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PHARMACEUTICALS AND PERSONAL CARE PRODUCTS: A REVIEW BASED IN OMAN

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Abstract

Pharmaceuticals and personal care products are being excessively in use. In return, their disposal is a difficult issue to deal with. Excessive/unused pharmaceuticals and personal care products (PPCP) are being disposed ineffectively and leaking into waterways and soil, which in return causes eminent environmental damages as well as harms animals and humans. This is a review article that explains what PPCPs are, their damages to environment and animals. It also includes treated Omani water analysis done by HPLC to determine the concentration of several different PPCPs present. Lastly, it also includes a survey carried out within Omani individuals to observe and understand people's awareness about PPCPs and a proper conclusion is drawn out of this analysis and survey on what kind of PPCPs are present in waterways and individuals' awareness on this topic. According to the survey results, suggestion and policy changes are listed in order to educate people/pharmacist/policy makers and scientist on this topic, to prevent further harm from PPCP.

Key words: PPCP, Pharmaceuticals, High Performance Liquid Chromatography (HPLC)

1. Introduction to PPCP

Pharmaceuticals and personal care products (PPCP) are wide range of products that are prescribed and non-prescribed drugs, medications, perfumes, cosmetics as well as every type of chemical that's being used in medicine, agriculture and cosmetics. Their chemical structures vary a lot. PPCPs have large and complex chemical formulas. According to Environmental Protection Agency, any product that is used for personal health/well-being or for cosmetics are referred to be under the category of PPCP, even the changed form of a parental chemicals called metabolites that are excreted by humans as well as animals are included in the category too. (Water QA, 2013). Endocrine disruptor chemicals (EDC) are within the

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PPCP group too, in which their presence cause the worst consequences if present/leak into the environment.

There are hundreds of different PPCP and they all have different chemical structures. Different types of PPCP have different functional groups, such as hydroxyl, amine or ketone groups (Avila, 2015). The activity of the functional groups don't matter much, because as they get into the environment, its toxicity, solubility and polarity changes with small alteration in the formula, thus whole the chemical property of PPCP changes. So, the change in the functional groups and its activity determines in which part of the environment PPCP get accumulated (Kümmerer, 2009). PPCP that get accumulated in an acidic environment act different, than if it get accumulated in a basic environment. Pharmaceuticals contain several different types of active ingredient (AI), beside the AI, it also contains organic and inorganic compounds, stabilizers, diluents. Medications such as synthetic hormones , EDC have different chemical structure as well. Their effects will be discussed in coming chapters.

Tones of wide range of PPCP are being produced worldwide. For instance, Around 6000 tones/year of musk is being produced, which is used as a scenting agent in detergents. Triclosan which is found in shaving creams and toothpastes (Avila, 2015) is another commonly used PPCP. Figure 1 below shows the distribution of personal care products sold around globe in 2010.

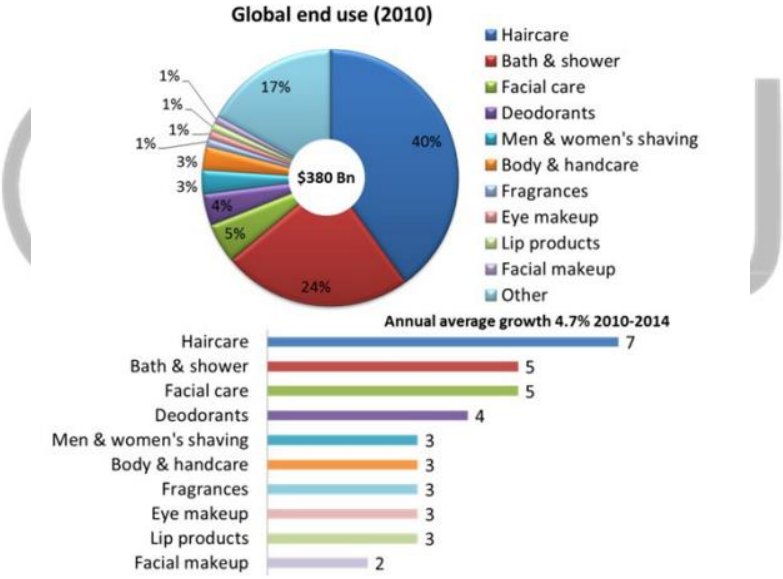

Figure 1 Most sold Personal Care Products (Yang, 2018)

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			Global	
Product	**Active Ingredient**	**Use**	**Rank**	**Sales (US $ Billion)**
Nexium	Esomeprazole	Gastroesophageal reflux disease	4	7.5
Abilify	Aripiprazole	Major depressive disorder	7	7.0
Crestor	Rosuvastatin calcium	High cholesterol and high triglycerides in the blood	3	8.3
Advair Diskus	Fluticasone propionate, salmeterol xinafoate	Asthma in patients 4 years and older	1	8.9
Cymbalta	Duloxetine hydrochloride	Major depressive disorder and general anxiety disorder	10	5.8
Humira	Adalimumab	Rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, and plaque psoriasis	2	8.5
Enbrel	Etanercept	Rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis	5	7.5
Remicade	Infliximab	Rheumatoid arthritis, psoriatic arthritis, ulcerative colitis and Crohn's disease	6	7.3
Copaxone	Glatiramer acetate	Multiple sclerosis	18	4.5
Neulasta	Pegfilgrastim	Neutropenia	20	4.3
Rituxan	Rituximab	Non-Hodgkin's lymphoma or chronic lymphocytic leukemia	–	–
Singulair	Montelukast sodium	Seasonal allergic rhinitis and perennial allergic rhinitis	16	4.7
Atripla	Efavirenz, emtricitabine, and tenofovir disoproxil	Human immunodeficiency virus (HIV)	–	–
OxyContin	Oxycodone hydrochloride	Moderate to severe pain		
Spiriva	Tiotropium	Breathing difficulties caused by chronic obstructive pulmonary disease (COPD)	13	5.1
Avastin	Bevacizumab	Patients with certain types of colorectal and lung cancers	11	5.4
Plavix	Clopidogrel bisulfate	Prevent blood clots after a recent heart attack	12	5.2
Januvia	Sitagliptin	Type 2 (non insulin-dependent) diabetes	–	–
Lantus	Insulin glargine	Type 1 (insulin-dependent) or type 2 (non insulin-dependent) diabetes	8	6.6
Truvada	Tenofovir disoproxil and emtricitabine	HIV	–	6.0
MabThera	Rituximab	Rheumatoid arthritis	9	4.3
Glivec	Imatinib mesilate	Blood cancer	19	
Lipitor	Atorvastatin	High cholesterol, and to lower the risk of stroke, heart attack	14	5.1
Herceptin	Trastuzumab	Breast cancer	15	5.0

Figure 2 Most sold pharmaceuticals (Yang,2018)

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The most sold personal care product was hair products in 2010 around globe, as reported by Yang. Moreover, figure 2 shows highly ranked pharmaceuticals sold globally in 2015. Number 1 sold pharmaceutical is said to be Advair Diskus that is used in the treatment of asthma. (Yang, 2018).

2. PPCP Information/Data About Oman

Sultanate of Oman has proven tremendous amount of improvement in the health sector in the last 30 years. In 1970s there were only 2 hospitals and 12 clinics were available, while in 2016 Ministry of Health is having 49 hospitals all around the Sultanate. (MOH, 2016). The following map shows the distribution of health care services in the capital city of Sultanate.

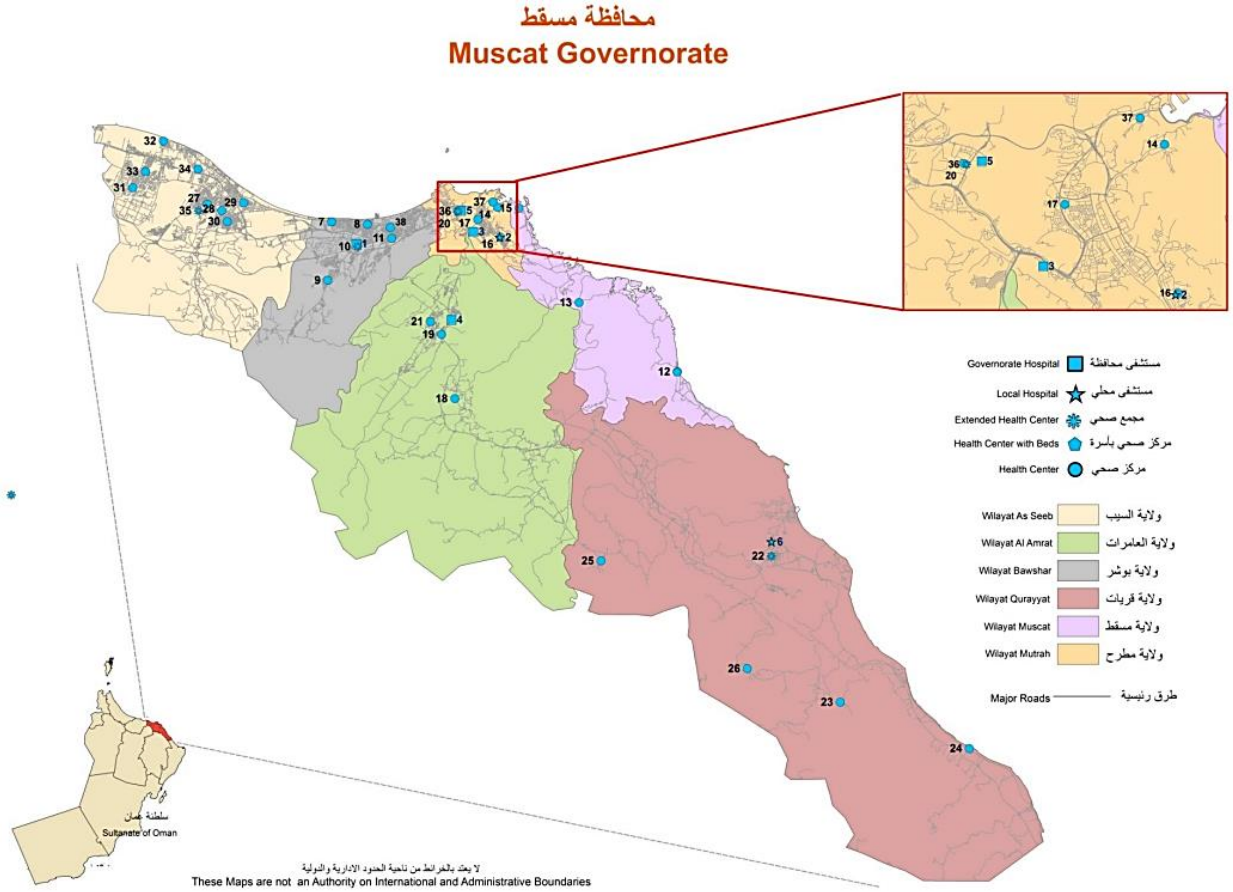

Figure 3 Distribution of Health Care Facilities in Muscat (MOH, 2016)

Environmentally speaking, more hospitals mean more biological waste and pharmaceutical waste, but its inevitable need with the elevation of population and economic development. Furthermore, pharmaceuticals sold in Oman differs from the world pattern, since every specific region has their own disease due to the different life styles and climate conditions. Ministry of Health, having a collaboration with World Health Organization had established a statistics paper of pharmaceutical country profile for Oman in 2011, authored by Ph. Sawsan Jaffer. It was recorded in pharmaceutical company profile of Oman that, there are 62 hospitals and 400 licensed pharmacies around Sultanate. Moreover there are 4 pharmaceutical companies in Oman manufacturing medicines with producing pharmaceutical starting materials and repacking of finished product without discovery of new active substances. The recorded

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mean number of patients receiving prescribed drugs in public hospitals was 2.5 per patient in 2011. (Jaffer, 2011)

Curriculum	%
% of medicines prescribed in outpatient public health care facilities that are in the national EML (mean)	97.5
% of patients in outpatient public health care facilities receiving antibiotics (mean)	48.2
% of patients in outpatient public health care facilities receiving injections (mean)	6.9
% of medicines adequately labelled in public health facilities (mean)	65.2

Figure 4 Properties of Prescribed Medicine in Oman (Jaffer, 2011)

Figure 4 above shows that 97.5% of patients that are prescribed with medicine within the public hospitals, get their medicines free of charge from pharmacies. Indicating almost all Omani patients have easy access to pharmaceuticals when prescribed. 65.2% of medicines were found to be labeled properly, so patients don't receive wrong medicines. People having easy access to pharmaceuticals have both pros and cons, which will be discussed in coming chapters. Table 1 below, was obtained from Ministry of Health, Oman's website data and gives information on how much hospitals all around Oman had spent on pharmaceuticals as well as to equipment in 2016. 7,547 thousand Omani Rials were spent on pharmaceuticals just in the capital city of Sultanate of Oman, Muscat. Not to forget to mention that this data doesn't include amount of money spent on pharmaceuticals in pharmacies.

Table 1 Consumption at Hospitals in Oman (MOH, 2016)

Governorate	الأدوية Drugs	أدوات المختبرات Laboratory Items	الأدوات الجراحية والجراحية الإستهلاكية* Surgical Instruments and Consumables*	الإجمالي الكلي@ Grand Total@	محافظة
Muscat	7,547	991	2,869	11,407	مسقط
Dhofar	4,418	855	2,165	7,438	ظفار
Musandam	504	203	162	869	مسندم
Al Buraymi	1,096	285	526	1,907	البريمي
Ad Dakhliyah	3,347	695	2,428	6,471	الداخلية
North Al Batinah	5,493	1,073	2,482	9,048	شمال الباطنة
South Al Batinah	2,705	603	1,329	4,636	جنوب الباطنة
South Ash Sharqiyah	2,773	813	1,380	4,966	جنوب الشرقية
North Ash Sharqiyah	1,851	491	1,134	3,476	شمال الشرقية
Adh Dhahirah	1,745	484	822	3,051	الظاهرة
Al Wusta	198	68	69	334	الوسطى
Royal Hospital	21,974	2,700	6,526	31,200	المستشفى السلطاني
Khawlah Hospital	8,316	393	12,694	21,403	مستشفى خولة
Central	5,106	2,293	389	7,788	المركزي
Grand Total	67,073	11,947	34,975	113,995	المجموع

(Note: Thousands Rials)

Explicitly, all the wastes coming out of these healthcare units need to be managed ecofriendly. Different types of PPCP, having different structural and chemical formulas get dumped into the environment to get rid of them. Each one of them acts adversely with the new surroundings in environment. Their effects, consequences and waste management strategies will be discussed in the further chapters.

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3. Various Types of PPCP

There are naturally occurring toxic PPCP, beside the synthetic ones. From the naturally occurring compounds, many other samples are manufactured and some of them are as follows;

3.1 Naturally Occurring PPCP

Phytoestrogen; These are the type of estrogen consumed by women to reduce the risk of breast cancer or cardiovascular diseases. While, even trace concentrations of these causes infertility in some animals such as sheeps. (Bucheli, 2018)

Ptaquiloside; Is another naturally occurring carcinogenic compound produced by plants in environment. It's used in the manufacturing of cosmetics and creams (Bucheli, 2018). Despite ptaquiloside is more toxic and dangerous than pesticides, very little preventative precaution is taken and people are not aware of it as much as they are aware of pesticides.

Pyrrolizidine Alkaloids; This is another compound found in the pollens and flowers. Many cosmetic products are made up with pyrrolizidine alkaloids and they are carcinogenic. They are even found in honey with an approximate amount of 95 μg/g.

Saposins; Saposins are found in the plant roots. They are mainly used as a foaming agent in soaps and bathing gels. Due to its antimicrobial properties also used in medicine.

Besides these naturally occurring compound's hazard to environment, the naturally occurring PPCPs are very dangerous to humans, especially if its directly via skin connection.

3.2. Synthetic PPCP

Synthetic PPCP include a vast range of chemicals from cosmetics, perfumes, pesticides to hormone regulatory medicines. Anything man made, used in veterinary medicine, health, well-being and cosmetic is referred to be a synthetic PPCP.

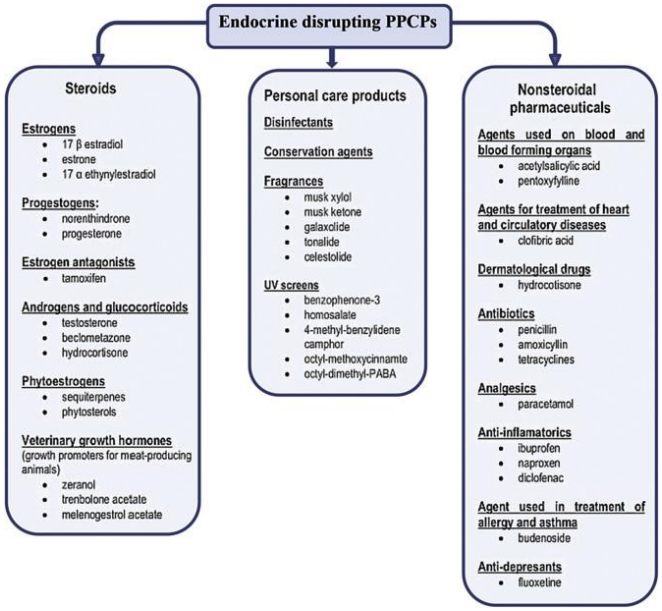

Figure 5 ED-PPCP (Ebele,2017)

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4. Sources of PPCP

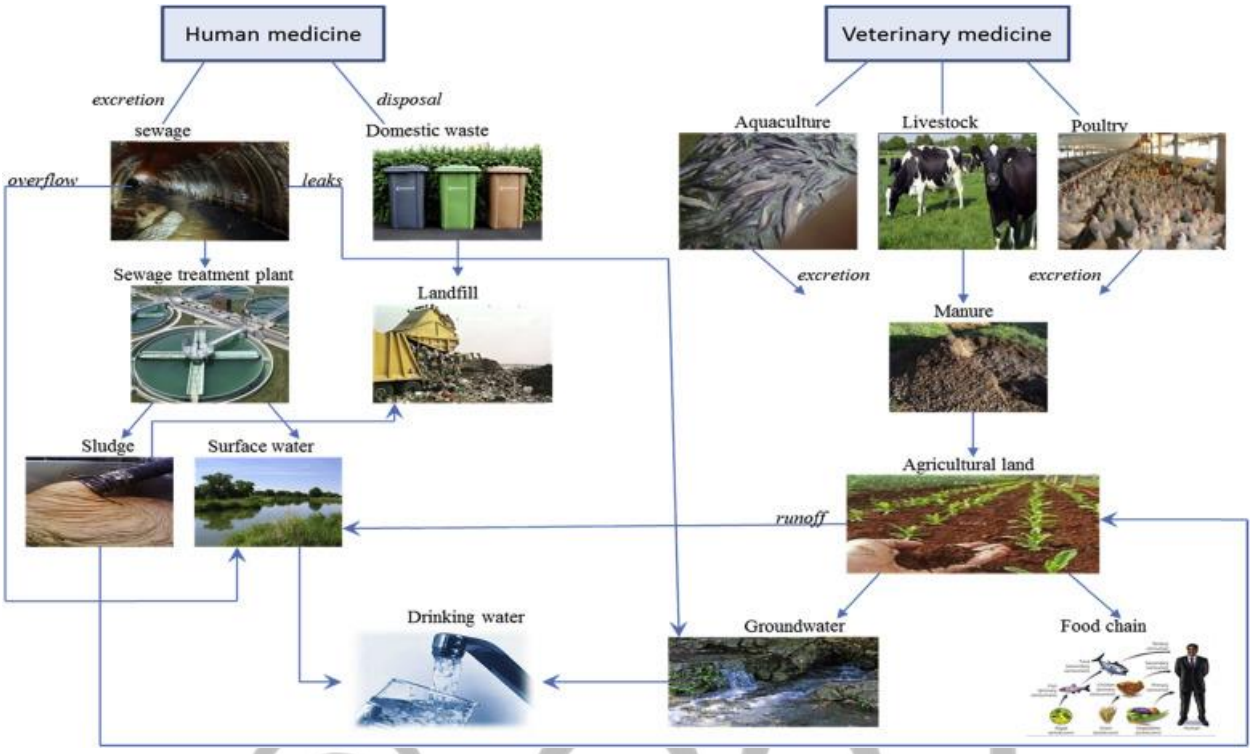

Figure 6 Sources of PPCP Into Environment (Ebele,2017)

PPCP are being used worldwide. The reasons and needs of why PPCPs are being used was discussed in the previous chapter. If the route of how PPCP arrive into environment is known, then systems could be developed to prevent the entry into environment or make them less harmful. When pharmaceuticals are used by humans or animals, they get excreted into the sewage and the treatments plants do not have proper filter system to stop PPCP into reaching to aquatic ecosystems. Whereas, in the landfilling technique to dispose the expired pharmaceuticals, depending on to the chemical structure of the PPCP, it may either run off to the ground water or can be taken up by plants while it stays in the soil and find their way into the food chain as well (Avila, 2015).

Beside from waste water treatment plants and run offs to waters, there are another ways PPCP get accumulated in environment. As reported by Hourger the phytoestrogens such as isoflavones are being produced by plants at around 600 tons annually (Hourger, 2011) which is a natural source.

Presence of PPCP in environment, can be classified in 3 different categorizes; PPCP in soil, water and air. The following chapter focuses on PPCP in soil and water.

5. PPCP in Waters

Various concentrations of PPCP are found in water, lakes, rivers. Environmental fact sheet of New Hemisphere reported several different routes of PPCP to environmental waters as following: The un-metabolized medicines get excreted from human to the drainage and sewage systems; extra medicines

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get flushed into the sink; washing gels, soaps, sun creams, body lotions used during bathing; veterinary drugs used for the animal treatment; PPCP that get discharged improperly by the pharmaceutical companies itself. (Drive, 2010) All these are unavoidable part of the world living system and cannot be stopped, but their consequences and effects could be minimized if there is a clear understanding of how they find their ways into environment.

Usually sewage treatment plants are not engineered in a way to remove the PPCP from water. Waste water treatment consists of 2 steps. First step is called the primary treatment, in which the wastewater is settled down to remove the solid particles. Whereas, in secondary step biological process is used to purify the water. In primary stage the large floating solid particles are separated from water by screening the water, following the entry of water to grit chamber where smaller particles such as sand, pebbles are removed from water by settling them down in chamber and then sewage is allowed to enter to the sedimentation tanks where the suspended solids get removed by sedimentation to the bottom of the tank. The sediment can either be used as a fertilizer or disposed to the landfills. In secondary stage, introduction of bacteria treats the wastewater by feeding on the organic material and producing a non-harmful by product, which takes place in trickling filters. Trickling filter is 3-6 feet deep stones on which bacteria grow. As a last step before the water is dumped back into waterways, Chlorine is added, to remove the odor and to kill pathogenic bacteria present. As United States Environmental Protection Agency reported "New emerging pollution problems have placed additional burden on wastewater treatment facilities." (EPA, 1998) As described above, the wastewater treatment systems only remove the mechanical pollutants and the organic particulate matter. Pharmaceuticals and personal care products are inorganic thus existing wastewater treatment plants are no longer effective for the contemporary new raising pollutants.

5.1. PPCP In Oman Waterways

In 1984, Sultanate of Oman had established Ministry for Environment and Water with the royal Decree of 45/84, which made Sultanate the first country to establish such a Ministry amongst other Arab countries. (Ahmed, 2017). With such an attempt, it can be stated that Oman is giving priority and is devoted to be one of the leaders in Arab World to treat water ecofriendly.

In Oman, there are more than 350 wastewater treatment plants (WWTP) running which belong to government as well as to private sectors. Out of 300 WWTPs, 10 of them are present in Muscat city. All WWTPs across Oman are using the similar treatment process that's being used worldwide, which is explained in the previous paragraph. Thus, these WWTPs could be said the primary route for PPCPs to enter to the environment. As Baawin reported, the amount of wastewater collected from domestic and commercial territories to the wastewater treatment plants was 21,993 m^3/day in 2016. (Baawin, 2013). In Oman, after Haya Water had established the sewage netrwork project 86% of the localities have been connected to sewer systems. (Zekri, 2014) .Although, PPCPs are present in tiny amounts as parts per million (ppm) in waters, since large volumes of wastewater is brought to the WWTPs and PPCP's physiochemical properties neither change nor break down, minute but continuous amounts of discharge of PPCP take place into the environment, especially to the waterways as effluent and to the soil as sludge. Thus conceivably, presence of PPCP even as ppm don't make them an innocent pollutant.

Antonette Arvai had carried out a research to see how 42 different pharmaceutical compounds have been treated and are present in Great Lakes of America and found out that only 6 chemical compounds

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(herbicides, antibiotics, anti-inflammatory drugs) were removed by the treatment plants and contain minute amount in lakes, caffeine and natural estrogen were removed successfully by the sewage treatment plant, whereas the remaining 70% of pharmaceuticals aren't being removed by sewage treatment plants. (Bienkowski, 2013). However, sophisticated treatment methods such as Nano-filtration or reverse osmosis are capable of removing pharmaceuticals from water beside other pollutants during wastewater treatment process. It was reported that Nano-filtration removes upto 90% of pharmaceuticals from water. (Kosutic, 2013). Narbaitz and his colleagues developed Cellulose acetate membrane and compared its removal capacities on ibuprofen, carbamazepine and sulfamethazine with thin film composite nano-filtration (TFC NF) membrane and concluded that, TFC NF membrane had higher flux rates and much better removal capacities on tested pharmaceuticals. (Narbaitz, 2013). Lab scale experiments are ongoing, more effective treatment methods are being in search but are difficult to apply on large scale due to high amount of energy production and cost. It was recorded that Seeb sewage treatment plant uses advanced treatment techniques in the plant that is the ultrafiltration membrane technology and author added that other plants are under construction to add this tertiary treatment stage to their plants as well. (Ahmed, 2017). This is an indication that soon in Oman, the leakage of pharmaceuticals into environment due to the treatment plants will decrease since the advanced membrane technologies are capable of removing the pharmaceuticals from effluents.

It was reported that macrolides and sulfonamides were the main types of antibiotics present in Sultanate's waters. PPCP concentrations varied between 0.01 to 14.5 µg/L. (Al Riyami, 2018). Due to rapid elevations in agriculture and lack of fresh water resources, Oman uses the water effluent in agriculture and landscaping. But as also seen from table 1, the main usage of treated wastewater is landscaping that's discussed in chapter 2.1. It was recorded that, treated wastewater is being used in irrigation as well as to avoid saltwater intrusion problem in the Coastal sides of Oman. (Baawain, 2013). Seawater shouldn't reach and mix with Oman's aquifers because Oman is already seeking to preserve its own freshwater resources. However, Oman having an extensive coastline of 3,165 km long, hence saltwater intrusion is ineludible and a big challenge. Al-Makhtoumi and his colleagues had tested the treated wastewater to mollify seawater intrusion along Al-Jamma Aquifer. 60,000 m^3 of treated wastewater was injected daily for 4 months period and 8 months' time was given for recovery. This cycle was repeated for over 20 years and he Al-Makhtoumi concluded that injection of treated wastewater had withdrew saline interface for 875m far. (Al-Maktoumin, 2015).

5.2. Effects of PPCP Present in Water

Although very small concentrations of PPCP are present, they are yet considered as psedu-persistent pollutant (Barcelo, 2007). When PPCP enter into the environment, water, soil or even human body, their physio-chemical properties alter which in return changes their properties and toxicities. Contaminated water has a damage both to the aquatic life, animals and humans that drink it continuously.

The detailed explanation on how PPCP find their route into waterways and surface waters was explained in chapter. In countries where no fresh water resources are available, finished drinking waters are produced by the treatment plants, which is the primary cause of PPCP such as antibiotics, mood stabilizers and many more being present in trace amounts within our drinking waters. (Lambert, 2012). Besides, even the fresh water sources such as rivers and lakes get contaminated by the PPCP. According to Associate Press in 2008, out of 35 lakes in the US, 25 of them were analyzed and detected different concentrations of PPCP. (Lambert, 2012). Another research was carried out by US. Geological Survey in between 1999 to

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2000 years, had detected that more than 80% of the 135 tested water streams were contaminated by 95 different types of PPCP. (Buxton,2002). Figure 5 shows the several different concentrations of PPCP present in 135 studied water streams in the US. Albeit, the presence of PPCP are in trace amounts in the drinking water, continuous ingestion of low concentration is still considered to be risky and dangerous to human health as well as to animals, which will be discussed in this chapter.

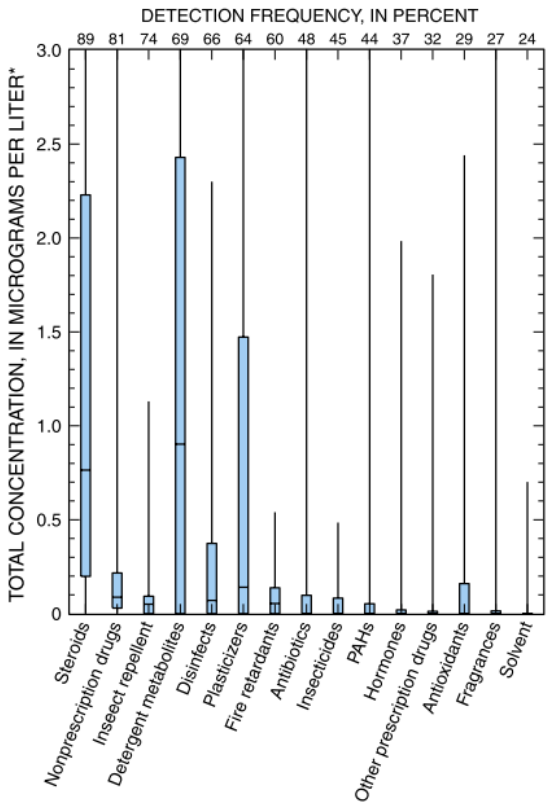

Figure 7 Concentration of PPCP According to US Geological Survey (Buxton, 2002)

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Table 2 Calculated Safety Ingestion Limits of PPCP (WQA, 2013)

Chemical	Type (EDC/PPCP)	Finished Water Concentration	Safety Level (DWEL)
Meprobamate	Anti-anxiety	3.8 – 42 ng/L	6000
Phenytoin	Anti-convulsant	2.3 ng/L	210
Atenolol	Beta blocker	1.2 – 18 ng/L	2700
Carbamazepine	Anti-seizure	6.3 ng/L	670
Naproxen	Analgesic	0.52 ug/L	40,000,000
Bisphenol A	Plasticizer	25 ng/L	72,000
Linuron	Herbicide	6 – 6.2 ng/L	8400
Nonyl Phenol	Surfactant	100 ng/L	16,000

Since, pharmaceuticals and personal care products are being consumed as life essentials and became part of our daily lives and thus PPCP are proven to be present in our drinking water, Water Quality Association(WQA) had come up with some calculations to provide us with maximum amount of ingestible PPCP concentration, which WQA named as "acceptable daily intake (ADI)". To calculate ADI, no-observed adverse effect level (NOAEL) is divided by lowest observed adverse effect level (LOAEL) and is multiplied with the uncertainty factor of a chemical which is specific for a chemical. (WQA, 2013). For instance, if a person has been drinking a water that contains an anti-anxiety drug called meprobamate, table 2 indicates, in each liter 3.8 to 42 Nano gram is present. If a person drinks more than 6000 L of the contaminated water with this drug that is around 8 continuous years, then the person is said to be at risk according to Water Quality Association's safety table.

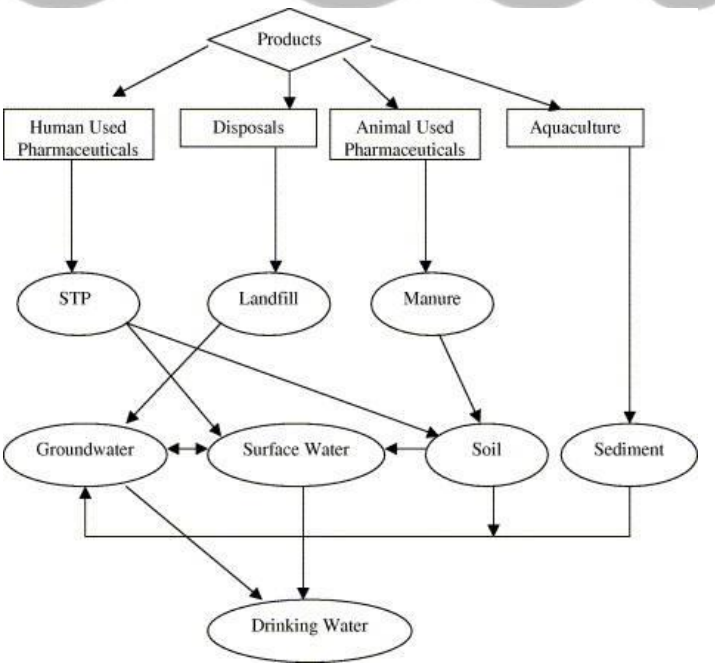

Figure 8 Sources of Pharmaceuticals in Environment (Colinmayfield, 2016)

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Morally talking people do not like the idea of ingesting pharmaceuticals like antibiotics or mood stabilizers especially from the water that they are drinking. Secondly, if the antibiotic residues are present in environment due to the continual ingestion and excretion of antibiotics, the genes may be passed to pathogenic bacteria causing antibiotic resistance. (Allen, 2013). Gratitude to recent studies going on to remove the antibiotic resistant genes from landfills that was done by Xinzhu at 2017 in Singapore. (Yi, 2017)

Moreover, endocrine disrupting pharmaceuticals (EDP) causes worse damage such as deformation in reproductive system of male fish. It was reported that male fish were feminized in British rivers at 1970s (Jabling, 2006). Which indicates that the PPCP have a toxic effects on different levels such as mutagenic and reproductive toxicity risk as well. Oetkan tested a drug named antiepileptic carbamazepine (CBZ) on a fresh water species and found that the drug even at very low concentrations had posed a potential threat chronic effect on C. Riparius specie (Oetken, 2005). The vulture population in the aquatics in India had decreased by 90%, it was then found that this was due to the high concentrations of diclofenac ingestion which was accumulated in waters due to high usage by people in India for the treatment of cattle in veterinary medicine. Since then, the usage of the drug was banned (Oak, 2013). Because of the lipophilic nature of pharmaceuticals they are hazardous to benthos as well. (Oetken,2005) Similar statement was also repeated by Al-Farsi saying that even though tiny amounts of PPCP don't cause direct harm to fish but are treacherous to phytoplankton. (Al-Farsi, 2017).

				
Pharmaceutical	Diclofenac	17α-Ethinylestradiol	Diclofenac	Sulfonamide
Therapeutic group	Analgesics	Synthetic estrogen	Analgesics	Antibiotic
Non-target organism	Vulture (Gyps bengalensis)	Fathead minnow (Pimephales promelas)	Rainbow trout (Oncorhynchus mykiss)	Maize (Zea mays) Willow (Salix fragilis)
Effects	Population collapse due to renal failure	Population collapse due to feminization of male fish	Strong reactions of liver, kidney, and gills	Adverse effects on root growth. Death of maize at high conc.
Study type	Wildlife	Whole-lake experiment	Laboratory	Greenhouse

Figure 9 Effects of EDP on Plants & Animals (Weber, 2014)

6. PPCP in Soil

There are 2 ways PPCP can reach to the soil. Its either when the water that contain PPCP gets in contact with the soil or when the solid waste get disposed into the soil as landfilling.

Due to the rapid increase of population there is increase of waste produced each year. According Hoornwerg's statistics the municipal solid waste produced (MSW) is 1.3 billion tons annually. This number is expected to increase to 2.2 tones billion/year in 2025. (Hoornweg, 2012). Three management methods are there for the huge amount of waste produced; Composting for recycle purposes, combustion in which electricity/steam can be produced from or landfilling. (Manual, 2016). Out of these 3 management

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methods, landfilling is the most preferred one because all the waste product is being lost whereas the 2 other methods are sustainable and waste is turned into a useful product. According to EPA Statistics in 2005 the chemical waste produced was 29.1 million tones. (EPA, 201). Figure 4, show how OECD countries manage their solid waste. 59% of the solid waste is filled in lands. The soils are being exposed to large amounts of chemicals and PPCP. Thus huge amounts of chemical waste is produced, which cannot really get treated by the treatment plants because of their nature; stable and non-biodegradable. Thus, when landfilled into the soil, PPCP stay there for long times and most of the pharmaceuticals are in their active forms.

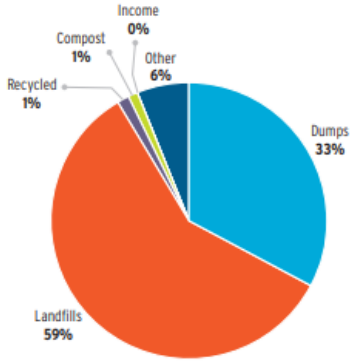

Figure 10 Waste Managment Methods (Messiha, 2005)

The other route PPCP can enter into soil is by using the treated water as mentioned earlier for irrigation purposes. 3.6 $X10^6$ m^3 of treated wastewaters from treatment plants are being re-used in US. (Miller, 2016). As mentioned earlier, the treatment plants cannot treat the pharmaceuticals well, and using effluent for the landscape irrigation eventually leads PPCP get transferred into the soil. They may be taken up by plants.

From using hundreds of pharmaceuticals in treatments of humans and animals to using pharmaceuticals in fish farming, PPCP find their way into the soil. (Al-Farsi, 2017) . Moreover, after PPCP find their way into soil, by depending onto the contaminant's physiochemical properties, plants uptake them. Usually, the area called an exodermis present in the root of the plant doesn't let the uptake of the solutes present but the PPCPs enter to the root from an area called the Rhizophere in the root and gets translocated from the root to other parts of the plants and eventually gets accumulated. Coupled chromatography system is used to analyze the PPCP in plants.

6.1. PPCP In The Lands of Oman

Oman environmental Service Holding company called Be'ah was established in 2007. Royal Decree by 46/2009 quote, had given Be'ah the permission and responsibility to deal with the solid waste in Oman.

It was reported on Be'ah's data sheet that, it receives 1.2kg /capita/day of municipal solidwaste, 4500 tonnes/year of healthcare waste, 1.5 million tones/year of industrial waste and 2 million/tone/year of municipal solid waste. (Be'ah, 2017). PPCPs make up a large amount of this solid waste, especially the healthcare waste that Be'ah receives. Figure 2 below shows the landfills all around the Sultanate of Oman.

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As its seen clearly from the figure, there are 12 numbers of landfilling station currently and 1 landfill station present in Al-Amrat within Muscat governorate, which is 60,000 square meter large. (Ahmed,2017). From waste characterization and generation of Be'ah, the total amount of the waste produced on 2016 was 675,756 tones and in 2017 this increased to 685,654 tones. (Be'ah Data, 2017). Hence, the fast elevations in volumes of solid waste will result in demanding of more landfill stations across Sultanate. A compost is made which fills the station. The compost consists of a mixture of green waste which is generated by Muscat Municipality and sludge that is the byproduct of water treatment plants such as Haya Water.

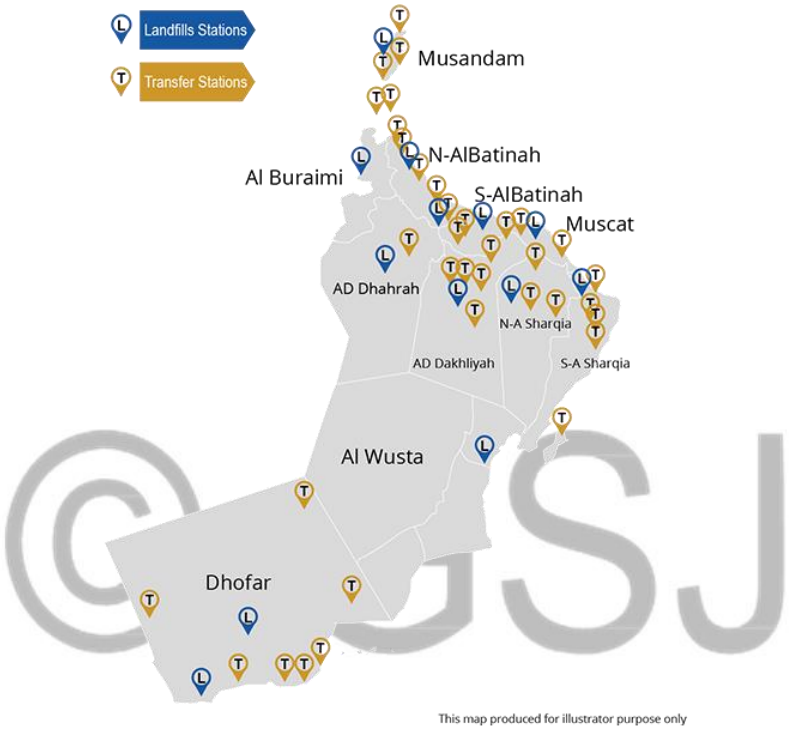

Figure 11 Landfills around Oman (Bea'ah,2017)

Table 1 below, provides information on wastewater effluent in Oman. As it can be seen, the effluents from wastewater treatment plants are mainly used for landscaping, which is responsible for the accumulation of PPCPs in soil. Main application of treated effluent is landscaping but recent years due to the increase in agriculture, the treated water is being used in irrigation as well. (Al-Riyami, 2018).

Table 3 Effluent Information (Baawain,2014)

Waste Water Treatment Plant	TE (m^3/day)	Sludge (ton/day)	Main TE Application
Al Ansab	21,000	66	Landscaping
Darsayt	18,000	33	Landscaping
Rusayl Ind	800	2	Landscaping
Salalah STP	20,000	35.5	Recharge Wells
Raysut Ind.	150	150	Landscaping
Sohar STP	6600	6600	Landscaping
Sohar Ind.	300	300	Landscaping

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Compound	Spiked concentration	Planting media	Test samples	Measured concentrations	Instrumental analysis
Amoxicillin trimethoprim	1 mg/kg	soil	Lettuce and carrot	Not detected in both samples 6 μg/kg (lettuce) 5.3 μg/kg (whole carrot)	LC-MS/MS
20 PPCPs including 16 pharmaceutical compounds, 3 personal care products and 1 herbicide	0.5 μg/l	Nutrient solution	Lettuce Spinach Cucumber chilli pepper	0.2–29 ng/g (leaves) for 13 PPCPs 0.04–34 ng/g (leaves) 12 PPCPs 0.05–70 ng/g (leaves & stems) 17 PPCPs 0.1–69 ng/g (leaves & stems) 15 PPCPs	UPLC-ESI-MS/MS
	5 μg/l	Nutrient solution	Lettuce Spinach Cucumber chilli pepper	All PPCPs were detected in the roots of the four crops, the highest detected concentration was 92×10^2 ng/g. some of the PPCPs was detected in the leaves and stems of all four vegetables, the highest detected concentration was 58×10^2 ng/g	
Sulfamethoxazole, trimethoprim, caffeine and Ibuprofen	500 ng/l	Nutrient solution	iceberg lettuce and spinach	Detected but not available	HPLC–ESI–MS/M
Sulfamethoxazole Ibuprofen and caffeine	Spike mix compounds	soil	sweet potatoes and carrot	0.05–0.24 ng/g (roots of both cops) Detected in higher concentration in leaves than roots Detected in both crops (leaves and roots) But not available	LC-MS
Sulfamethoxazole and trimethoprim	232.5 μg/l	Nutrient solution	cabbage	138.26 ng/g (root) 20.10 ng/g (leaf) 91.33 ng/g (root) 11.42 ng/g (leaf)	LC/ESI/MS
	Spiked mix compounds	soil	tomato fruit and cucumber fruit	Not detected in both crops	LC–MS/MS
Sulfamethoxazole and trimethoprim	0.25 mg/l (mix with other chemicals) 1 mg/l (individual)	Nutrient solution	Pea, cucumber	Detected in both crops (not available)	LC-ESI-MS/MS
Sulfamethoxazole	No spiked compounds	Soil (amended with animal manure)	radish, rape, celery, coriander	radish leaf (0.9–2.7 μg/kg), rape leaf (0.2 μg/kg), not detected in both celery and Coriander	LC-ESI-MS/MS
Ibuprofen	1.27 mg/l	Soil (amended with yellow-water)	ryegrass and soil	Not detected in both	GC–MS
	100 ng/l	nutrient solution	lettuce, spath	Detected in both crops (not available)	GC–MS
Caffeine and Ibuprofen	Spiked mix with other compounds	soil	tomato fruit and cucumber fruit	Detected in both crops	LC–MS/MS
Carbamazepine, diclofenac, fluoxetine, propranolol, sulfamethazine and triclosan	No spiking	soil	Ryegrass Radish (roots and leaves)	Detected in both crops in order Carbamazepine (33 μg/g) > propranolol > triclosan > fluoxetine > diclofenac. Carbamazepine (52 μg/g) > triclosan > diclofenac > propranolol > fluoxetine	Not available
Sulfamethazine	0, 50, and 100mg/ml	Soil amended with manure	Corn Potato lettuce	Detected in all crops 0.1–1.2 mg/kg	HPLC
Chlortetracycline and tylosin	20 μg/l	Soil amended with manure	Corn, lettuce potato, cabbage and green onion	chlortetracycline only detected in small range 2–17 μg/kg in all crops	ELISA method
Bisphenols A (BPA), diclofenac sodium (DCL), naproxen (NPX), and 4-nonylphenol	BPA, DCL, NPX at, respectively, 46.4, 237.4, 178.2, or 110.4 ng/l	hydroponic	Lettuce and collards	For both crops the concentrations were ranged 0.22 ± 0.03 to 927 ± 213 ng/g, in order of BPA > NP > DCL > NPX	HPLC

Figure 12 Amounts of PPCPs Present In Plants (Al-Farsi, 2017)

Pharmaceuticals contain 2 main ingredients, that are the active pharmaceutical ingredient (API) and the excipient. API is a specific component that is responsible for giving the desired effect to the body and excipient carries the drug, in other words the drug media. (Vandel,2013). Pharmaceuticals are designed in a way to be active for long periods, effective and stable. So after these wastewaters get disposed into the environment as landfills, they will still be in active form and thus even their minute amounts will cause enough damage to the soil. Besides the damage, because of drug's stability property even when they are put into landfills they stay there for many years and do not degrade. This can reach to the plants, animals and even into our food chain. Figure 12 above shows a study Al-Farsi had carried out on varies plants across Oman and the amount of 100 different PPCPs presence within them. (Al-Farsi, 2017). Ibuprofen and caffeine was the most abundant PPCP present in plants in Sultanate. As it can be seen from the

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following figure that significant amount of PPCPs were detected in plants, that should not be neglected and overlooked for the health concerns. Due to the land fillings, improper solid waste management methods PPCPs have leaked into our environments. The effects of PPCPs in soil is discussed in the next heading.

6.2. Effects of PPCP in Soil

Because treatment plants not treating the PPCP from effluent well is, effluent water containing PPCP and this contaminated water is being used in agriculture for irrigation, which is the main reason for the uptake of PPCP by plants. Due to the toxicities of PPCP, the amount of bacteria in soil decreases, decreasing the quality of the soil because the soil lacks of protozoa which in return slows down the decomposition of plants (Al Farsi, 2017). The accumulation of these contaminations accumulated within the roots and plant tissue can be calculated by the phenomenon called the root calculation factor (RCF) and bio-concentration factor (BCF). Al-Farsi had also reported that, the PPCP enter into our food chain. When pharmaceutical is excreted from the human body, it's called a metabolite. Most metabolites are found as inactive compounds in the environment except some of them (Kummerer, 2010). Prodrugs, such as sulfasalazine that is used in the treatment of Colitis is still in its active form. By using US EPA model, human exposure could also be calculated as well. Ingesting the pharmaceuticals have severe effects on human health, such as ingesting antibiotics through this way can cause antibiotic resistance, thus can lead to a death since surgeries or transplantations can't be done because there is an inhibition of antibiotics caused by the resistance. (Al-Farsi, et al., 2017) If the PPCP are not taken by the plants, they could run off to the underground water or could even degrade. But some reported that, the degraded from of these PPCP could be as toxic or even more toxic than its originals (Sengelov et al, 2003). As a sequel, by being aware of the soil contamination by PPCP and their routes of entry to the soil and to food chain, it could be possible to prevent the incident. For instance, fungi is responsible for the degradation of PPCP in the soil. Such techniques could be used to avoid the toxicity effect of PPCP in soil. (Kummerer, 2010)

7. PPCP Analysis on Influent & Effluent Water In Oman

Analysis was done using high performance liquid chromatography with triple quadruple mass spectrophotometry. The reason for this is that, from literatures it was noted that, pharmaceuticals contained in trace amounts. Thus to be able to detect the trace amounts of pharmaceuticals, this technique was the most applicable.

In Sultan Qaboos University (SQU), there are 4 HPLC/MS/MS are present, distributed around the university in college of medicine, college of agriculture and marine science, college of science and CAARU center.

5 liters of influent and effluent water was obtained from Haya water, to analyze the concentrations of 6 chemicals present in them, that are; The analysis was carried out using the high performance liquid chromatography with triple quadruple mass spectrophotometry, was carried out in the CAARU Center at Sultan Qaboos University. Reverse phase method was used, gas temperature was 300^{o}C, gas flow was 5 l/min.

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7.1. Procedure:

1. SPE cartridge were first activated by passing 3 ml of methanol and 10 ml of dissolved water.

2. 250 ml of sample water (effluent and influent) that was collected from Haya Water Company were passed through activated SPE cartridge.

3. The point calibration was prepared of 10, 50 and 100 ppb. Of the pharmaceuticals that's desired to be tested. (Caffeine, Ibuprofen, paracetamol, diclofenac)

4. They were run in reverse phase HPLC/MS/MS at 300^{o}C, gas flow of 5 l/min. The column used was 5mm spherical, C18 3.9 x 150 mm.

7.2. Results:

The following shows their concentrations within influent and effluent water samples. Results also give an indication of how well the treatment plants work. The concentrations of PPCP are within the safety limit according to the WHO fact sheet.

Table 4- Concentrations of pharmaceuticals in Influent & Effluent

	Concentration in ppb			
Sample ID	Paracetamol	Caffeine	Diclofenac	Ibuprofen
Inlet	0.85	15.04	0	0.12
Outlet	0	0.08	0	0

As it was expected, and noted from the literature reviews, there was presence of paracetamol and ibuprofen in sewage (influent of Haya) water sample of 0.85 and 0.12 ppb respectively. The highest concentration of pharmaceutical that was present in influent water was caffeine in 15.04 ppb amount. Whereas, very shockingly none of the pharmaceuticals were present in the effluent except 0.08 ppb of caffeine.

8. Survey

A survey was carried out on 73 university level students within Oman to check their awareness on PPCP. Following 8 questions were asked.

8.1. Survey Questions & Replies

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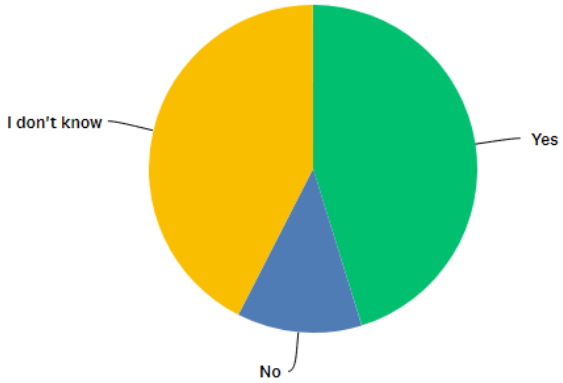
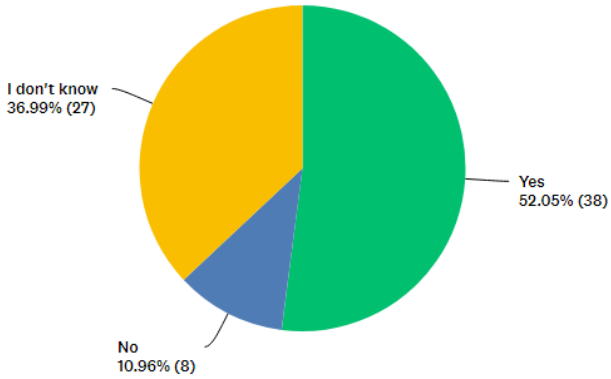
1- Are pharmaceuticals harmful to soil?



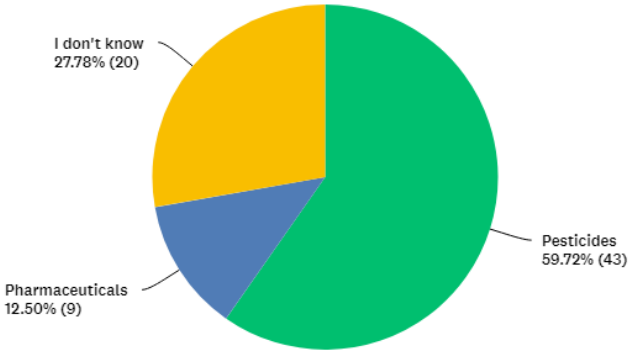
2- Are pharmaceuticals harmful to water?



3- What is the open form of PPCP?

16 participants gave the correct answer of Pharmaceuticals and Personal Care Products answer.

4- Which one harms the environment more a- Pesticides b- pharmaceuticals c- I don't know



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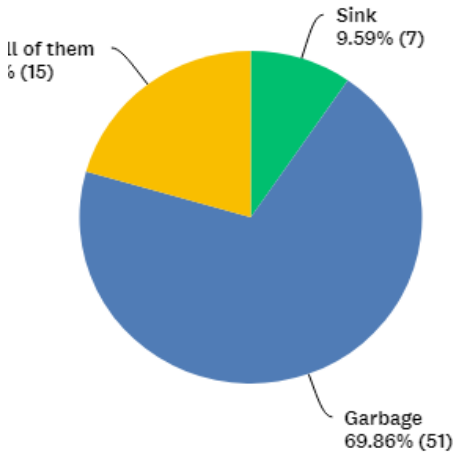
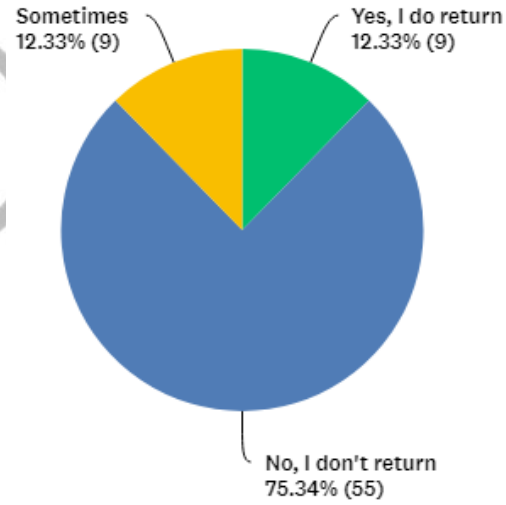
5- I discharge excess/expired pharmaceuticals into a- Sink b- Garbage c- I use them all



6- I return expired/ excess pharmaceuticals back to pharmacy?



7- I have been informed how to dispose the pharmaceuticals before handing them in?

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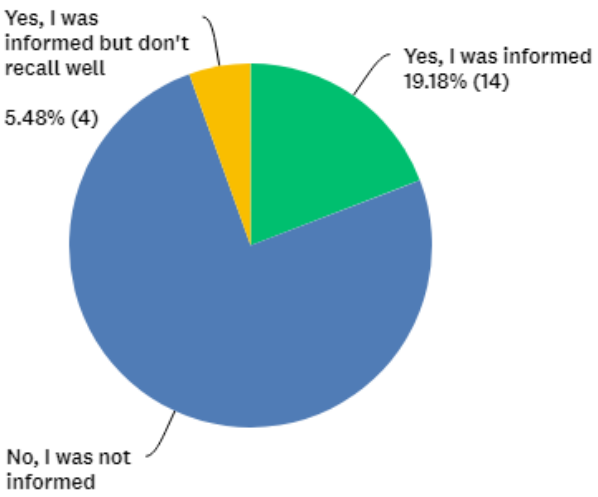
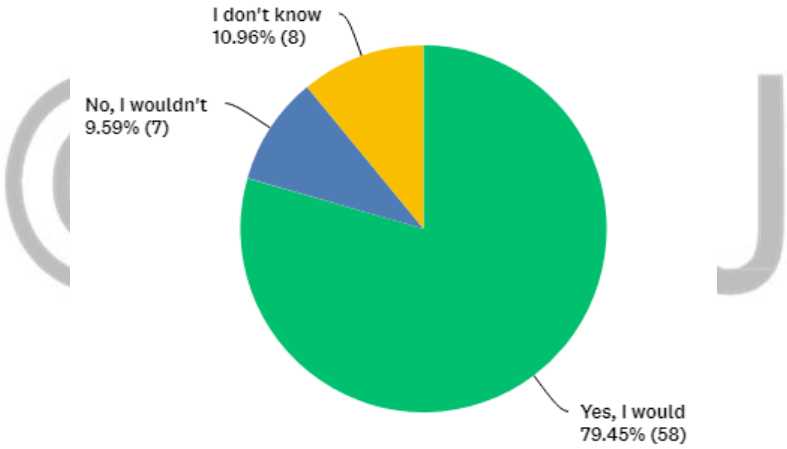


8- If medicine recycle program was launched, would you give your unused/extra medicine back?



8.2. Survey Result Analysis

A survey had been carried out among 73 people, within 7 days. …. Was the respondent rate.

Among the 73 university level students, 45.21% of them gave the correct answer saying, pharmaceuticals are harmful to soil, while the 12.33% gave a wrong answer saying that, pharmaceuticals are not harmful and remaining 42.47% chose the choice if I don't know. While surprisingly, for question 2, 52% knew that pharmaceuticals are harmful to water. However didn't know that pharmaceuticals could be harmful to soil as well in question 1. Out pf 73 university student, 16 of them knew the open form of the abbreviation PPCP, which is an expected amount, because it's more of an environmental terminology. 59.7% of the participants marked that pesticides are more harmful than pharmaceuticals, which is the wrong choice. Only 12% of the participants knew that pharmaceuticals are more dangerous. The reason behind it, is that people

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are not being informed and not aware of pharmaceuticals' harm as much as they are being aware of pesticides. Almost 70% of the participants throw their excess or unused pharmaceuticals to garbage, meaning its going more into the landfilling rather than directly into the sink. Which is a better choice, because as discussed earlier, its more likely for a pharmaceutical to accumulate into environment via water. Only 12% of participants, return their excess/expired/unused pharmaceuticals back into pharmacies. Which is a very little amount. 75% said that, no proper was explained on safely disposing the pharmaceuticals, which is probably a reason for patients throwing their extra medicine to garbage instead of returning them back to pharmacies. Lastly, participants were asked if they would participate in a medicine recycling program, to return their extra medicines back 79.45 % were willing to commit. If there is a will, then there is definitely a hope towards a better change.

9. Recommendations & Policy Changes

Despite these questions were asked on university level students, as it can clearly be seen from the survey results, people are unaware of pharmaceuticals and personal care products and their hazards and danger to the environment. Awareness of public must be increased by writing more about these on newspapers and talking about PPCP and their hazards on environmental platforms on TVs. Mass changes are necessary to create a real impact, and this can only be done by motivating people from the platform they have access to most, like social media and advertisements on TVs as well. On the other hand, Pharmacist must give indications on what to do with extra/unused or expired medicines while handling them to patients. The reason why, students knew more about pesticides than PPCP is because it's in the syllabus and in text books. With new emerging diseases and cures, the syllabus in schools must be updated to nowadays issues.

Besides public, in industrial area more advanced treatment technologies such as ultra and Nano filtration membrane techniques could be used. Continuous quality checkup must be done on and around the landfilling areas. Strict regulations must be followed to persevere a healthy aquatic and soil quality.

Manufacturing PPCP must be shifted to a greener chemistry, more of natural resources must be used instead of chemicals ones. It’s both healthier for our body as well as to our environment.

10. Conclusion

PPCP, their abundance, occurrence and effects are studied throughout the article, both globally and specifically within Oman. It was found that 0.85, 15.04 and 0.12 ppb of paracetamol, caffeine and ibubrofen is present in Oman’s wastewaters respectively. Despite, from the literature studies it was proven that pharmaceuticals don’t get treated and removed by waste water treatment plants, unless advanced treatment methods are used. The reason why effluent water didn’t contain other pharmaceuticals was because, as reported by Ahmed uses the advance treatment methods to clean the influent water. Although the ppcp presence are in trace amounts, human and environment’s continuous exposure to them makes them a serious environmental and health issue. Serious precautions must be

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taken and their entry to environment must be minimized. Otherwise, continuous leakage and accumulation of these toxic substances will destroy aquatic lives, soil, get into the food chains and our bodies eventually. Since their effects are known, researches must find new sources to manufacture medicines and policy makers must be stricter on rules and regulations regarding to PPCP presence in environment.

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