorexia, weight loss, insomnia, and addition (Heal *et al.,* 2013). The number of ADHD stimulant prescriptions, including amphetamine, has annually increased from 2007-2011 by 39%, from 34.8 million to 48.4 million prescriptions in the United States (NFLIS, 2011). Amphetamine is also commonly used as a recreational drug for its psych-stimulant effects on the central nervous system (Heal *et al.*, 2013). Amphetamine users experience increased alertness, wakefulness, insomnia, energy, self-confidence, decreased appetite, enhanced mood, well-being, and euphoria (De la Torre *et al.*, 2004). According to the European Monitoring Center for Drugs and Drug Addition (2013), 12.4% of young adults aged 16- 34 abused amphetamine in 2011-2012 in the UK. Methamphetamines may also be an important source of amphetamines, which is a metabolite (Barnes *et al.*, 2008).

In the Minnesota lakes report, amphetamines were detected at a maximum concentration of 0.0291μg/L (Ferrey, 2015). High levels of amphetamines have been shown to impact microbial communities by altering chemotaxic responses in certain bacteria, and stimulating behavioral changes, interfering with catecholamine production, photosynthesis, and nitrogen capabilities in aquatic algae (Chet *et al.*, 1973, Rosi-Marshall *et al.*, 2015). Although some effects in aquatic organisms have been described, there appear to be large data gaps regarding how environmentally relevant levels of amphetamines may be affecting aquatic ecosystems (Rosi Marshall *et al.*, 2015). Huerta-Fontela *et al.*, 2008 have demonstrated that amphetamines can be effectively treated through drinking water treatment processes.

Carbamazepine is an anticonvulsant for patients suffering from seizures (MedlinePlus, 2012). More recently, it has also been used to treat bipolar depression. Bertilsson and Tomson, 1986 found that 90% of a single oral dose was excreted in urine in the form of metabolites. A screening of 27 different surface waters in Germany revealed concentrations of 0.05μg/L to 3.2μg/L. Highest reported concentrations were those found near wastewater treatment plants. In surface waters, carbamazepine degrades slowly by photo-degradation with a half-life of about 100 days (Bahlmann *et al.*, 2009). Ecotoxicological studies have demonstrated that high carbamazepine can cause immobilization of *Daphnia magna,* which had an EC50 of 0.11μg/L. For humans, the predicted no observed effect level, generated using geo-referenced models P*h*ATE™, of carbamazepine through drinking water and fish consumption is 226,000 μg/L (Cunningham *et al.*, 2010).

Gemfibrozil is a lipid regulating agent prescribed to patients undergoing diet changes to reduce their cholesterol or fat intake (MedlinePlus, 2014, DailyMed, 2015). Less than2% is excreted unchanged in the urine (Citron Pharma LLC 2015). The maximum concentration detected in the

Minnesota Lakes study was 0.00207μg/L (Ferrey, 2015). Fang *et al.*, 2012 detected gemfibrozil in influent, effluent, and groundwater. They noted that land application of sewage containing gemfibrozil, following treatment in a wastewater treatment plant, was a source of groundwater pollution. Studies of goldfish converted from 475μg/M using a molecular weight of carbamazepine of 236.27 g/mol (Kim *et al.*, 2016b) reported that gemfibrozil between 1.5μg/L and 1,500μg/L taken up from the water reduced plasma testosterone levels by 49-72% (Mimeault *et al.*, 2005).

Morphine is an opiate prescribed for pain relief. Additionally, morphine is found in poppy seeds and is a metabolite of heroin (Boleda *et al.*, 2009). In the human body, less than 10% is excreted unchanged (Buclin *et al.* 2009). Wastewater treatment plants can remove up to 73% of morphine from untreated sewage (Boleda *et al.*, 2009). In one article, Zuccato and Castiglioni (2009) synthesized data on selected illicit drugs in surface waters all over the world. They found that morphine levels ranged from zero μg/L in Belgium to 0.010 μg/L in Germany. High levels of morphine have been shown to have a stimulating effect on certain fish such as *Macropodus opercularis,* resulting in erratic swimming and circling (Csanyi *et al.*, 1984). Morphine has also been shown to reduce the phagocytic activity in mussel hemocytes, potentially weakening the immune system (Gagné *et al.*, 2006). Little data exists on the ability of water treatment facilities to clear morphine.

Phenazone is an analgesic and antipyretic administered as mouth and eardrops. In humans, approximately 3.3% is excreted unchanged with the rest breaking down into 4-hydroxy-antipyrine, norantipyrine, 3- hydroxymethl-antipyrine, and 3-carboxy-antipyrine (Danhof and Breimer, 1979). Reddersen *et al.*, 2002 routinely detected phenazone in groundwater samples in Berlin, Germany at 3μg/L, suspected to have originated from a nearby pharmaceutical plant. High levels of phenazone did not have any acute effects on fish, daphnia, or algae, but chronic effects are still unknown. Redderson *et al.*, 2002 also found that the treatment process at the local water treatment plant was able to effectively remove 90% of phenazone from the drinking water. The last 10% remaining in drinking water posed notoxicological threat for humans at such low concentrations (Reddersen *et al.*, 2002).

Sulfamethoxazole and trimethoprim are used to treat bacterial infections in humans. Physicians prescribe them individually or together in a drug called Sulfatrim (PharmGKB, 2015).

Sulfamethoxazole can also be used as an antibiotic agent for animals. Cribb and Speilberg, 1992 found that humans excrete 54% of ingested sulfamethoxazole unchanged. In source and finished water sites from the Scioto River Basin in Ohio, sulfamethoxazole was detected in 16 samples at levels below 0.005μg/L (Finnegan *et al.*, 2010). Humans metabolize trimethoprim, another antibiotic, and excrete 80% unchanged. Ferrey, 2015 reported that trimethoprim was found in Minnesota lakes at a maximum concentration of 0.00175μg/L in 2013. Liguoro *et al.,* 2012 found that high levels of trimethoprim caused growth inhibition in *Lemna minor*, swimming activity inhibition in *Poecilia reticulata*, and reproduction and growth inhibition in *Daphnia magna*. However, researchers concluded that environmental concentrations below 1μg/L are unable to evoke appreciable biological effects in various aquatic organisms (De Liguoro *et al.*, 2012).

Warfarin is an anticoagulant, commonly administered to patients with deep vein thrombosis, atrial fibrillation, and recurrent stroke or heart valve prosthesis. Less than 1% is excreted unchanged in the urine and none is found in the feaces (Merad, 1988). Carmona *et al.*, 2014 detected warfarin in wastewater treatment effluent, surface water, and drinking water in the Turia River basin in Spain. They cited septic systems, domestic solid wastes, wastewater treatment plants, commercial-industrial discharges, and animal agriculture as possible source of warfarin pollution into these bodies of water. In surface water, warfarin levels reached 0.015μg/L, which was consistent with levels detected in 23 other surface waters in Spain. Little data from either toxicity or QSAR studies regarding the effects of warfarin on aquatic organisms. With regards to human health, Carmona *et al.,* 2014 also noted low level warfarin contamination in mineral and drinking waters, posing a possible threat to human health.

2.6.4 Agricultural or Veterinary Chemicals: Sulfamethazine, Sulfrachlorpyridazine, and Thiabendazole

Sulfamethazine is an antimicrobial and antibacterial agent used in veterinary medicine. Sulfamethazine is typically excreted in the urine as a combination of the unchanged compound and several metabolites (Bevill *et al.*, 1977). It is not used in human medication. Manure fields are a point source of pollution for sulfamethazine in surface waters (Hirsch *et al.*, 1999). According to Carstens *et al.,* 2013, sulfamethazine has a 2.7- day half-life in pond water, broken down by photodegredation and sorption to sediment. Carstens *et al.,* (2013) found sulfamethazine in 26 out of 52 surface water samples at levels as high as 0.48µg/L. Another study found that *Daphnia magna* had a NOEC, no observed effect level, of 3,300 µg/L. Concentrations exceeding this caused growth sympathomimetic drugs produce physiological effects similar to those caused by the activity or stimulation of the sympathetic nervous system (Ji *et al.*, 2012).

Sulfrachlorpyridazine is a broad-spectrum sulfonamide antibiotic used in swine and cattle industries. In a study of 20 river waters samples from River Trent at Shardlow, Derbyshire, UK, no sulfrachlorpyridazine was found (Blackwell *et al.*, 2004). Few literature sources describe sulfrachlorpyridazine in surface waters or their effects on aquatic ecosystems or human health. Only one study explored the presence of sulfrachlorpyridazine in seafood and found that exposure to 0.020µg/L had a 91.2% recovery rate (Gehring *et al.*, 2006).

Thiabendazole is a fungicide and parasiticide primarily used in veterinary medicine and agriculture. In humans, little thiabendazole is excreted in either urine or feces following metabolism. Runoff is a likely source. In surface waters in the Suerte River Basin in Costa Rica, nearby several banana plantations, researchers reported a range of 1µg/L to 3µg/L (Castillo *et al.*, 2000). In Trenton, New Jersey, a more urban environment, researchers found concentrations of thiabendazole below 0.0011µg/L in sewage effluents (Albrecht and Franco-Paredes 2014, Kim *et al.*, 2016a). In a review of thiabendazole as a potential seed treatment, Moore *et al.*, (2006) noted that thiabendazole is persistent and immobile in aquatic environments. Its only mode for degradation is photolysis. Moore *et al.*, 2006 also reported that rainbow trout and bluegill sunfish had a NOAEC of 12µg/L and Daphnids had an EC50 310µg/L. Thiabendazole was shown to interfere with growth and reproduction of these organisms. According to Moore *et al.*, 2006, data gaps exist for the effects on aquatic plants. The United States Environmental Protection Agency Re-registration Eligibility Decision (RED), (2002) concluded that the presence of thiabendazole in food or drinking water does not pose a threat to humans.

2.6.5 Personal care product: Triclosan

Triclosan is a common antibacterial agent, has been found in soaps, has been detected in river water, groundwater, sediments, biota samples of fish, and human breast milk (Adolfsson-Erici *et al.*, 2002, Banerjee *et al.*, 2016). In the Minnesota lakes report, triclosan was detected at a maximum concentration of 0.00575μg/L. High levels of triclosan have also been shown to cause sub-lethal effects in certain fish including jaw locking, quiescence, and erratic swimming movements, which can significantly affect their ability to obtain food and evade predators (Orvos *et al.*, 2002, Fritsch *et al.*, 2013, E. Werner I., Davies R., Beggeli S., Feng W., Pessah I. 2013). Triclosan is also a significant environmental source of dioxins, which are unintentional byproducts of organochlorines manufacturing that have carcinogenic and endocrine-disrupting properties (Ferrey, 2015).

2.6.6 Methods of analyzing PPCPs

Solid-phase extraction (SPE) is a separation technique used to extract compounds from a mixture of impurities. SPE is used to concentrate and purify samples for analytes of interest from several matrices. The separation ability of solid phase extraction is based on the preferential affinity of desired analyte, usually, to a solid phase through which the test sample is passed. The solid phase is selected so that the impurities in the sample are un-retained on the solid phase (adsorbent/stationary phase) while the analyte of interest is retained on it. Analytes that are retained on the stationary phase can then be eluted from the solid phase extraction cartridge with the appropriate solvent. High-performance liquid chromatography (HPLC) is a separation technique used to separate components of a mixture from each other by taking advantage of a variety of physiochemical interactions of analytes in the mixture between two phases. One phase is held stationary in a column while the mixture to be analyzed is introduced into another phase that is moved over the stationary phase. All standards and replicate samples will be analyzed using reverse phase HPLC with a filtered and degassed mobile phase and absorbance detection. Quantitation will be done by first generating a calibration curve prepared using known caffeine standards run under the same conditions as the samples. Before preparing the calibration curve, separations conditions must be optimized to ensure that the caffeine peak is adequately resolved from other components in the sample in minimal time. Optimization of the method involves changing parameters like mobile phase composition and flow rate until the required separation quality is reached. (Abdul *et al.,* 2006).

CHAPTER THREE

MATERIALS AND METHODS

3.1 The Study Area

The study was carried out in Ekiti State, South western Nigeria. Ekiti state is a tropical state, located between longitudes 40°51′ and 50°451′ East of the Greenwich meridian and latitudes 70°151′ and 80°51′ North of the Equator with a land size covering an area of 5887.890km^2. The state is endowed with water resources, some of which are Ero, Ureje, Egbe and Itapaji dams which serve as major sources of capture fisheries (Daramola *et. al.*, 2007). Ureje dam in Ado Local Government Area with water capacity of 4,930 m^3/ day was used for the study.

3.2 Sample Collection

Water sample was collected from Ureje dam in Ado-Ekiti in pre-cleaned glass bottles rinsed with methanol. During collection, each bottle was rinsed three times with the dam water and then filled by inverting the bottle into the water beneath the surface. After collection, the sample was stored in a cooler until returning them to the laboratory, where it was refrigerated at 2C degrees until digestion. Fish sample (Tilapia guineensis) was collected from Ureje dam in Ado-Ekiti in a clean bowl and it is being iced until returning to Federal University Oye-Ekiti (Ikole Campus) laboratory. On getting to the laboratory, the fish was dried in an oven and was weighed.

3.3 Materials used

- Bottles
- Icepacks
- Beakers
- Filter paper
- Test kits
- Questionnaires
- Tetraoxosulphate(IV)acid (H_2SO_4)
- Ntric acid (HNO_3)
- Potassium chloride (KCl)
- Coppersulphate(VI)acid ($CuSO_4$)

- Methanol
- High Performance Liquid Chromatography (Inifnity1260)
- Caffeine aqueous stock standard solution at 1000µg/mL (ppm).

3.4 Digestion of the samples

The samples were digested in Federal University Oye-Ekiti (Ikole Campus) Laboratory before taken down to Chemistry department in Ekiti State University Ado-Ekiti for further analysis.

3.4.1 Digestion of water sample

25 mil of water and 10 mil of HNO_3 were mixed in different beaker and taken to the digestion block and was boiled for 30 minutes at 150^0C. It was cooled for some minutes before storing it in a sample bottle for further analysis.

3.4.2 Digestion of fish sample

1 gram of fish sample + 3 gram of potassium chloride (KCL) and 10 gram of copper sulphate (VI) acid ($CuSO_4$) + 25 mil of Conc. H_2SO_4 and was digested for 1hr 30 minutes at 420^0C. After full digestion, the sample was made up with distilled water and was stored in a sample bottle for further analysis.

3.5 HPLC Analysis of Caffeine

HPLC mobile phase and solvent: 50 mm potassium dihydrogen phosphate, acetonitrile and methanol which strictly is also the solvent for standards and 'test' material (filter a sufficient volume of all solutions with 0.45µm syringe filter before injections).

3.5.1 Methods

Preparation of Standards

The stock solution was diluted appropriately with the mobile phase to make 10.00mL each of 10, 20, 30, 40 and 50ppm caffeine standard solutions. The retention time for Caffeine to be detected is when the peak is at 8.86 retention time.

3.5.2 Chromatographic Analysis

HPLC Parameters

Mobile phase: 50 mm potassium dihydrogen phosphate (pH=2), 80% methanol and 20% deionized water.

Flow rate; 0.8 mL/min.

UV detector wavelength: 274nm.

Injection volume: 2.000μL.

3mL of the standard was obtained into a 5mL syringe. 2mL of the standard was introduced into the sample injector of the HPLC via a filter disc. Chromatogram was run (takes 9 minutes to elute). The retention time (tr), peak height (h) and peak area (A) for the caffeine peak was recorded. Repeated of the procedure with the rest of the standards was done. All HPLC output data was transferred on to a flash drive. The prepared laboratory sample was injected and the quality of the separation of the caffeine peak from any other components in the sample was noted.

3.5.3 Questionnaire survey

Questionnaire to determine Knowledge, Attitudes and Practices profile of the respondents as relates to PPCPs, the modes of disposing their contents and containers and possible consequences of improper disposal was designed (Appendix 1). The questionnaire was pre-tested and administered using Random sampling method.

The questionnaire consists of three parts:

- section A covered information about the demography of the respondent;
- section B was concerned with the knowledge about Pharmaceutical and Personal Care Products (PPCPs);
- Section C covered attitudes and practices about Pharmaceutical and Personal Care Products (PPCPs).

3.5.4 Data Analyses of Questionnaire results

- Questionnaires were distributed in Ureje dam vicinity in Ado-Ekiti.
- 35 questionnaires were retrieved back out of 41 administered and the percentage was determined.
- Received questionnaires were subjected to descriptive analysis using Excel.
- Results were presented in tables and pie charts.

CHAPTER FOUR

RESULTS AND DISCUSSION

Fish and water samples were collected from an urban dam, Ureje dam, in Ado local government area, Ekiti State. They were collected in the rainy season, in the month of August.

4.1 Samples from Ureje dam

4.1.1 Fish sample

The fish samples did not show detectable levels of caffeine. At the retention time of 8.87 minutes for caffeine, there was no peak on the graph, indicating the non-detection of caffeine in the samples analyzed. This is shown in Figure 4.1.

4.1.2 Water sample

The water samples also did not show detectable levels of caffeine. At the retention time of 8.87 minutes for caffeine, there was no peak on the graph, indicating the non-detection of caffeine in the samples analyzed. This is shown in Figure 4.2.

The water sample had a peak of 1.285 retention time which is similar to a peak of 1.193 retention time from the fish sample.

The study went further to carry out a questionnaire survey to find out how much individuals know about PPCPs, the modes of disposing their contents and containers they use and possible consequences of improper waste and drug disposal and to know if there is any relationship between the results obtained from the samples and the questionnaires.

Thirty-five (35) questionnaires were retrieved from a total of forty-one (41) that were sent out. The response rate was 85.37%.

4.2 Demography of the respondents

A pie chart showing the age distribution of the respondents is shown in Figure 4.3 with age range, 15-24 having the highest percentage (54%).

Males (51.43%) responded more than females (49.57%) as shown in Figure 4.4.

Christians rated the highest percentage (74%) amongst respondents as shown in Figure 4.5.

Figure 4.6 shows the educational levels of the respondents. They mostly comprised University degree holders (B. Sc.) and Higher National Diploma holders (54%).

66% and 34% of the respondents were single and married respectively as shown in Figure 4.7.Majority of the respondents were Students (20%) as shown in Figure 4.8.

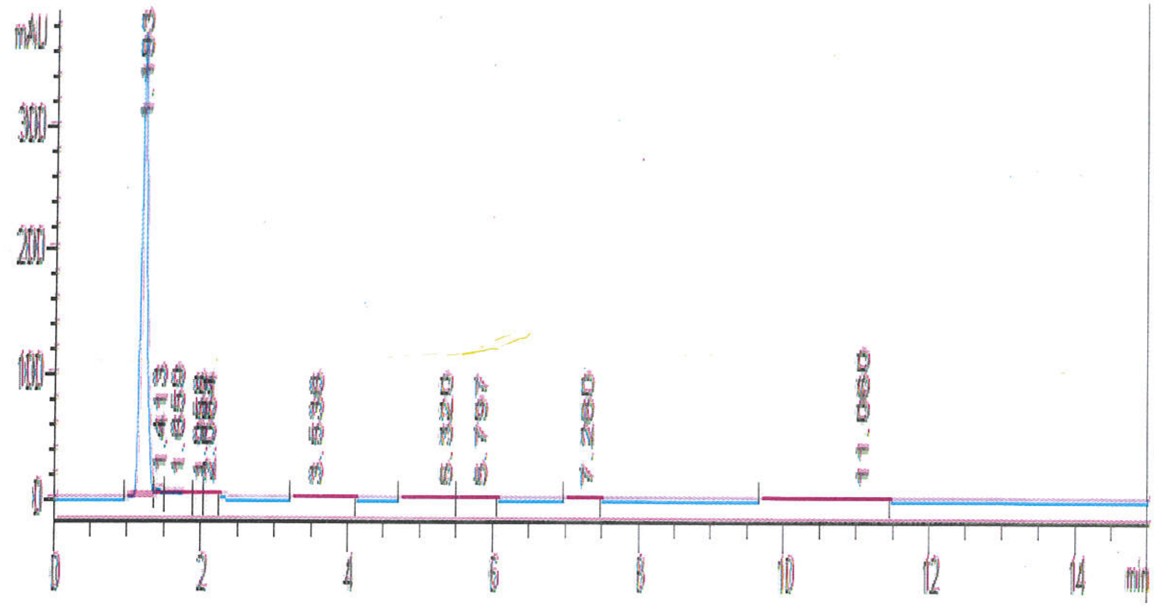

Fig 4.1: Chromatographic Graph of Fish sample

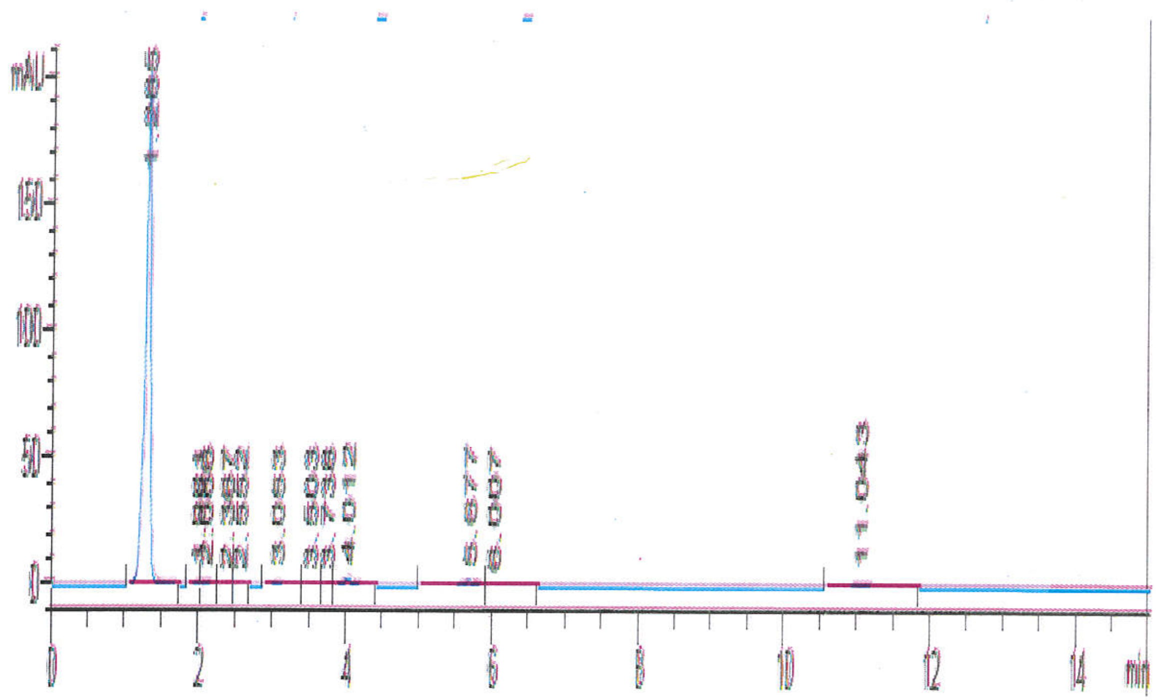

Fig 4.2: Chromatographic Graph of Water Sample

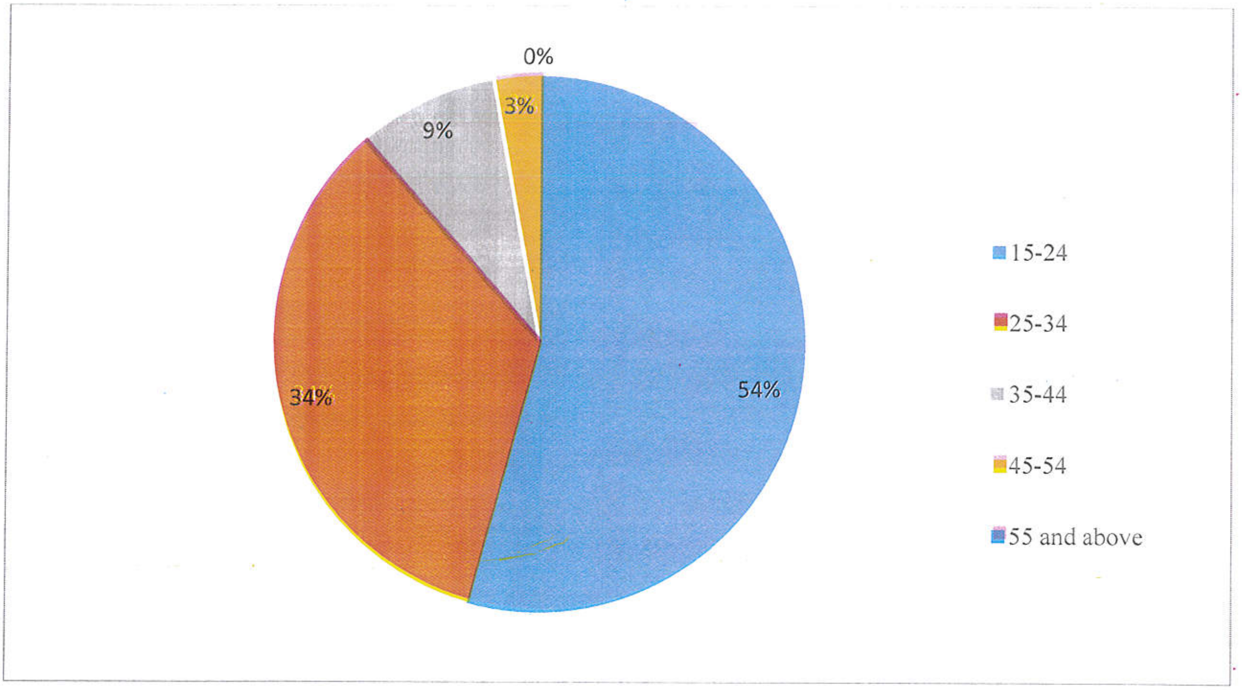

Fig 4.3: Total frequency distribution of the age group of the respondents

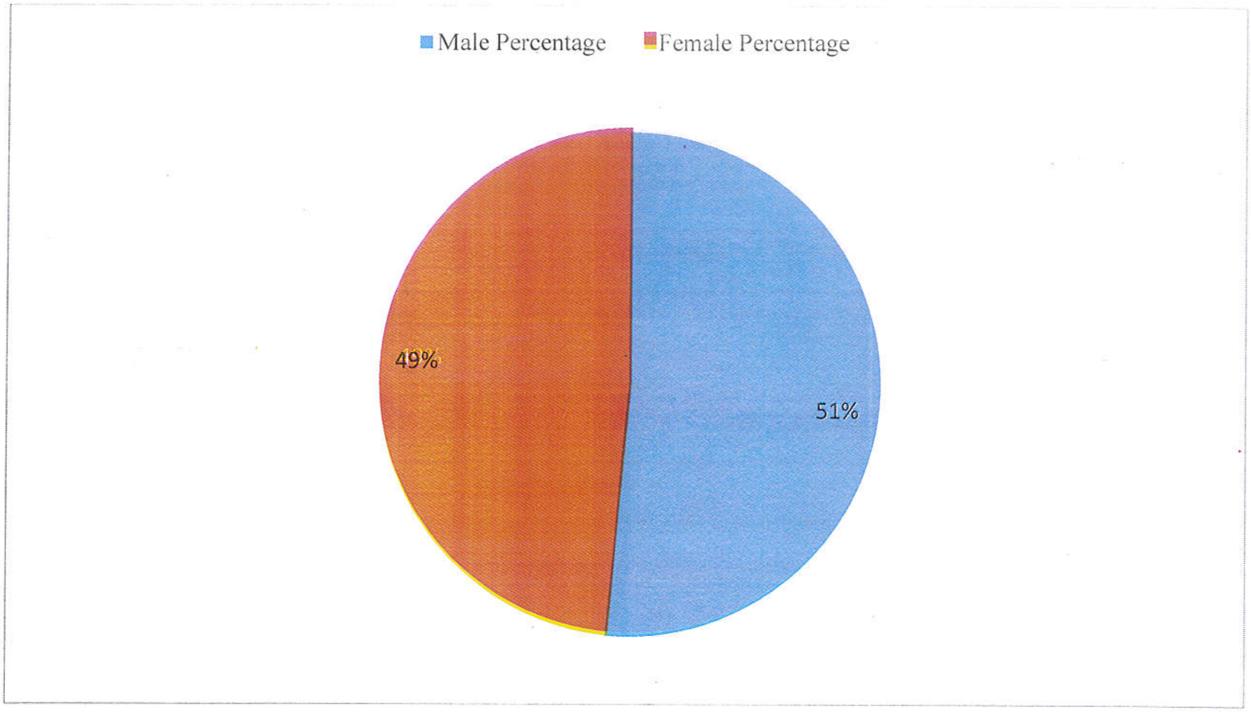

Fig 4.4: Total frequency distribution of the gender of the respondents

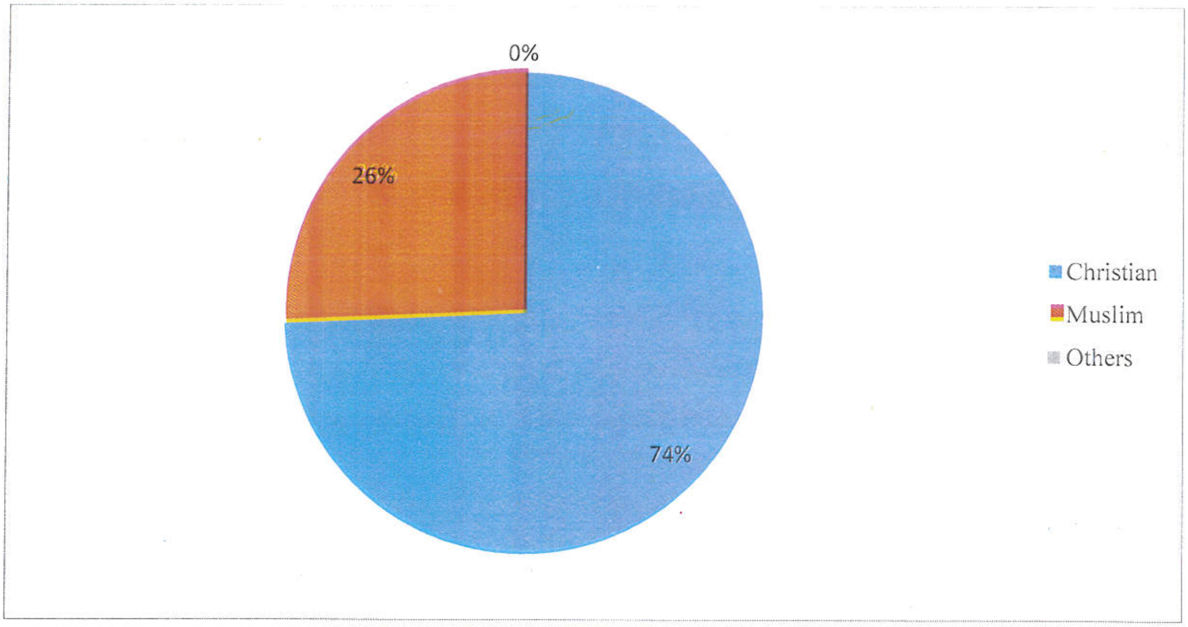

Fig 4.5: Total frequency distribution of the Religion of the respondents

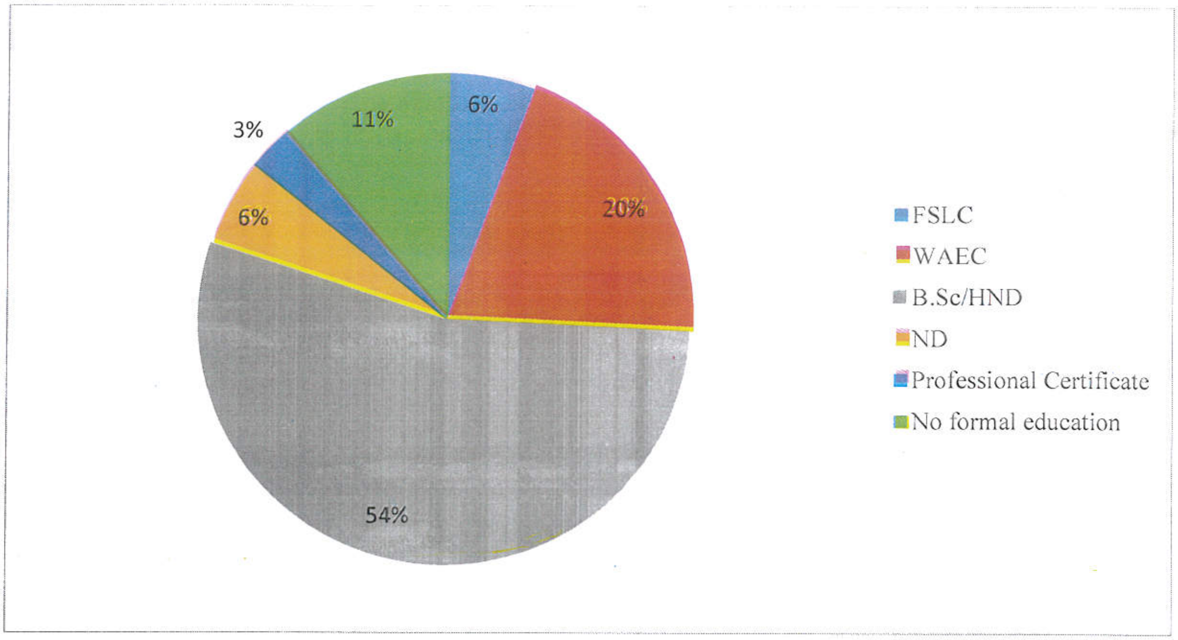

Fig 4.6: Total frequency distribution of the Educational levels of the respondents

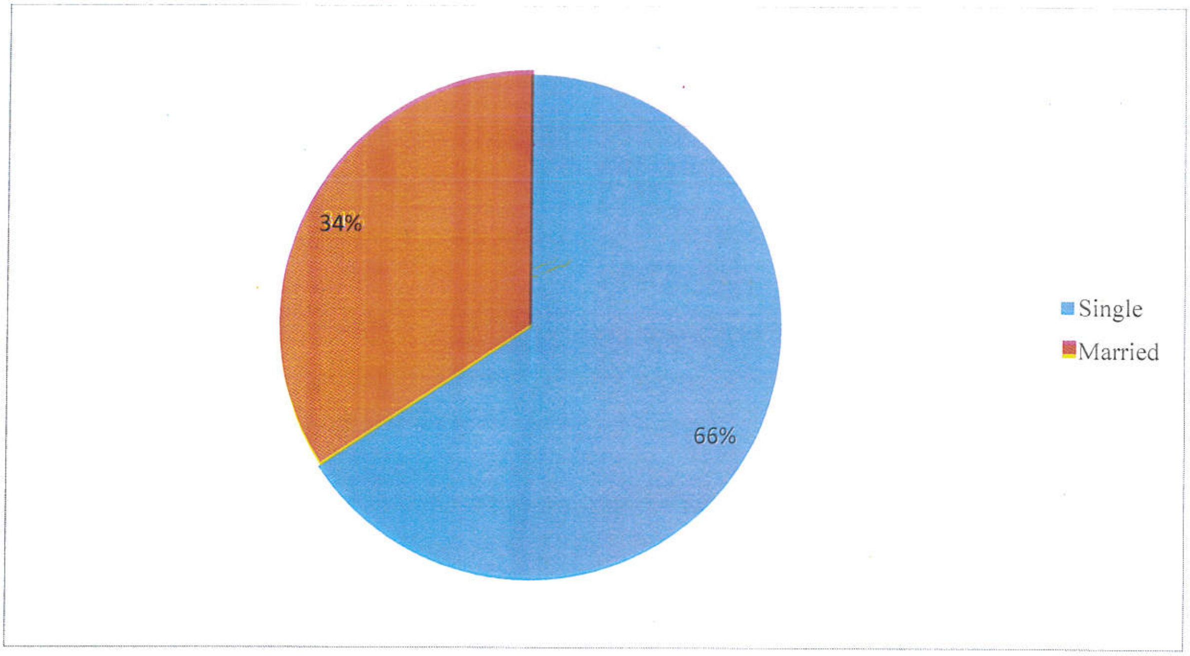

Fig 4.7: Total frequency distribution of the Marital status of the respondents

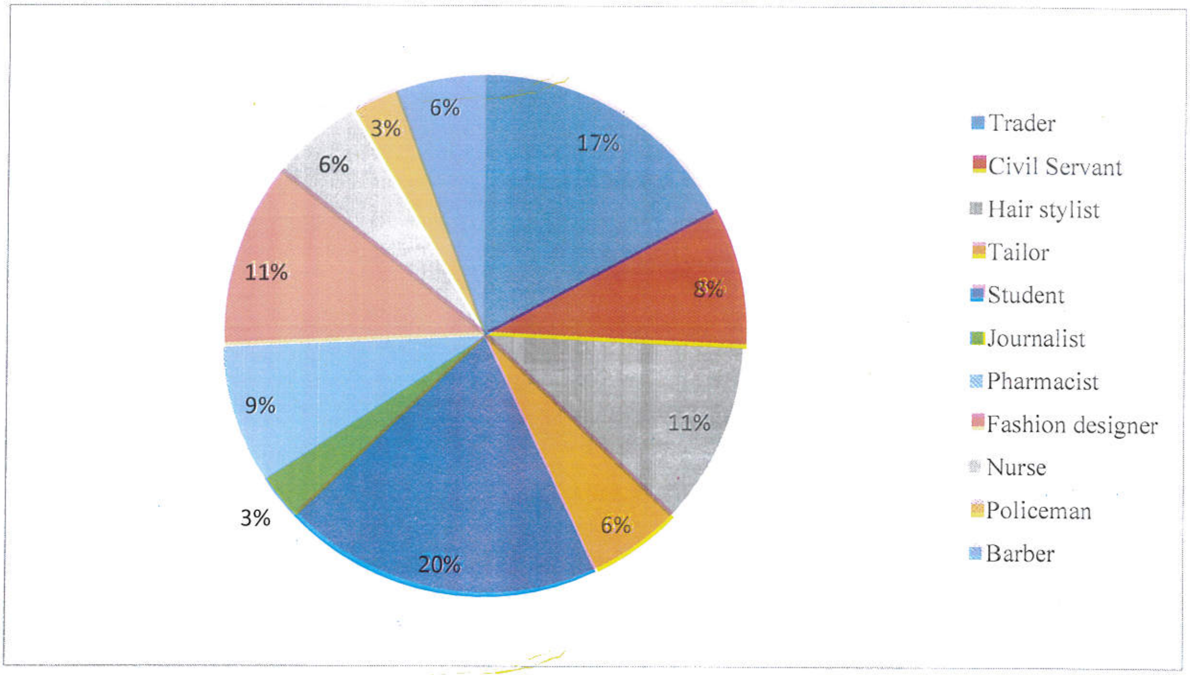

Fig 4.8: Frequency distribution of the Occupation of the respondents

4.3 Knowledge, Attitudes and Practices (KAP) profile

4.3.1 Knowledge of Pharmaceutical and Personal Care Products (PPCPs)

- 37% of the respondents had heard about PPCPs; 49% had not heard about them while 14% were not sure they had heard about PPCPs as shown in Figure 4.9.
- 34% of the respondents knew what they are; 46% do not know what they are while 20% were not sure they know what they are as shown in Figure 4.10.
- 34% of the respondents use PPCPs; 26% do not while 40% are not sure they use PPCPs as shown in Figure 4.11. Of those that use them, majority (54%) uses them often and of those that do not use them, 71% stated that they had never heard of them. These are shown in Figures 4.12 and 4.13.
- Many (54%) are not sure these PPCPs have effects on waterbodies and aquatic life while 14% do not know. Only 32% think these PPCPs have effects on waterbodies and aquatic life as shown in Figure 4.14.

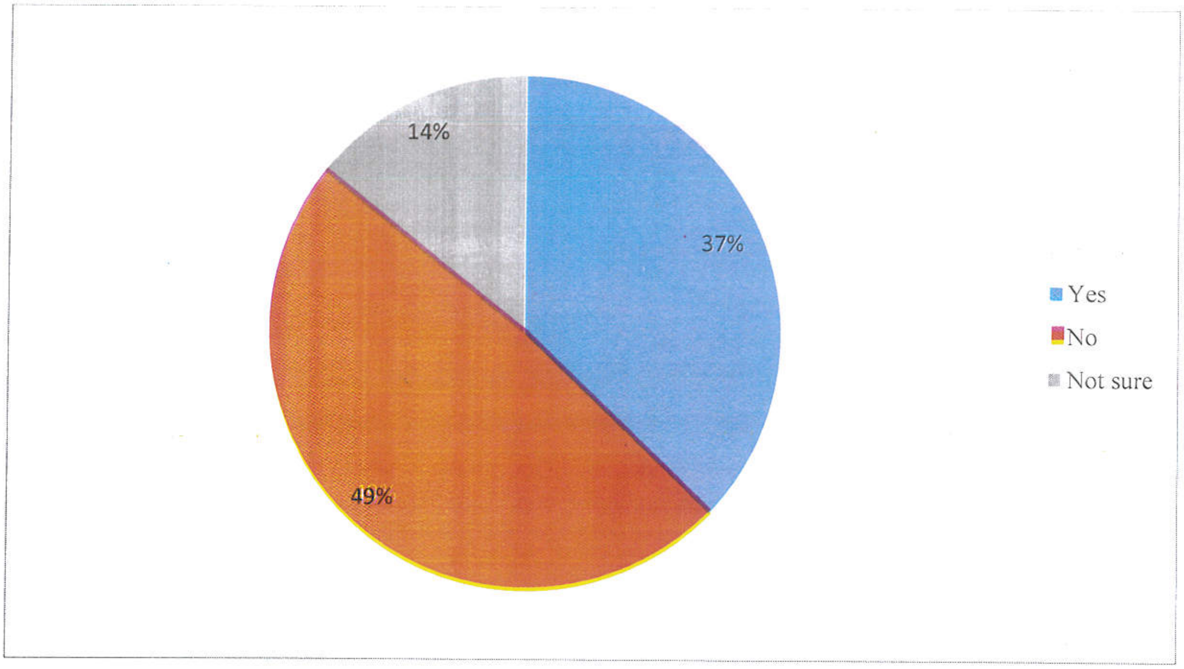

Fig 4.9: Awareness of PPCPs

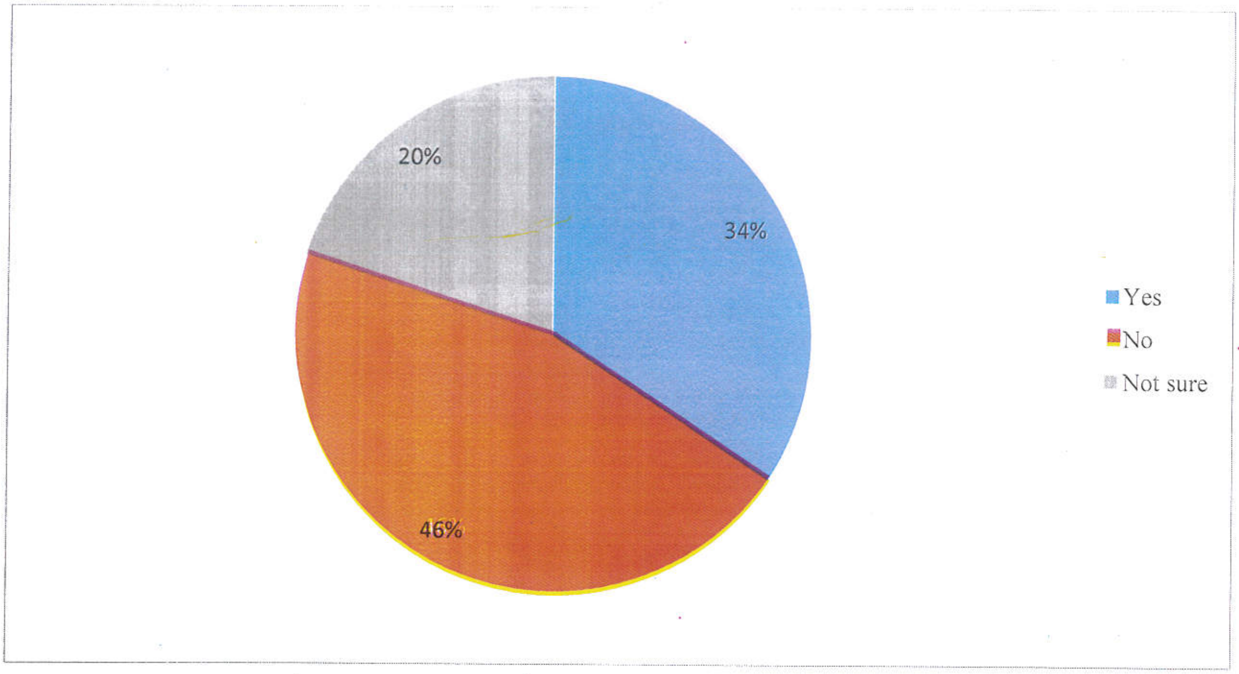

Fig 4.10: Knowledge of PPCPs

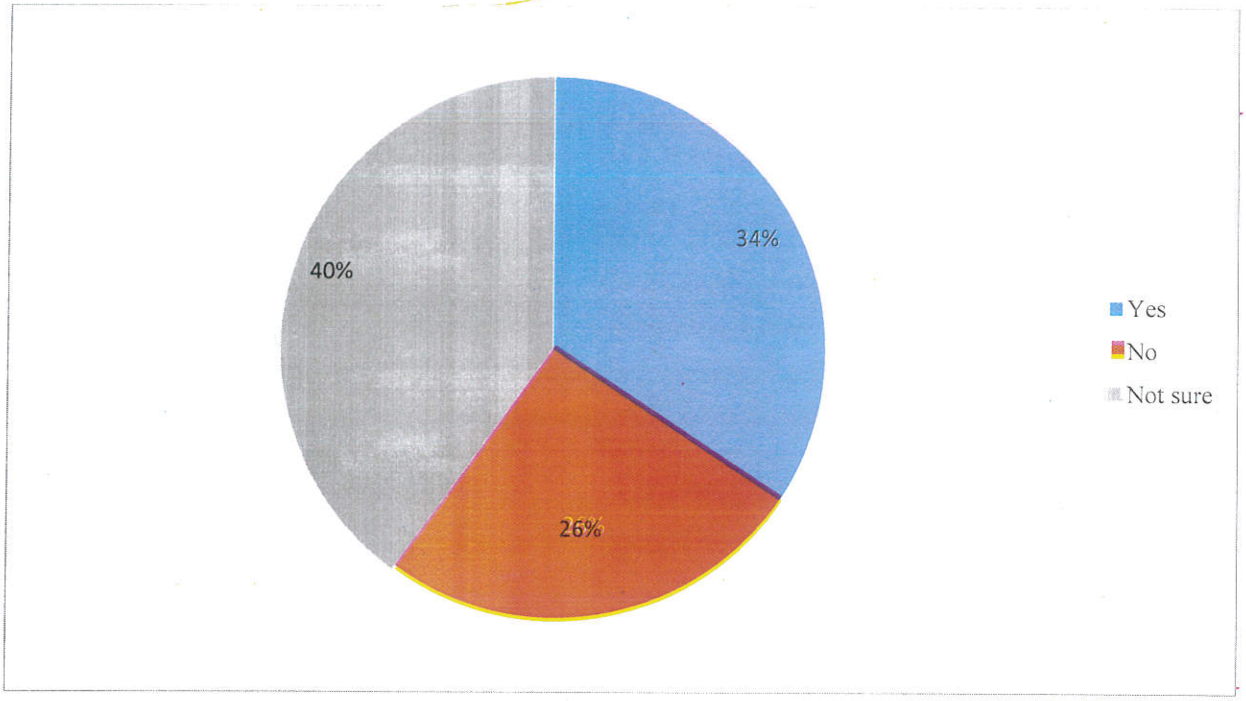

Fig 4.11: Use of PPCPs

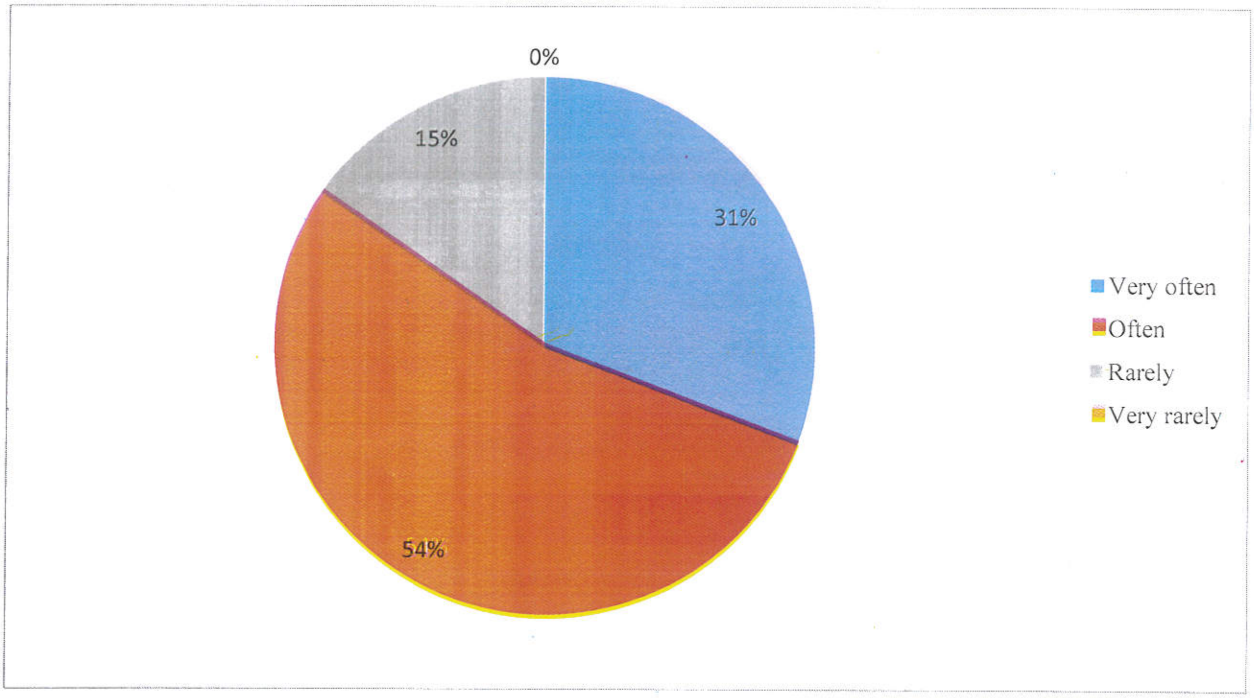

Fig 4.12: Frequency of PPCPs

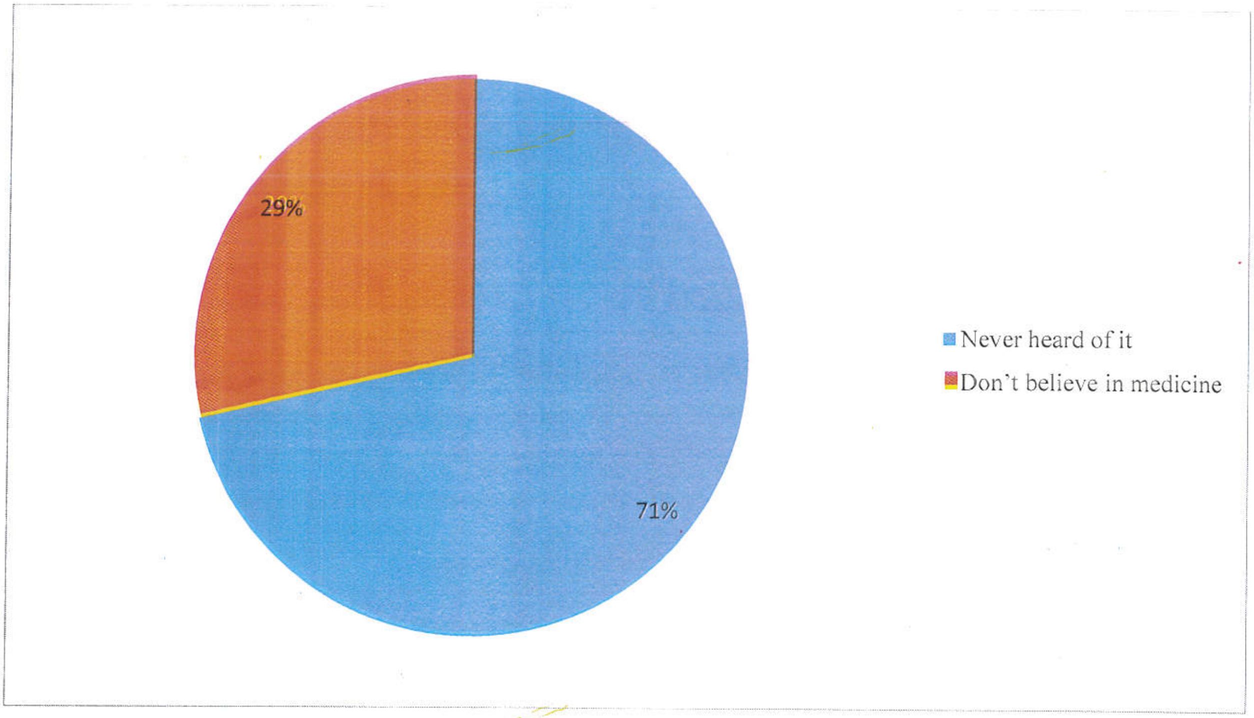

Fig 4.13: Reasons for not using PPCPs

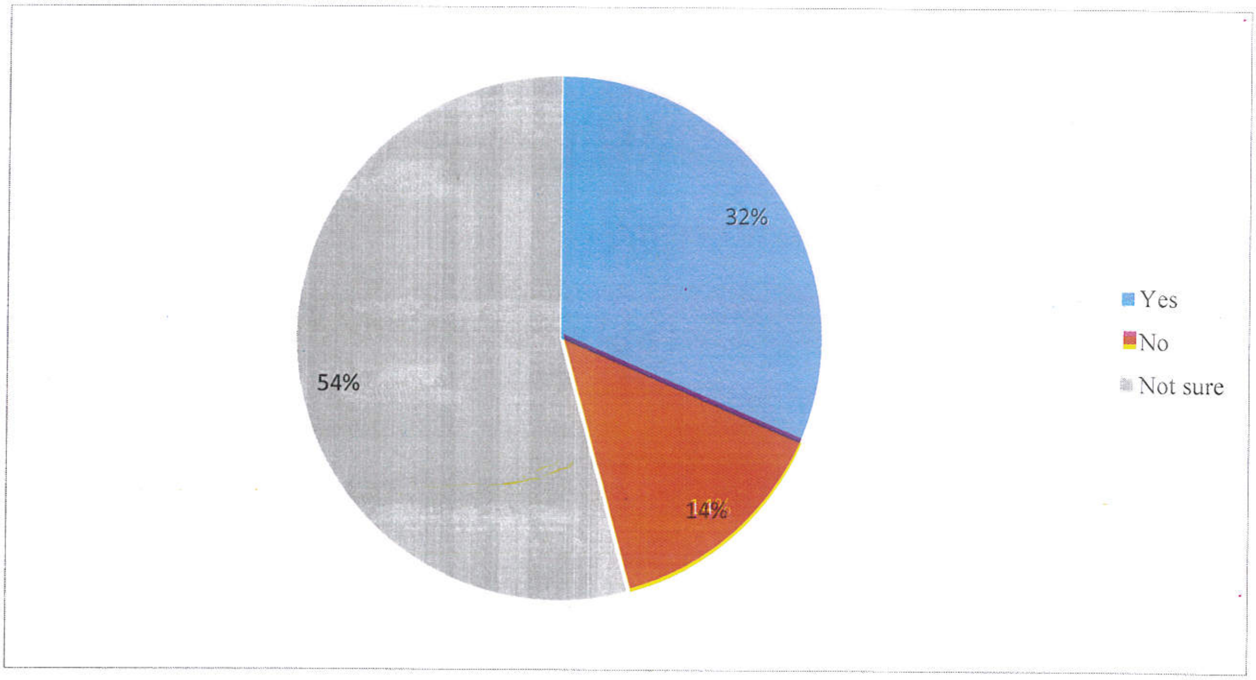

Fig 4.14: Effects of PPCPs on Waterbodies and Aquatic life

4.3.2 Attitudes and Practices towards Pharmaceutical and Personal Care Products (PPCPs)

- 77% of the respondents complete their drug dosages. Discontinuation of drug dosages when an individual feels recovered accounts for the largest percentage (57%) for not completing dosages, followed by individuals that do not take drugs (29%) and those that forget to do so (14%), as shown in Figures 4.15 and 4.16.
- 83% of the respondents use up their personal care products. 50% of the respondents who do not use up their products gave no reasons for that while 33% and 17% either lose interest in the products or feel like getting another as shown in Figures 4.17 and 4.18.
- Throwing in trash cans and then to garbage collection points rated highest (43%) among modes of disposing contents and containers of PPCPs. This was followed by throwing in bushes (26%), with returning to the pharmacy or supermarket not being an option (0%) as shown in Figure 4.19.
- It was observed that 57% of the people think that their mode of disposing these contents and containers is appropriate (Figure 4.20). This is further confirmed by the fact that 51% do not know the impact of inappropriate disposal of PPCPs (Figure 4.21). Figure 4.22 shows those that know there are impacts, mentioned contaminations of the environment.
- Only minority of 29% of the respondents perceive any risks between these contents and containers and the environment; 37% do not while 34% are not sure as shown in Figure 4.23.
- Figure 4.24 shows that only 6% are conversant with community drug-take-back programme that collects drugs for proper disposal. 83% do not know about it.

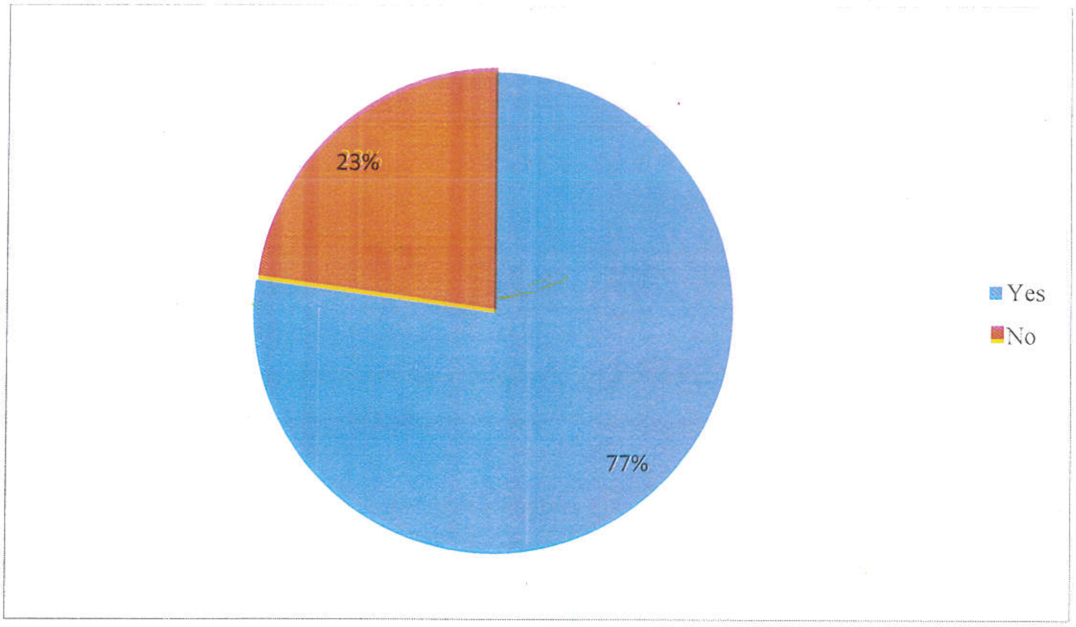

Fig 4.15: Completion of dosages

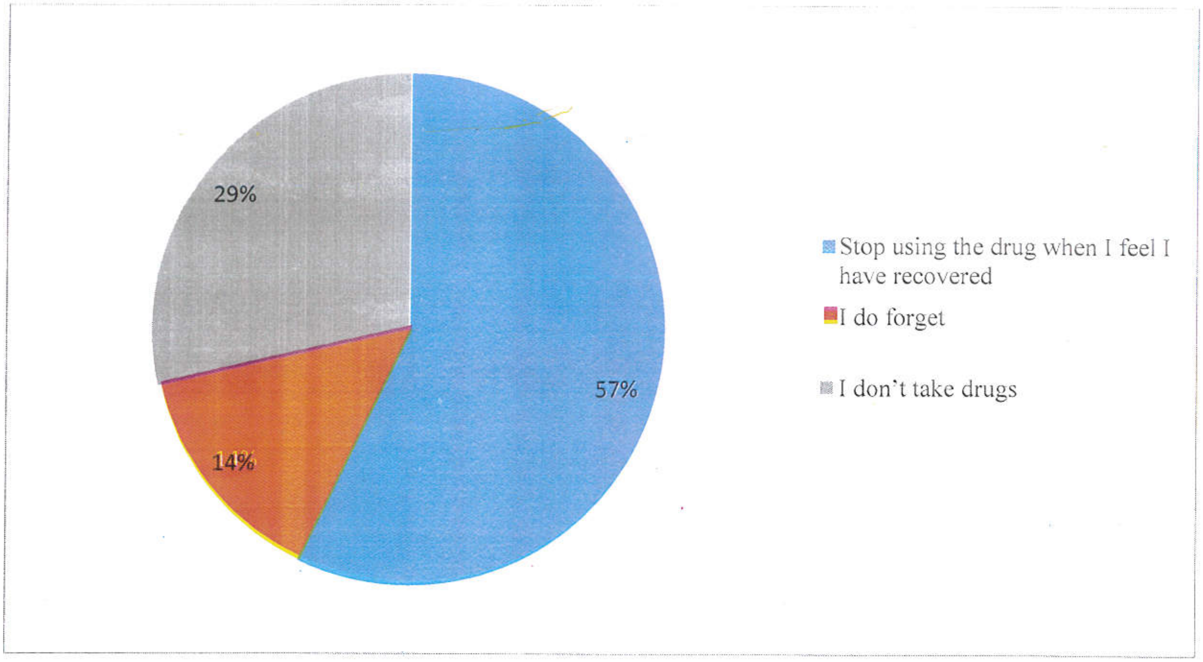

Fig 4.16: Reasons for not completing dosages

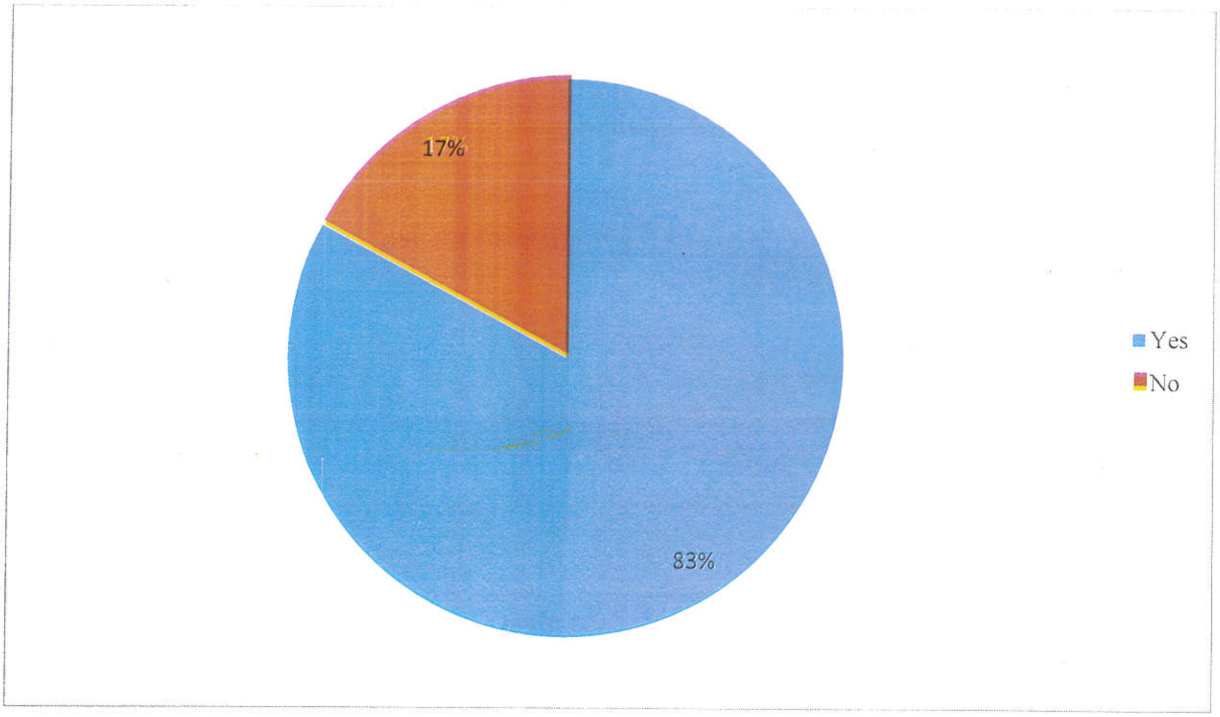

Fig 4.17: Use up of PPCPs

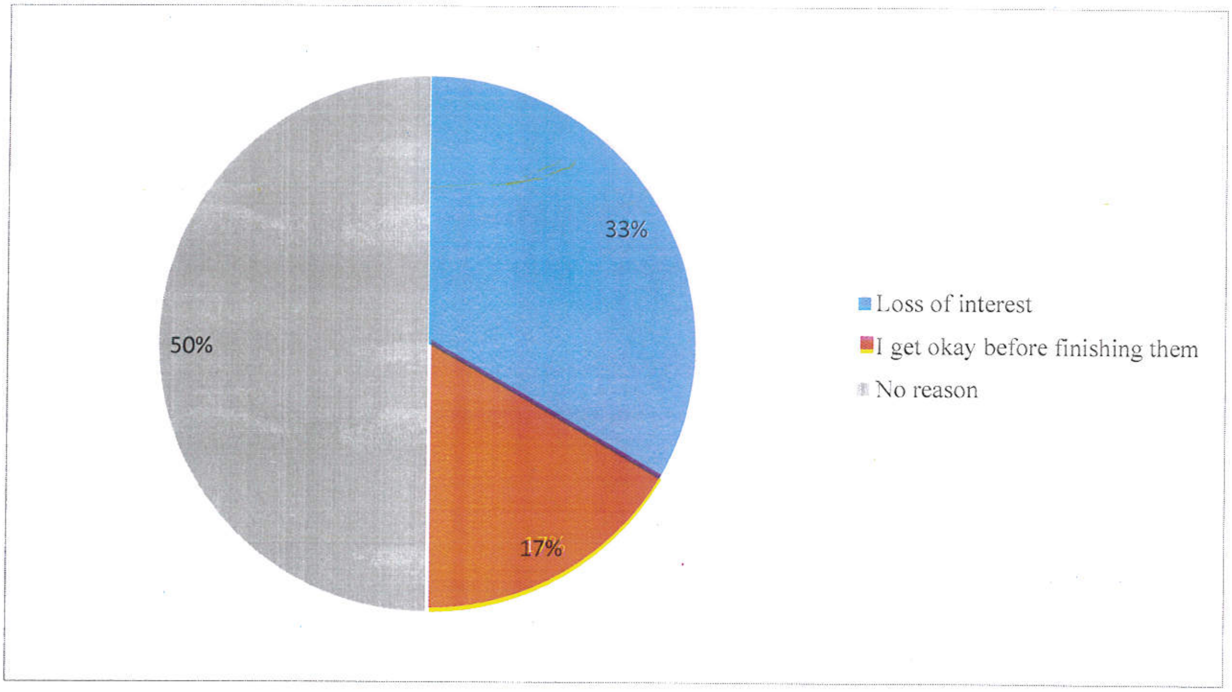

Fig 4.18: Reasons for not using up PPCPs

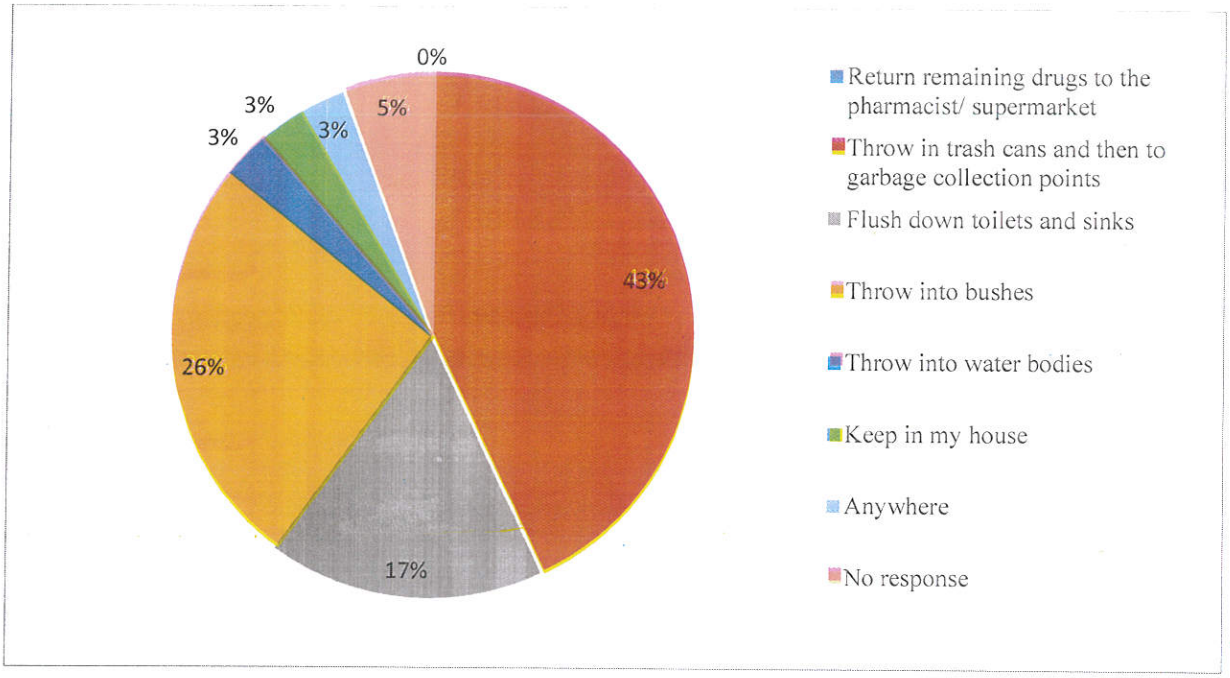

Fig 4.19: Modes of disposal

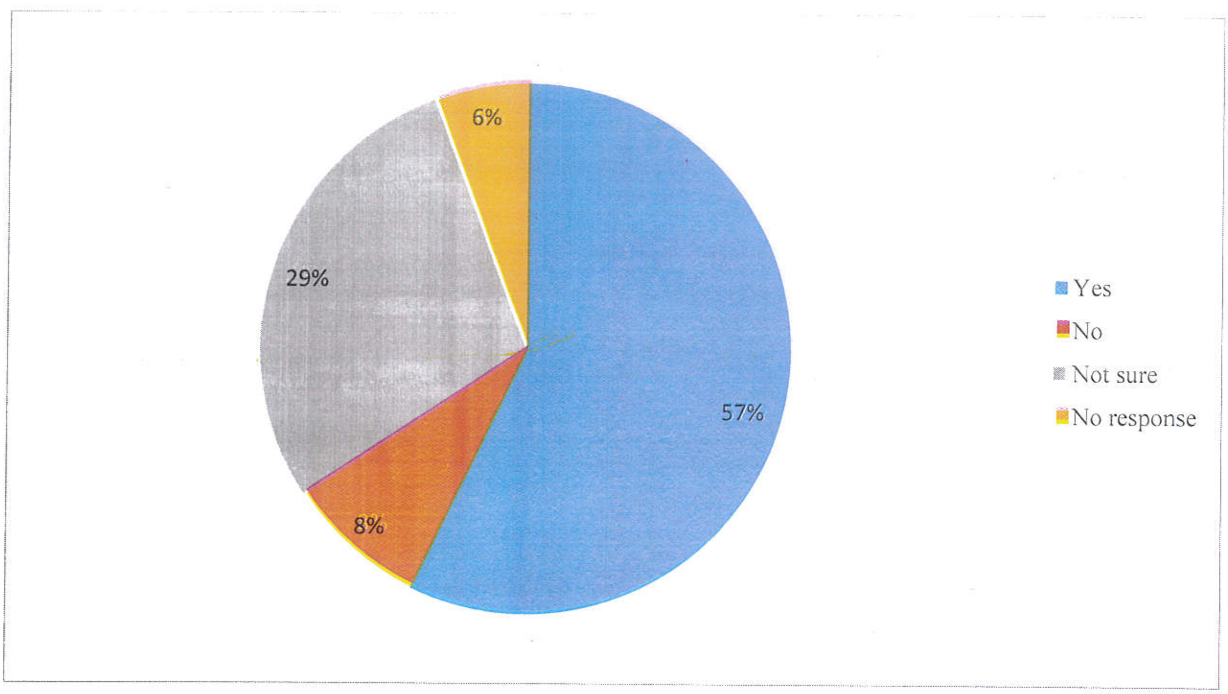

Fig 4.20: Appropriate modes of disposal

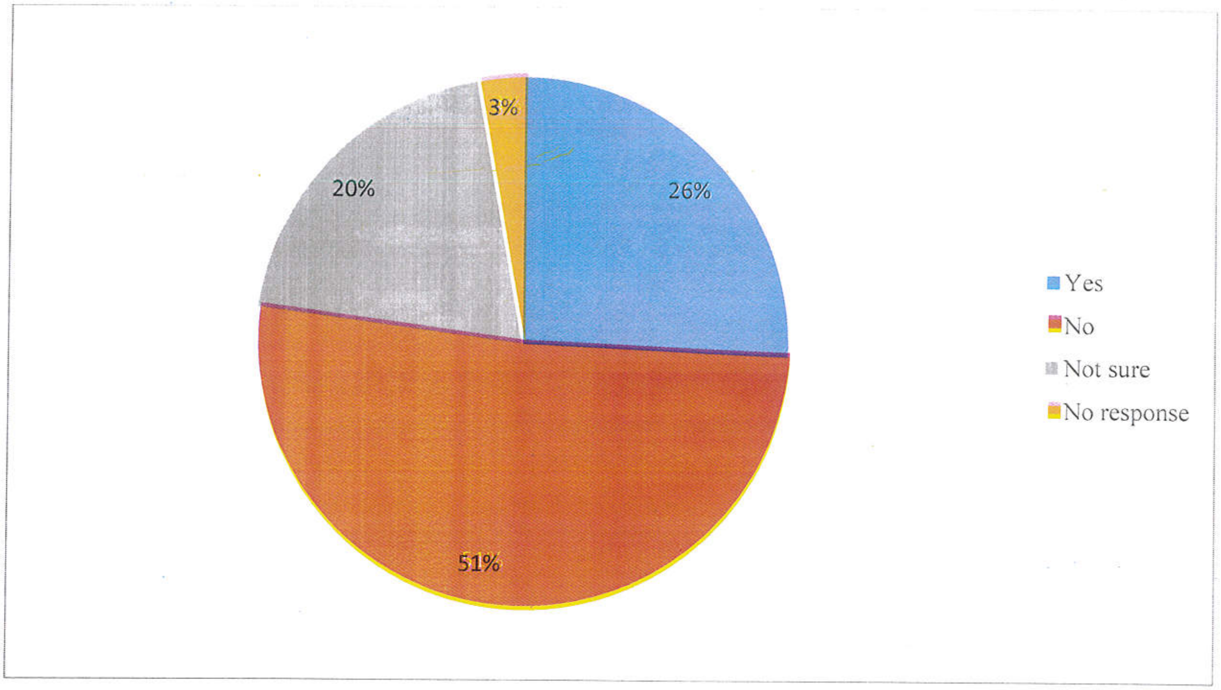

Fig 4.21: Impacts of inappropriate disposal

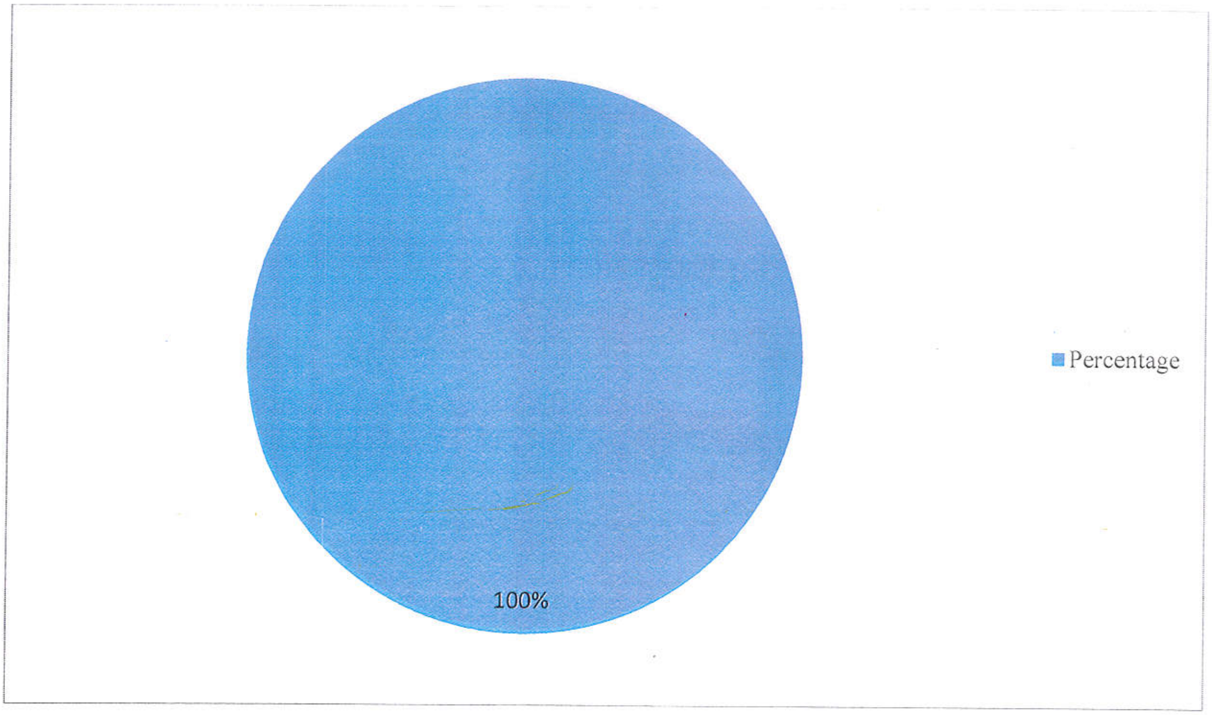

Fig 4.22: Contaminations of environment

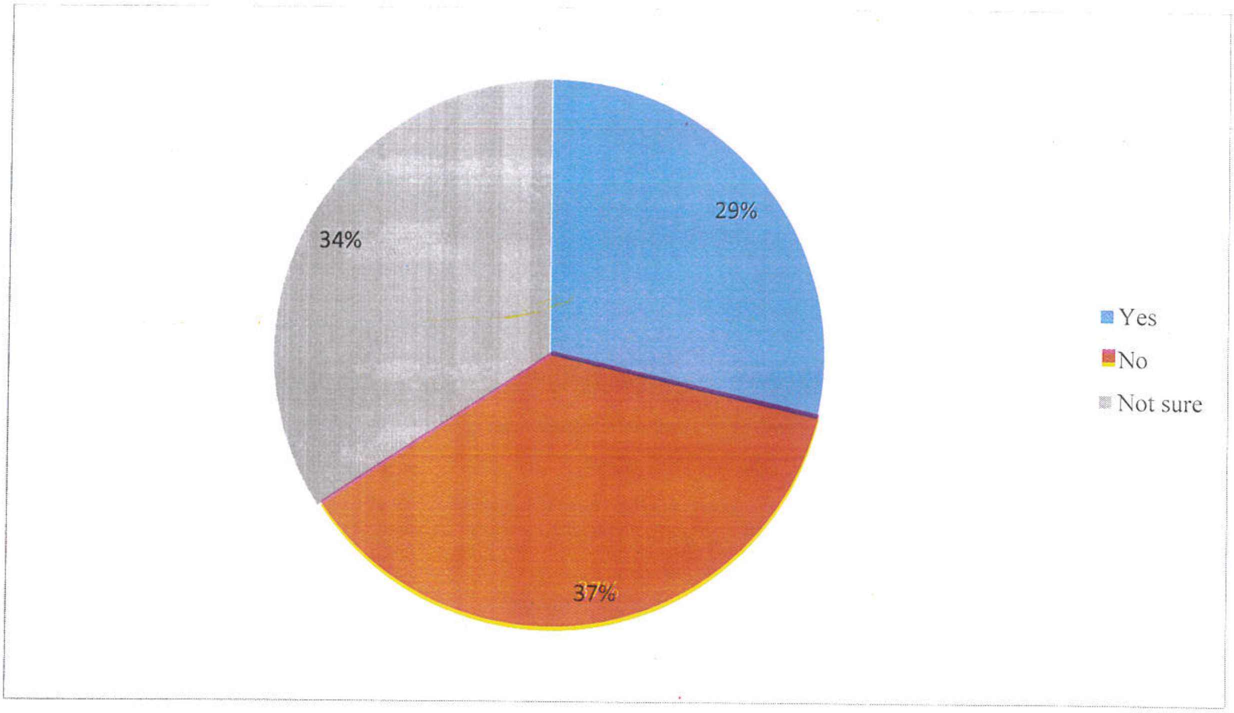

Fig 4.23: Perceiving risks of PPCPs

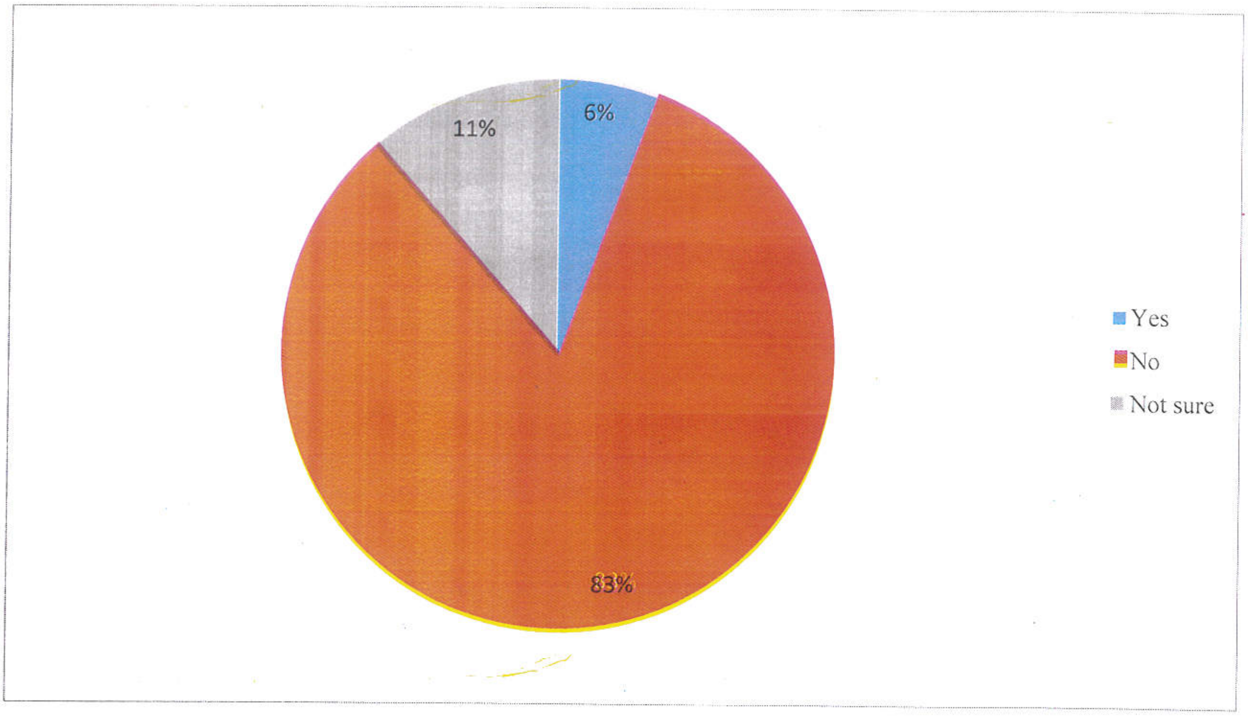

Fig 4.24: Awareness of drug-take-back system

- The use of jingles/medias rated highest (54%) in suggestions on ways of teaching the public on appropriate methods of disposal. This was followed by use of handbills, fliers and billboards (29%) with One-on-One information rating lowest (8%).
- 83% and 26% of the respondents are not aware that PPCPs and the chemicals they are made up of could have negative effects on fish in their environment and on humans respectively while 6% and 26% are aware of possible effects on fish and humans respectively. These are shown in Figures 4.26 and 4.27. Effects such as Cancer, Skin disorders and Blisters were mentioned. Use of jingles still rated highest as means of educating the public on the effects and consequences of these PPCPs.
- 68% of the respondents do not think that ways of proper disposal can be improved upon, although the optimistic ones (32%) suggested creating awareness on the dangers of inappropriate disposal as the best way of disposal, followed by burning and provision of bins by the government, as shown in Figure 4.29.

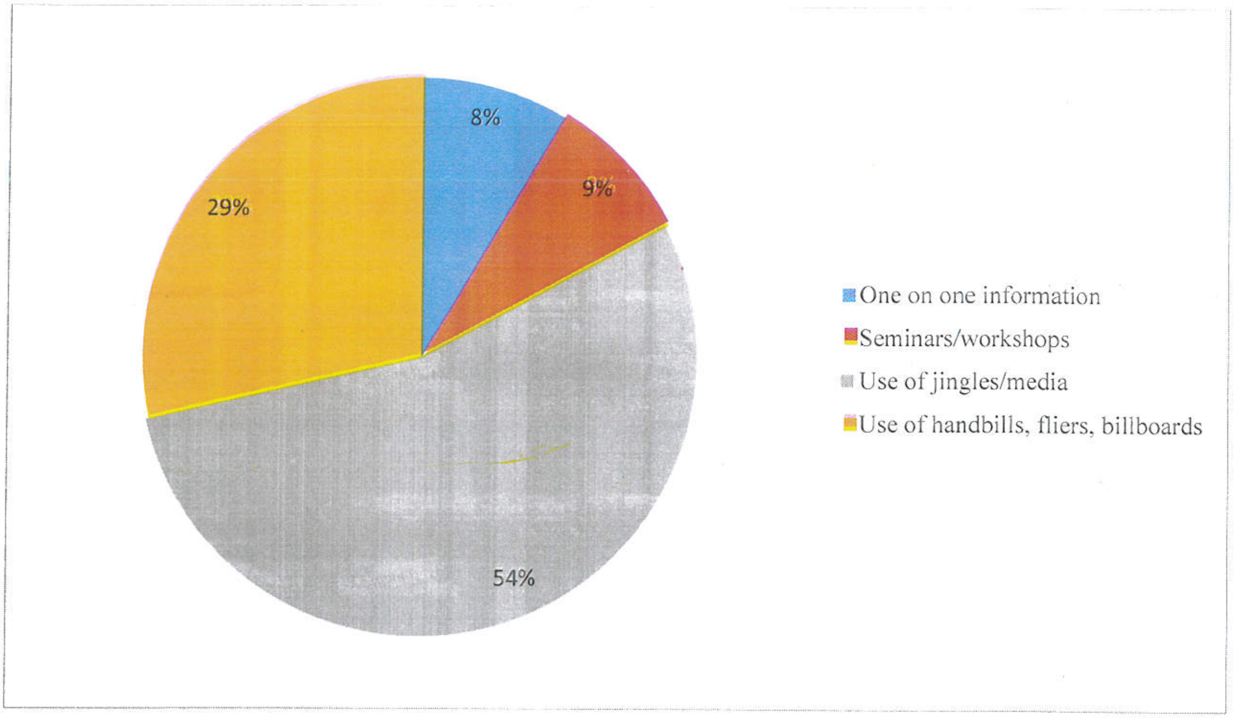

Fig 4.25: Ways of awareness creation

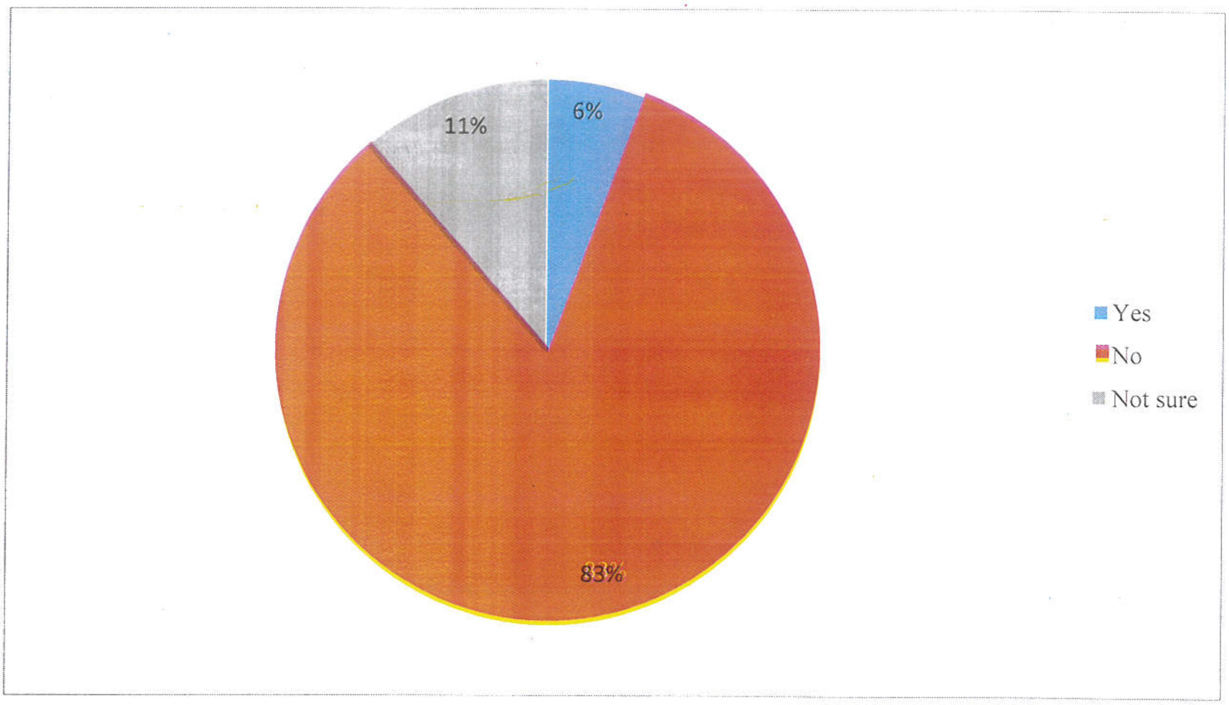

Fig 4.26: Awareness of the effects of PPCPs on fish in their environment

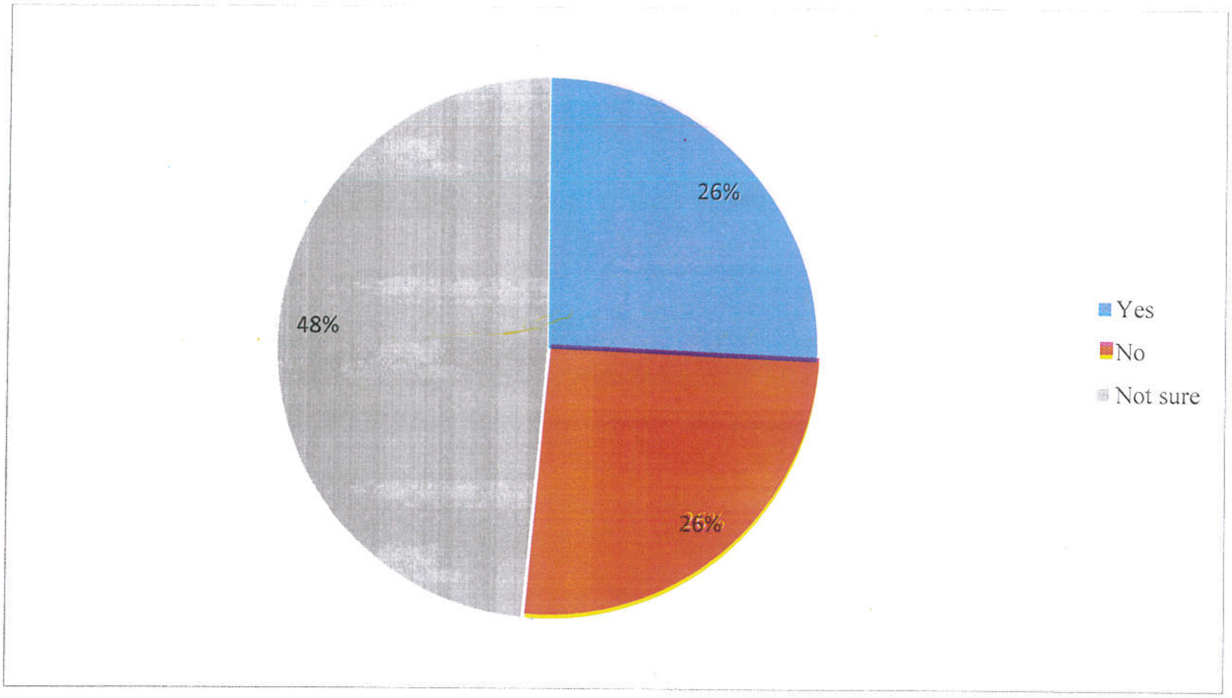

Fig 4.27: Awareness of effects of PPCPs on humans

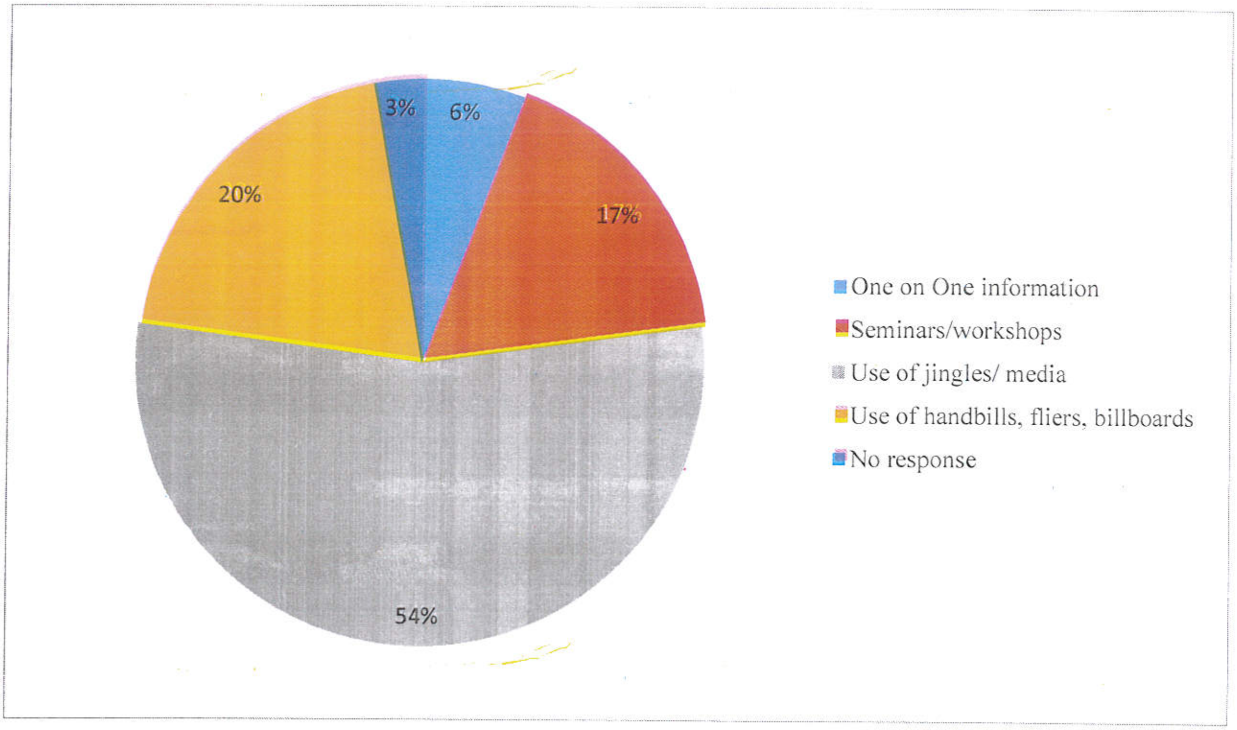

Fig 4.28: Ways of communicating effects and consequences to public

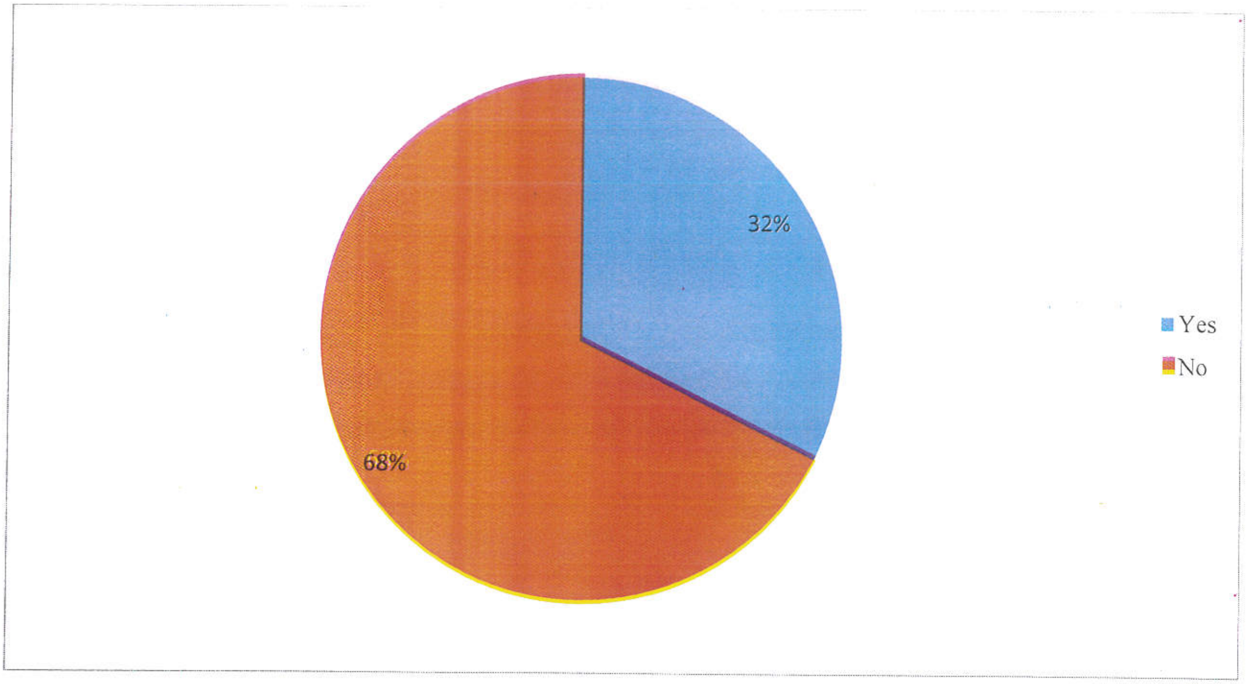

Fig 4.29: Perception about improving ways of disposal

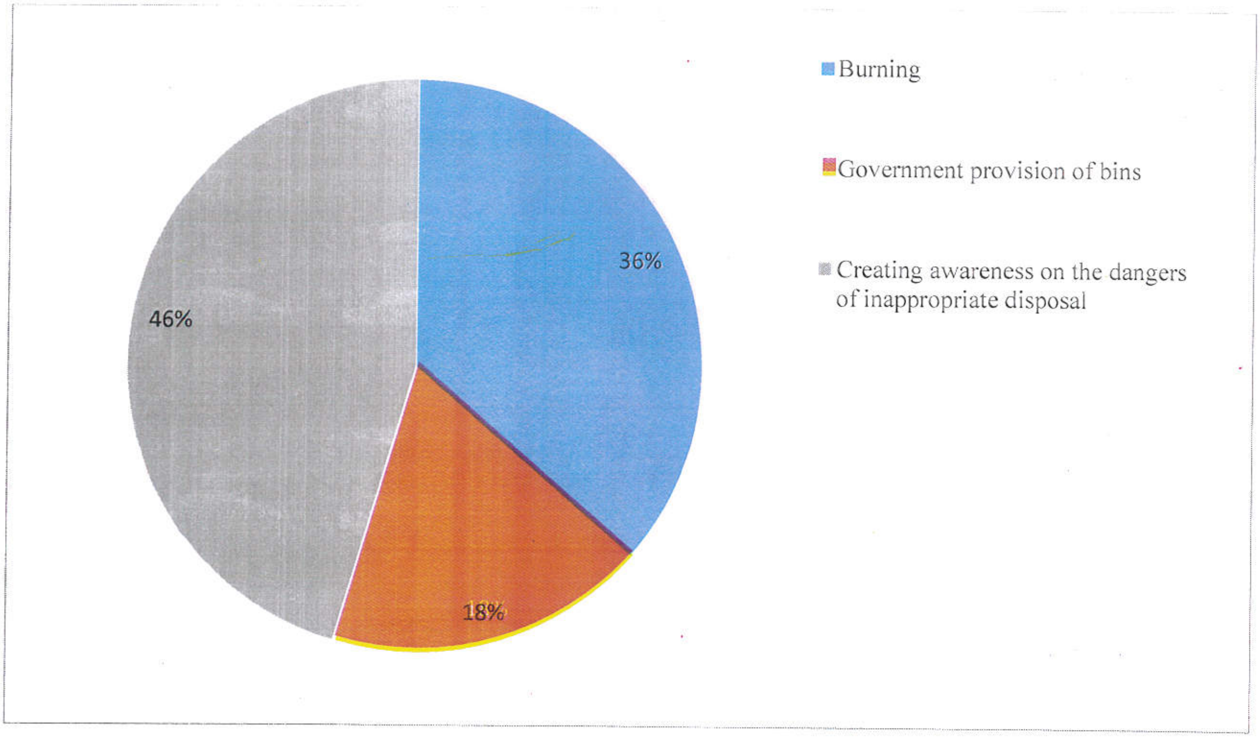

Fig 4.30: Suggested ways of improving on disposal methods

4.4 DISCUSSION

According to World Health Organization (2011), the consumption of more than 400-500mg of caffeine a day from fish, water and other food products may lead to insomnia, nervousness, restlessness, irritability, an upset stomach, a fast heartbeat and even muscle tremors in humans. Fish and water samples collected from Ureje dam did not show detectable levels of caffeine. This shows that fish and water from the dam are safe for human consumption, for human use and other purposes. The result of this study is contrary to the work done in surface waters by Edward *et al., 2015* in Barbados, West Indies who reported caffeine concentrations of up to 6.8 μg/L, with an average concentration of 2.0 μg/L in surface water. Also, in Swiss Lakes and rivers, Buerge *et al.*, (2003) detected caffeine in almost every sample, at concentrations ranging from 0.006μg/L to 650μg/L. It is worthy to note however, that about two (2) compounds were detected from the samples even though not identified.

For only 32% of the respondents to think these PPCPs have effects on waterbodies and aquatic life explains that many do not know what they are and so do not know their consequent effects on the environment.

Majority of the people dispose both containers and contents of PPCPs in the trash cans and then to garbage collection points. This was observed to be the best way they know about disposal. The fish and water samples were collected in the rainy season. The rains, flood, runoffs and winds may carry all these into the waterbodies causing damages to the ecosystem, aquatic organisms and consequently, humans (United States Geological Survey, 2014). The unawareness of majority of the respondents about the knowledge and effects of PPCPs and our waterbodies being seen as channels for waste disposal raise concerns about probable future occurrence and detectable levels of caffeine and/or other compounds in the aquatic ecosystem. In addition to surface water, groundwater is a widespread source for drinking water, and thus, the prevalence of PPCPs in groundwater should also be considered. According to the United States Geological Survey (USGS), PPCPs can move from septic systems into groundwater (Phillips *et al.*, 2015) as a result of continued inappropriate disposal of PPCPs. Results show that majority think disposing the PPCPs contents and containers in bushes, flushing down toilets and sinks, and trash cans is proper without knowing the implications. This explains why the community drug-take-back programme is not used by many and why individuals would think the methods of disposal they use are appropriate. This therefore lays more emphasis on the need for creation of awareness on the dangers of inappropriate disposal of PPCP. Moreover, bioaccumulation of these compounds grows from lower concentration to higher concentrations and could pose negative effects on the aquatic organisms and humans in future.

CHAPTER FIVE

CONCLUSION AND RECOMMENDATIONS

5.1 CONCLUSION

This study has demonstrated that Caffeine is not present in Ureje dam in Ekiti state. Moreover, many individuals do not have adequate knowledge of PPCPs. Significant research is still required to understand both the scope of the problem and its implications for the safety of public water supply and aquatic organisms. Baseline information on PPCPs (caffeine) in Ekiti State has been generated for future use. Individuals' knowledge and awareness on PPCPs have to be improved upon. Moreover, additional research needs to be taken to provide more conclusive evidence of risk and harm to fish and human health in Ekiti state and Nigeria as a whole. To make appropriate and cost-effective decisions regarding the level of PPCPs that are discharged to the environment in Ekiti state, cross-disciplinary cooperation will be needed between environmental scientists, medical scientists, engineers, and economists.

5.2 RECOMMENDATIONS

- Individuals and waste management boards should ensure proper-waste disposal.
- Individuals should be conscious to finish drug dosages or return to the appropriate channels. People should find out if any pharmacies in their communities will take back unused or expired medications. If no other disposal option exists, the medications should be altered in some ways and placed in trash. If the medications will be landfilled, they should be left in their original containers to reduce seepage, making sure all identifying information has been removed. Packaging in an obscure container such as an empty margarine tub or non-transparent bag and placing in trash is advised.
- Government should provide facilities for waste recycling.
- Education and creation of more awareness on the use, knowledge, effects, impacts and more on PPCPs should be emphasized and carried out.
- More research should be carried out to identify potentially harmful compounds present in aquatic ecosystem and study chemical synergies as well.

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APPENDICES

APPENDIX 1: PHARMACEUTICALS AND PERSONAL CARE PRODUCTS ASSESSMENT QUESTIONNAIRE

Dear Respondent,

This questionnaire is designed to obtain information on what individuals know about PPCPs, the modes of disposing their contents and containers and possible consequences of their actions. Please answer the questions with sincerity and tick appropriately. We guarantee the confidentiality of your response.

Thanks for your cooperation.

OLUKAYODE, TOYOSI LAWRENCE

SECTION A: DEMOGRAPHY

Location of respondent ....

Sex: Male [ ] Female [ ]

Age 15-24 [ ] 25-34 [ ] 35-44 [ ] 45-54 [ ] 55 and above [ ]

Religion: Christianity [ ] Islam [ ] Others (Please specify)....................................

Educational qualification: First School Leaving Certificate [ ], West African School Certificate Education [ ] University Degree [ ] No formal education [ ], Others (Please specify)...

Marital status: Single [ ] Married [ ]

Number of persons in your household: 1-3 [ ] 4 – 6 [ ] 7 & above [ ]

Your Occupation...

Number of years on your job...

SECTION B: KONWLEDGE ABOUT PHARMACEUTICAL AND PERSONAL CARE PRODUCTS (PPCPs)

1. Have you heard about PPCPs before? Yes [ ] No [ ] Not sure [ ]
2. Do you know what they are? Yes [ ] No [ ] Not sure [ ]
3. Do you use them? Yes [ ] No [ ] Not sure [ ]
4. If Yes, how often? Very often [ ] Often [ ] Rarely [ ] Very rarely [ ]
5. If No, please specify reason
6. Do you think they have any effects on our waterbodies and aquatic life? Yes [ ] No [ ] Not sure [ ]

SECTION C: ATTITUDES AND PRACTICES TOWARDS PHARMACEUTICAL AND PERSONAL CARE PRODUCTS (PPCPs)

1. a) Do you usually complete drug dosages when you buy them? Yes [ ] No [ ]
   b) If No, please give reason................................
2. a) Do you use up your personal care products before disposal? Yes [ ] No [ ]
   b) If No, please give reason.............................
3. How do you dispose them, that is, both contents and containers of PPCPs?
   -Return remaining drugs to the pharmacist/ supermarket [ ]
   -Throw in trash cans and then to garbage collection points [ ]
   -Flush down toilets and sinks [ ]
   -Throw into bushes [ ]
   -Throw into water bodies [ ]
   -Others specify...........................
4. (a) Do you think your method of disposing the contents and containers is proper? Yes [ ] No [ ] Not sure [ ]
   (b) If No, please suggest better ways...
5. (a) Do you know the impact of inappropriate disposal of PPCPs? Yes [ ] No [ ] Not sure [ ]
   (b) If Yes, please specify...
6. Do you perceive any risk these contents and containers could be to the environment? Yes [ ] No [ ] Not sure [ ]
7. (a) Are you aware of community drug take-back programme that collects drugs for proper disposal? Yes [ ] No [ ] Not sure [ ]

(b) If yes, how often do you make use of this service? Very often [ ] Often [ ] Rarely [ ] Very rarely [ ]

8. Do you think many individuals use other better ways of disposing drugs, contents and containers? Yes [ ] No [ ] Not sure [ ]
9. How do you suggest an awareness on appropriate ways of disposal can be taught to the public?
   -One on One information [ ]
   -Seminars/workshops [ ]
   -Use of jingles/ media [ ]
   -Use of handbills, fliers, billboards [ ]
10. Are you aware that these PPCPs and the chemicals they are made of could have negative effects on fish in their environment? Yes [ ] No [ ] Not sure [ ]
11. (a) Are you also aware that these PPCPs and the chemicals they are made of could have negative effects on humans? Yes [ ] No [ ] Not sure [ ]
    (b) If Yes, can you please mention them? ....
12. How do you suggest an awareness for these effects and consequences can be created?
    -One on One information
    -Seminars/workshops
    -Use of jingles/ media
    -Use of handbills, fliers, billboards
13. (a) Do you think ways of disposal can be improved upon? Yes [ ] No [ ]
    (b) If Yes, what ways do you suggest please?

APPENDIX 2: DESCRIPTIVE STATISTICS OF QUESTIONNAIRE TABLES

Table 1: Awareness of PPCPs

Awareness of PPC	Frequency	Percentage
Yes	13	37
No	17	49
Not sure	5	14

Table 2: Knowledge of PPCPs

Knowledge of PPC	Frequency	Percentage
Yes	12	34
No	16	46
Not sure	7	20

Table 3: Use of PPCPs

Use of PPCPs	Frequency	Percentage
Yes	12	34
No	9	26
Not sure	14	40

Table 4: Frequency of using PPCPs

Frequency of using PPCPs	Frequency	Percentage
Very often	4	31
Often	7	54
Rarely	2	15
Very rarely	0	0

Table 5: Reasons for not using PPCPs

Reason for not using PPCPs	Frequency	Percentage
Never heard of it	5	71
Don't believe in medicine	2	29

Table 6: Effects on water bodies and aquatic life

Response	Frequency	Percentage
Yes	11	32
No	5	14
Not sure	19	54

Table 7: Completion of drug dosages

Response	Frequency	Percentage
Yes	27	72
No	8	23

Table 8: Reasons for not completing dosages

Reason	Frequency	Percentage
Stop using the drug when I feel I have recovered	4	57
I do forget	1	14
I don't take drugs	2	29

Table 9: Use up of PPCPs

Response	Frequency	Percentage
Yes	29	83
No	6	17

Table 10: Reasons for not using up PPCPs

Response	Frequency	Percentage
Loss of interest	2	33
I get okay before finishing them	1	17
No reason	3	50

Table 11: Modes of disposal

Method of disposal	Frequency	Percentage
Return remaining drugs to the pharmacist/ supermarket	0	0
Throw in trash cans and then to garbage collection points	15	43
Flush down toilets and sinks	6	17
Throw into bushes	9	26
Throw into water bodies	1	3
Keep in my house	1	3
Anywhere	1	3
No response	2	6

Table 12: Appropriate modes of disposal

Response	Frequency	Percentage
Yes	20	57
No	3	8
Not sure	10	29
No response	2	6

Table 13: Impacts of inappropriate disposal

Response	Frequency	Percentage
Yes	9	26
No	18	51
Not sure	7	20
No response	1	3

Table 14: Perceiving risks of PPCPs

Response	Frequency	Percentage
Yes	10	29
No	13	37
Not sure	12	34

Table 15: Ways of awareness creation

Response	Frequency	Percentage
One on one information	3	8
Seminars/workshops	3	9
Use of jingles/media	19	54
Use of handbills, fliers, billboards	10	29

Table 16: Awareness of the effects of PPCPs in their environment

Response	Frequency	Percentage
Yes	2	6
No	29	83
Not sure	4	11

Table 17: Awareness of effects of PPCPs on humans

Response	Frequency	Percentage
Yes	9	26
No	9	26
Not sure	17	48