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STUDY OF THE EXISTENCE OF SOME PHARMACEUTICAL RESIDUE AND THE ASSOCIATED HUMAN RISKS

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Abstract

The modern study set out to measure the concentrations of some pharmaceutical residue in the ingesting water of the Beni-Suef Governorate in Northern Upper Egypt, the raw and outlet of the American-2, Raid Pasha, Idrasyah, and Foqai water therapy plants, as properly as to assess the risks related to these pharmaceutical compounds in the water. The water samples that accumulated from the 4 remedy plants uncooked consumption and treated water were both potentially toxicologically hazardous due to at least one medication. Metformin, Paracetamol, Salicylic Acid, Mefenamic Acid, Acetaminophen, and Caffeine all posed serious health dangers to human beings when ingested thru dealt with water, necessitating more care. The seasonal version results on the presences of medicinal compounds are extra extensive than the type of technological know-how used for water purification, as proven in Appendix, according to the ANOVA take a look at (two elements barring replication) of the plant's data. Seasonality can affect toxicological risk, and the toxicity of combined pharmaceutical residues is larger than that of person compounds. The use of more high-quality applied sciences ought to be taken into consideration due to the fact conventional DWTPs can only partly cast off and reduce the chance of pharmaceutical residues.

Keywords: Pharmaceutical residue; Drinking water; Human risks; Egypt

1. Introduction

Concern over drugs' fate and results on the environment is developing alongside the global demand for and manufacturing of medications. Pharmaceutically active resources (PhACs) can now be detected in water matrices at extremely low concentrations (ng/l), and numerous research have shown that PhACs are current in both floor and groundwater all over the world. (Andreozzi, et al., 2002; Daughton et al., 1999; Zwart et al., 2005; DeLorenzo et al., 2008; Maasz et al., 2019).

PhACs are mainly released into the aquatic environment by wastewater treatment plants (WWTP). (Madureira et al., 2011). Untreated sewage disposal, residues and effluents from animal husbandry fields, incorrectly disposed of medications, untreated effluent from the pharmaceutical industry, and hospital effluent are additional sources of contamination. (Marcial et al., 2003). After entering the environment, PhACs may undergo natural attenuation processes such as dilution, sorption, or chemical transformation depending on the physical-chemical properties of the compound, such as water solubility, lipophilicity, and vapor pressure, as well as environmental conditions, such as pH, temperature, and ionic strength (Lei et al., 2014, 2014; Lin, et al.,2018).

After ingestion, PhACs are transformed and expelled both in their natural state and as metabolites. Removal in WWTPs and DWTPs differs considerably because of their different physicochemical properties and degradability. PhACs are found as a result of incomplete removal in drinking water and surface water. (Bejarano et al., 2016; Dammann et al., 2011). According to several recent investigations, PhACs have been discovered in water matrices at concentrations varying from ng/l to g/l. The German Federal Environment Agency released a review in 2011 that included information from environmental monitoring in Germany. (UBA). 156 drugs were discovered in drinking water, groundwater, and surface water, and the analysis confirmed their existence. (Webb et al., 2001). Worldwide, several review articles have emphasized aquatic monitoring of PhACs in China, the European Union, the United States, the United Kingdom, and

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the European Union (Kristensen et al., 2005, Mendoza et al., 2014, Wu et al., 2014), and have demonstrated how frequently these compounds are found. It was shown that natural rivers are in fact contaminated with PhACs using data from 2003 to 2011 gathered by Kummerer (2004) in the United Kingdom, India, Spain, the United States, France, Brazil, Austria, and Sweden. According to Bouissou et al., non-steroidal anti-inflammatory drugs (NSAIDs), b-blockers, antidepressants, and antibiotics are the therapeutic classes that have been the focus of the most study (2014). The harmful effects caused by these compounds have been recorded in the international literature since it was known that these molecules can have negative effects on ecosystems at concentrations as low as nanograms per liter (Camacho et al., 2014). But according to the research, these steps aren't always enough to guarantee PhACs removal. Drinking water treatment plants (DWTP) may apply a barrier to prevent PhACs reintroduction to the human body (Carlsson et al., 2006; Kantiani et al., 2008).

Although scientific trials make sure that human biological results are properly understood (Lahnsteiner et al., 2006), there are uncertainties concerning the environmental threat posed by PhACs due to the fact there is little information available about their destiny and behavior in the environment, such as their uptake, metabolism, and excretion fees (pharmacokinetics), and their target affinity and useful effects (pharmacodynamics)(Lange et al., 2006; Zhang et al., 2012). Moreover, little is known about the long-term effects of indirect exposure from drinking water.

Therefore, the danger of PhACs contamination to the environment and to human health have to be evaluated. Risk assessments for each human health and the surroundings (HRA and ERA) focus on how poisonous resources have interaction with dwelling matters whilst taking into account a variety of physiological features (such as respiration, transport, and signaling) and critical building blocks (such as DNA, proteins, membranes, and cells). The foundation for toxicity data extrapolation is toxicity measures (such as no found impact stages or concentrations), which take into account interindividual variability, interspecies variability, variations in exposure time, variations in endpoints, achievable synergistic effects, systematic errors, assumptions, and random errors (Zhang et al., 2017).

Applications for Environmental Assessment of Human Drugs and Biologics" (Zhang et al., 2017), which are still in impact today. The European Medicines Agency (EMEA), in addition to the FDA, affords pointers for the advent of risk assessments. The manner was constantly developed till the "Guideline on the environmental hazard assessment of pharmaceutical merchandise for human use" (EMEA, 2006) (Doc. Ref. EMEA/CHMP/SWP/4447/00 corr. 2) was published. The manner was once in the beginning based totally on Directive 65/65/EEC and then improved in 93/39/EEC. The US Environmental Protection Agency (USEPA) produced "Guidelines for the Health Risk Assessment of Chemical Mixtures" in 1986, which served as the first set of HRA guidelines. Since then, the organization has made changes and enhancements and posted extra materials. The World Health Organization (WHO) introduced the "WHO Human Health Risk Assessment Toolkit: Chemical Hazards" in 2010, with the aim of supporting users in locating, obtaining, and using the records required to consider chemical hazards, exposures, and the related health risks.

Through the computation of chance quotients, most pharmaceutical concentrations in either drinking water or source water had been compared to DWEL values associated with various age periods. To provide a conservative "worst-case" scenario approach, most determined concentrations had been used. For each age range, the DWEL and RQ values have been estimated. The age vary that was once related with a higher risk quotient for all drugs was once from 0 to three months. Given that there is a considerable distinction between the concentrations found and the estimated DWEL values, which is steady with the findings of the WHO and other human fitness danger assessments, these values imply that the prescription drugs observed in the water samples analyzed do not pose any danger to the consumer's health.

In order to improve the accuracy of hazard assessment, the categorization of human fitness risks

was primarily based on the contrast of threat quotients (RQs) for which a number of lifestyles stages had been taken into consideration. The life levels that had been chosen have been primarily based on these that the U.S. EPA counseled in the record "Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants." (EPA, 2005). By dividing the best possible concentration of every drug discovered in the samples with the aid of its corresponding Drinking Water Equivalent Level, RQ had been calculated for each the capsules quantified in the ingesting water samples and the tablets quantified in the source water samples. In the tournament that there was once an operational difficulty with the WTPs, the stages detected in raw water were used as a worst-case scenario. A chance associated with unintended publicity by using consuming water is indicated by way of an RQ rating higher than 1. According to the Wyoming Water Rules and Regulations"
book (DEQ, 2005), the DWELs have been estimated.

$$RQ = \frac{C_s}{DWEL} \quad (1)$$

$$DWEL = \frac{ADI \times BW \times HQ}{DWI \times AB \times FOE} \quad (2)$$

Where HQ is the Hazard Quotient assumed to be 1, DWI is the Drinking Water Intake (L/day) where age specific values were used in accordance with the U.S. EPA "Exposure Factor Handbook" (EPA, 2011), and AB represents the presumed gastrointestinal absorption rate. Cs is the concentration of the pharmaceutical compound found in the sample. ADI is the Acceptable Daily Intake (mg/kg day). The present study aimed to evaluate the levels of some pharmaceutical residue in drinking water of Beni Suef Governorate, Egypt and the associated human risks.

2- Material and Methods

Sampling: the water samples were collected in the period of study (from Jun. 2021 to Apr. 2022). All water samples were collected by a water-column sample device from the middle of the water level in 2-L amber salinized glass bottles with Teflon-faced caps.

Due to the compatibility of the sorbent types, one liter of each sample was acidified by adding 100% formic acid to a pH range of 3.5–4.0. Before filtering, samples were mixed with internal standards (Citalopram-d6, Carbamazepine-d10, E2-13C3, and N-ethyloxazepam); the final concentration for each standard was 5 ng/l; these were utilized for sample quantification. Samples were vacuum filtered through a GF/F 0.7-m glass microfiber filter (#516-0345, VWR) after being spiked using internal standards.

The Auto Trace 280 automated SPE system was used to perform solid phase extraction (SPE) on the samples. With the help of a stream of inert nitrogen gas, SPE extracts were evaporated (APHA, 2017).

An ACQUITY UPC2 supercritical fluid chromatography system (Waters) and a Xevo TQ-S Triple Quadrupole Mass Spectrometer were used for analytical measurements and detection. TargetLynx XS software analyzed the data after they had been evaluated by MassLynx software (V4.1 SCN950) (APHA, 2017).

Individual substances' potential environmental dangers were assessed using a hazard quotient. The following equation illustrates how HQ values were determined using both measured environmental concentration (MEC) and anticipated no effect concentration (PNEC):

$$HQ = MEC / PNEC \quad (3)$$

Based on the mean effect or lethal concentration (EC50 or LC50) or the non-observed effect concentration (NOEC), respectively, PNEC was calculated for both acute and chronic effects. As recommended in the literature, the toxicity endpoint was divided in both instances by safety factors.

In order to determine the worst-case scenario for HQ calculation, the lowest PNEC values and the maximum concentration of pharmaceutical chemicals in the analyzed waters were taken into consideration. High risk (HQ > 1), medium risk (0.1 HQ 1), low risk (0.01 HQ 0.1), and insignificant risk (HQ 0.01) were the groups into which the risk was divided (Zhang et al., 2017).

2. Results and Discussion

2.1 Pharmaceutical residues of American-2 WTP:

The present study showed that, the levels of some pharmaceutical residue in drinking water that produced from the American-2 WTP, and also evaluate the associated risks of these compounds in drinking water, as shown in Table (2) and Figure (2).

Pharm. Cpds	MDL (µg/l)	LOQ (µg/l)	Precision (≤ 5%)	Accuracy (%)	Bias (± µg/l)
Metformin	0.1	0.1	3.6	93.2	0.02
Paracetamol	0.1	0.1	4.6	94.5	0.01
Salicylic acid	0.1	0.1	4.4	91.8	0.03
Acetaminophen	0.1	0.1	4.8	96.1	0.02
Caffeine	0.1	0.1	3.3	91.1	0.01
Ketoprofen	0.1	0.1	2.8	93.1	0.02
Clotrimazole	0.1	0.1	3.8	94.2	0.02
Mefenamic acid	0.1	0.1	3.1	95.5	0.01
Triclosan	0.1	0.1	4.1	92.4	0.02
Propranolol	0.1	0.1	4.7	91.2	0.03
Warfarin	0.1	0.1	4.2	94.6	0.02

Table (1): The quality control criteria for the test methods

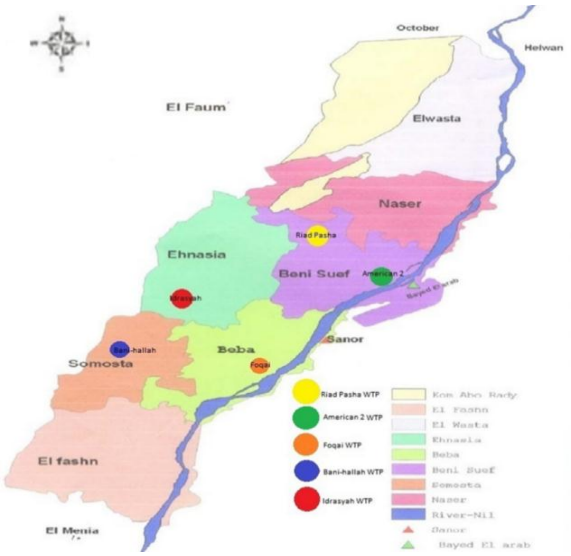


Figure 1: Map of sampling sites in a Beni Suef

The results of raw and outlet of the American water treatment plant (WTP) illustrated in Tables (2 and 3), the levels of pharmaceutical residue in raw and outlet water were as the following; Metformin were 0.134 and 0.092 mg/l, Paracetamol 0.178 and 0.138 mg/l , Salicylic acid 0.033 and 0.021 mg/l, Acetaminophen 0.093 and 0.076 mg/l, Caffeine 0.112 and 0.072 mg/l, Ketoprofen 0.068 and 0.041 mg/l, Clotrimazole 0.029 and 0.017 mg/l, Mefenamic acid 0.043 and 0.024 mg/l, Triclosan 0.071 and 0.045 mg/l, Propranolol 0.039 and 0.027 mg/l , Warfarin 0.088 and 0.056 mg/l, as shown in Tables (2, 3). The reduction percentages of the pharmaceutical compounds as the water treatment in the American2 WTP, was illustrated in Figure (2). The ANOVA test (two factors without replication) of the data of the plant showed that, the seasonal variation effects on the presences of pharmaceutical compounds are the major than the type of technology used for water purification, as indicated in Table (5).

From the findings, a seasonal trend in the awareness of pharmaceutical residue in natural water sources can be seen. Because of the minimal rainfall during this time, which reduces river drift and concentrates these pollutants, the iciness season had the best possible concentration of pharmaceutical residue. Additionally, this season's low temperatures motivate the spread of infectious disorders, leading to extended stages of pharmaceutical residue consumption. Pharmaceutical residue awareness begins to decline with the arrival of spring and reaches its lowest values in the summer, which is marked with the aid of a high rainfall index, growing dilution, and high temperatures that may additionally pace up the biodegradation of prescribed drugs due to multiplied microbial activity (Bejarano et al., 2016).
The toxicological risk potential associated with pharmaceutical residues was somewhat reduced by conventional DWTP (Table 2).

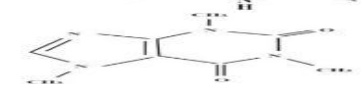
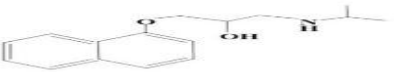
Compound Name	Stricture Formula	Therapeutically Class	Medicine Use
Metformin		Anti-diabetic	Initial oral therapy in type to diabetes mellitus
Paracetamol		Miscellaneous analgesics	Treatment of pain or fever
Salicylic acid		Analgesics –Anti-inflammatory	Stimulating the pain
Acetaminophen		Analgesics	Treatment of headaches, other specific pains and fiberile illness
Caffeine		Psyco-Stimulant	Stimulating the pain
Ketoprofen		Anti-inflammatory	Reduction of pain
Clotrimazole		Anti-mycotic	Treatment of Candida al bicans and other fungal infections
Mefenamic acid		Analgesics –Anti-Inflammatory	Treatment of primary dysmenorrhea
Triclosan		(PPCP) personal product compound Bactericides/disinfectants	soaps, deodorants, shampoos, cosmetics, textiles, plastics, surgical sutures
Propranolol		Beta-blocker	sinus tachycardia, arrhythmias and obstructive cardiomyopathy and, more recently, in the treatment of angina pectoris
Warfarin		Non-steroidal anti-inflammatory	Treatment of chronic-heart failure, Prevent blood clots

Table 2: Selected pharmaceutical compounds

Pharm. Cpds	LC50 (mg/l)	MEC (mg/l)	PNEC	HQ	Risks
Metformin	64	0.134	0.064	2.09	High
Paracetamol	100	0.178	0.1	1.78	High
Salicylic acid	100	0.033	0.1	0.33	Medium
Acetaminophen	60	0.093	0.06	1.55	High
Caffeine	50	0.112	0.05	2.24	High
Ketoprofen	100	0.068	0.1	0.68	Medium
Clotrimazole	100	0.029	0.1	0.29	Medium
Mefenamic acid	80	0.043	0.08	0.54	Medium
Triclosan	80	0.071	0.08	0.89	Medium
Propranolol	80	0.039	0.08	0.49	Medium
Warfarin	100	0.088	0.1	0.88	Medium

Table (3): Pharmaceutical residues and associated human risks of American-2 WTP intake

Pharm. Cpds	LC50 (mg/l)	MEC (mg/l)	PNEC	HQ	Risks
Metformin	64	0.092	0.0644	1.4	High
Paracetamol	100	0.138	0.1	1.38	High
Salicylic acid	100	0.021	0.1	0.21	Medium
Acetaminophen	60	0.076	0.067	1.2	High
Caffeine	50	0.072	0.054	1.4	High
Ketoprofen	100	0.041	0.1	0.41	Medium
Clotrimazole	100	0.017	0.1	0.17	Medium
Mefenamic acid	80	0.024	0.08	0.30	Medium
Triclosan	80	0.045	0.08	0.56	Medium
Propranolol	80	0.027	0.08	0.34	Medium
Warfarin	100	0.056	0.1	0.56	Medium

Table (4): Pharmaceutical residues and associated human risks of American-2 WTP outlet

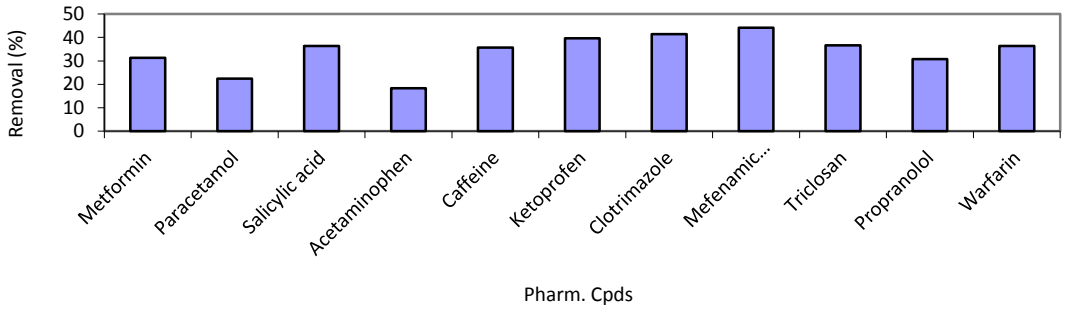


Figure (2): Removal percentages of pharmaceutical risks in American-2 WTP

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Months	362201.6	10	36220.16	455.0592	5.8E-141	1.873923
Phs Cpds	21023.41	22	955.6094	12.00599	6.13E-27	1.590867
Error	17510.77	220	79.59439			
Total	400735.8	252				

Table (5): ANOVA test for the data of American 2 WTP

2.2 Pharmaceutical residues of Riad pasha WTP

The present study showed that, the levels of some pharmaceutical residue in drinking water that produced from the Raid pasha WTP, and also evaluate the associated risks of these compounds in drinking water, as shown in Table (6) and Figure (3). The results of raw and outlet of the Raid pasha WTP illustrated in Tables (6 and 7), the levels of pharmaceutical residue in raw and outlet water were as the following; Metformin were 0.282 and 0.214 mg/l, Paracetamol 0.312 and 0.228 mg/l , Salicylic acid 0.072 and 0.044 mg/l, Acetaminophen 0.162 and 0.122 mg/l, Caffeine 0.198 and 0.108 mg/l, Ketoprofen 0.112 and 0.069 mg/l, Clotrimazole 0.055 and 0.048 mg/l, Mefenamic acid 0.078 and 0.054 mg/l, Triclosan 0.132 and 0.083 mg/l, Propranolol 0.066 and 0.046 mg/l , Warfarin 0.143 and 0.108 mg/l, as shown in Tables (5 and 6). The reduction percentages of the pharmaceutical compounds as the water treatment in the Raid pasha WTP, was illustrated in Figure (3). The ANOVA test (two factors without replication) of the data of the plant showed that, the seasonal variation effects on the presences of pharmaceutical compounds are the major than the type of technology used for water purification, as indicated in in Table (8).

Social and monetary motives can additionally be linked to the greater concentration of pharmaceutical residues, in addition to climate-related issues. Higher tiers of the human development index (HDI) and gross domestic product per capita (GDP per capita) are linked to higher concentrations of pharmaceutical residue. These variables replicate the population's doable for consumption, therefore it stands to purpose that the more money a household makes, the better their access to fitness care will be, without delay affecting how a whole lot pharmaceutical residue they consume. On the different hand, no correlation between the concentration of pharmaceutical residue and the coverage of the WWT used to be found. This could be as a result of various organic and physical strategies that degrade contaminants in a water supply. For instance, these systems' low go with the flow pace inhibits aeration, which impairs cardio procedures and can also sluggish the pace at which chemicals degrade. Due to the lowered floor location to quantity ratio, which reduces the amount of sunlight available, photodegradation techniques additionally occur to a lesser level. Additionally, given that the hydraulic retention duration in the water supply is longer, the accumulation of pharmaceutical residue may also be brought on with the aid of their adsorption on colloidal or suspended particulates (Maasz, et al, 2019).

Other factors, such as water body preservation and wastewater treatment system, may be major players in addition to seasonality and socioeconomic conditions (Lin, et al, 2018).

Pharm. Cpds	LC50 (mg/l)	MEC mg/l)	PNEC	HQ	RQ
Metformin	64	0.282	0.064	4.41	High
Paracetamol	100	0.312	0.1	3.12	High
Salicylic acid	100	0.072	0.1	0.72	Medium
Acetaminophen	60	0.162	0.06	2.70	High
Caffeine	50	0.198	0.05	3.96	High
Ketoprofen	100	0.112	0.1	1.12	High
Clotrimazole	100	0.055	0.1	0.55	Medium
Mefenamic acid	80	0.078	0.08	0.98	Medium
Triclosan	80	0.132	0.08	1.65	High
Propranolol	80	0.066	0.08	0.83	Medium
Warfarin	100	0.143	0.1	1.43	High

Table (6): Pharmaceutical residues and associated human risks of Riad pasha WTP intake

Pharm. Cpds	LC50 (mg/l)	MEC mg/l)	PNEC	HQ	Risks
Metformin	64	0.214	0.064	3.34	High
Paracetamol	100	0.228	0.1	2.28	High
Salicylic acid	100	0.044	0.1	0.44	Medium
Acetaminophen	60	0.122	0.06	2.03	High
Caffeine	50	0.108	0.05	2.16	High

Ketoprofen	100	0.069	0.1	0.69	Medium
Clotrimazole	100	0.048	0.1	0.48	Medium
Mefenamic acid	80	0.054	0.08	0.68	Medium
Triclosan	80	0.083	0.08	1.04	High
Propranolol	80	0.046	0.08	0.58	Medium
Warfarin	100	0.108	0.1	1.08	High

Table (7): Pharmaceutical residues and associated human risks of Riad pasha WTP outlet

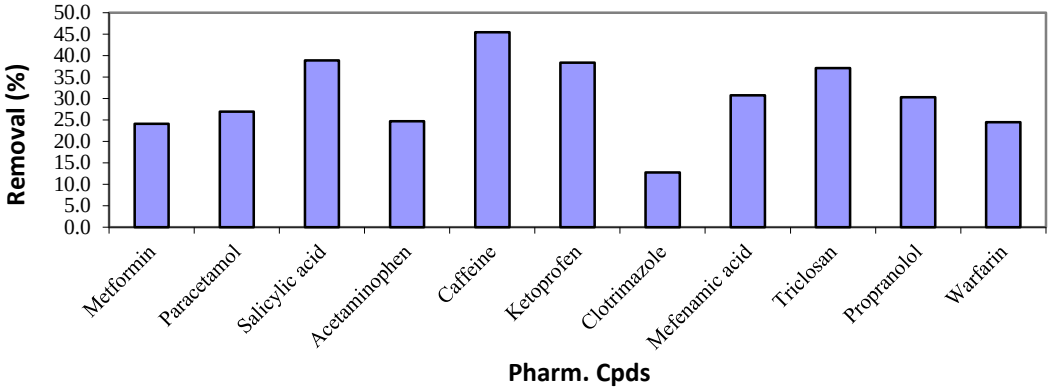


Figure (3): Removal percentages of pharmaceutical risks in Riad pasha WTP

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Months	684065.9	10	68406.59	1037.603	4.9E-179	1.873923
Phs Cpds	36096.9	22	1640.768	24.88745	8.32E-48	1.590867
Error	14504.06	220	65.92752			
Total	734666.9	252				

Table (8): ANOVA test for the data of Riad Pasha WTP

2.3. Pharmaceutical residues of Idrasyah WTP

Consumption, therefore it stands to purpose that the The present study showed that, the levels of some pharmaceutical residue in drinking water that produced from the Idrasyah WTP, and also evaluate the associated risks of these compounds in drinking water, as shown in Table (8) and Figure (4). The results of raw and outlet of the Idrasyah WTP illustrated in Tables (9 and 10), the levels of pharmaceutical residue in raw and outlet water were as the following; Metformin were 0.128 and 0.098 mg/l, Paracetamol 0.161 and 0.141 mg/l , Salicylic acid 0.055 and 0.045 mg/l, Acetaminophen 0.109 and 0.092 mg/l, Caffeine 0.072 and 0.061 mg/l, Ketoprofen 0.066 and 0.052 mg/l, Clotrimazole 0.033 and 0.027 mg/l, Mefenamic acid 0.036 and 0.028 mg/l, Triclosan 0.061 and 0.043 mg/l, Propranolol 0.034 and 0.026 mg/l , Warfarin 0.066 and 0.047 mg/l, as shown in Tables (9 and 10). The reduction percentages of the pharmaceutical compounds as the water treatment in the Idrasyah WTP, was illustrated in Figure (4). The ANOVA test (two factors without replication) of the data of the plant showed that, the seasonal variation effects on

the presences of pharmaceutical compounds are the major than the type of technology used for water purification, as indicated in Table (11). Lin et al. (2018) claim that due to the inherent homes of the chemicals, the clarification manner (which includes coagulation, flocculation, sedimentation, and filtration) is usually no longer a key pathway by which pharmaceutical residue in filtered-water samples are degraded or removed. The lower elimination efficiencies of fluconazole (log Kow=0.40) and prednisone (log Kow=1.46) can be defined by the low awareness of pharmaceutical residue in superficial water and the hydropholic behavior of the pharmaceutical residue with low log Kow (3.0), as these compounds are not anticipated to be adsorbed to the particles however to dissociate in the aqueous phase and stay away from the adsorption technique (Maasz, et al., 2019). The most typical pharmaceutical residues found in handled water had been these two.

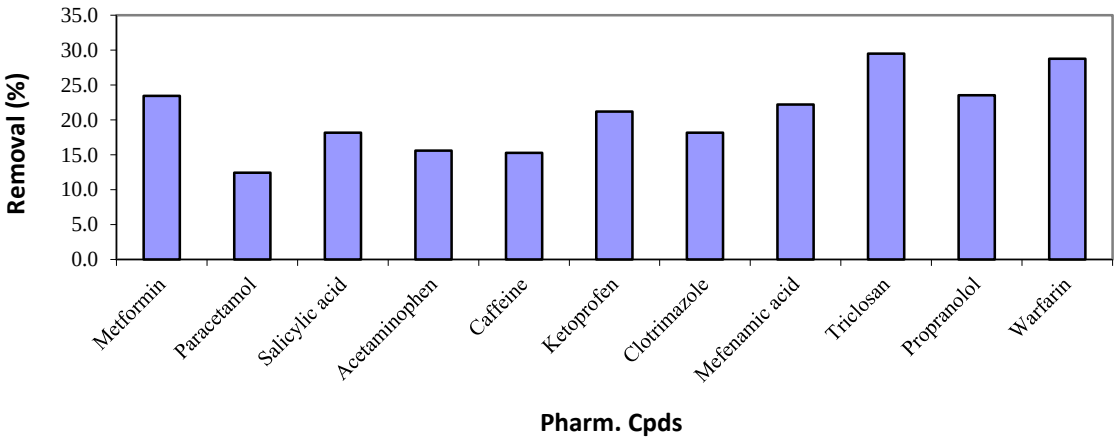
Pharm. Cpds	LC50 (mg/l)	MEC mg/l)	PNEC	HQ	Risks
Metformin	64	0.128	0.064	2.00	High
Paracetamol	100	0.161	0.1	1.61	High
Salicylic acid	100	0.055	0.1	0.55	Medium
Acetaminophen	60	0.109	0.06	1.82	High
Caffeine	50	0.072	0.05	1.44	High
Ketoprofen	100	0.066	0.1	0.66	Medium
Clotrimazole	100	0.033	0.1	0.33	Medium
Mefenamic acid	80	0.036	0.08	0.45	Medium
Triclosan	80	0.061	0.08	0.76	Medium
Propranolol	80	0.034	0.08	0.43	Medium
Warfarin	100	0.066	0.1	0.66	Medium

Table (9): Pharmaceutical residues and associated human risks of Idrasyah WTP intake

Pharm. Cpds	LC50 (mg/l)	MEC mg/l)	PNEC	HQ	Risks
Metformin	64	0.098	0.064	1.53	High
Paracetamol	100	0.141	0.1	1.41	High
Salicylic acid	100	0.045	0.1	0.45	Medium
Acetaminophen	60	0.092	0.06	1.53	High
Caffeine	50	0.061	0.05	1.22	High
Ketoprofen	100	0.052	0.1	0.52	Medium
Clotrimazole	100	0.027	0.1	0.27	Medium
Mefenamic acid	80	0.028	0.08	0.35	Medium
Triclosan	80	0.043	0.08	0.54	Medium
Propranolol	80	0.026	0.08	0.33	Medium
Warfarin	100	0.047	0.1	0.47	Medium

Table (10): Pharmaceutical residues and associated human risks of Idrasyah WTP outlet

Figure (4): Removal percentages of pharmaceutical risks in Idrasyah WTP



Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Months	222978.6	10	22297.86	1152.196	6.1E-184	1.873923
Phs Cpds	11888.62	22	540.392	27.92363	1.17E-51	1.590867
Error	4257.549	220	19.3525			
Total	239124.8	252				

Table (11): ANOVA test for the data of Idrasyah WTP

2.4. Pharmaceutical residues of Foqai WTP

The present study showed that, the levels of some pharmaceutical residue in drinking water that produced from the Foqai WTP, and also evaluate the associated risks of these compounds in drinking water, as shown in Table (12) and Figure (5). The results of raw and outlet of the Foqai WTP illustrated in Tables (12 and 13), the levels of pharmaceutical residue in raw and outlet water were as the following; Metformin were 0.174 and 0.141 mg/l, Paracetamol 0.222 and 0.165 mg/l , Salicylic acid 0.094 and 0.077 mg/l, Acetaminophen 0.1 and 0.082 mg/l, Caffeine 0.137 and 0.112 mg/l, Ketoprofen 0.087 and 0.064 mg/l, Clotrimazole 0.097 and 0.072 mg/l, Mefenamic acid 0.063 and 0.044 mg/l, Triclosan 0.115 and 0.086 mg/l, Propranolol 0.078 and 0.059 mg/l , Warfarin 0.083 and 0.063 mg/l, as shown in Tables (12 and 13). The reduction percentages of the pharmaceutical compounds as the water treatment in the Foqai WTP, was illustrated in Figure (5).

The ANOVA test (two factors without replication) of the data of the plant showed that, the seasonal variation effects on the presences of pharmaceutical

compounds are the major than the type of technology used for water purification, as indicated in Table (14).

Due to chlorine's high reactivity with most important and secondary amines, it has been observed that some pharmaceutical residues can be eliminated pretty successfully the use of chlorination. Wu et al. (2014) declare that compounds without the imidazole team have higher chlorination efficiencies due to the fact the absence of this team encourages the deactivation of the fragrant ring and amplifies the chlorine reaction. The

chlorine attack on this compound is averted by the presence of a bromide in one of the fragrant rings in location of chlorine and via replacing a benzene ring with a pyridine ring. This may want to account for the increased removal of betamethasone, loratadine, and enrofloxacin.

Pharm. Cpds	LC50 (mg/l)	MEC mg/l)	PNEC	HQ	Risks
Metformin	64	0.174	0.064	2.72	High
Paracetamol	100	0.222	0.1	2.22	High
Salicylic acid	100	0.094	0.1	0.94	Medium
Acetaminophen	60	0.1	0.06	1.67	High
Caffeine	50	0.137	0.05	2.74	High
Ketoprofen	100	0.087	0.1	0.87	Medium
Clotrimazole	100	0.097	0.1	0.97	Medium
Mefenamic acid	80	0.063	0.08	0.79	Medium
Triclosan	80	0.115	0.08	1.44	High
Propranolol	80	0.078	0.08	0.98	Medium
Warfarin	100	0.083	0.1	0.83	Medium

Table (12): Pharmaceutical residues and associated human risks of Foqai WTP intake

Pharm. Cpds	LC50 (mg/l)	MEC mg/l)	PNEC	HQ	Risks
Metformin	64	0.141	0.064	2.20	High
Paracetamol	100	0.165	0.1	1.65	High
Salicylic acid	100	0.077	0.1	0.77	Medium
Acetaminophen	60	0.082	0.06	1.37	High
Caffeine	50	0.112	0.05	2.24	High
Ketoprofen	100	0.064	0.1	0.64	Medium
Clotrimazole	100	0.072	0.1	0.72	Medium
Mefenamic acid	80	0.044	0.08	0.55	Medium
Triclosan	80	0.086	0.08	1.08	High
Propranolol	80	0.059	0.08	0.74	Medium
Warfarin	100	0.063	0.1	0.63	Medium

Table (13): Pharmaceutical residues and associated human risks of Foqai WTP outlet

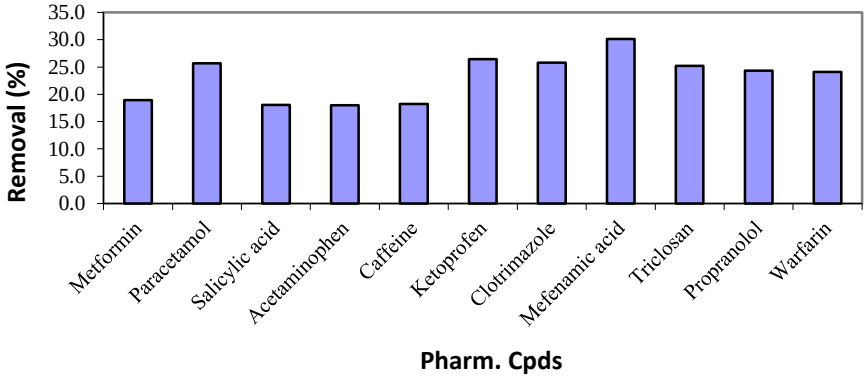


Figure (5): Removal percentages of pharmaceutical risks in Foqai WTP

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Months	702826.2	10	70282.62	382.0134	4.9E-133	1.873923
Phs Cpds	57600.26	22	2618.194	14.2309	3.17E-31	1.590867
Error	40475.48	220	183.9794			
Total	800901.9	252				

Table (14): ANOVA test for the data of Foqai WTP

Conclusion

As hint quantities of drugs had been determined in the floor and consuming water of all evaluated water sources, pharmaceutical residue air pollution is a reality in Egypt's natural waters. The presence and attention of pharmaceutical residues are influenced by using seasonality and neighborhood socioeconomic factors.

Since only one of the studied pharmaceutical residues was once non-toxic to any trophic degree and roughly 60% have been extraordinarily poisonous to at least one level, the toxicity possible verifies the worry over these compounds.

At least one drug uncovered the raw and processed water from the 4 assessed water sources to some degree of toxicological environmental concern. Metformin, Paracetamol, Salicylic Acid, Mefenamic Acid, Acetaminophen, and Caffeine all precipitated serious fitness risks to people when ingested thru treated water, necessitating greater care. The ANOVA test (two elements besides replication) of the plant's data revealed that the kind of technology employed for water purification is less necessary than the seasonal variable impacts on the presences of medicinal chemicals.

Seasonality can have an effect on toxicological risk, and blended pharmaceutical residues have a higher toxicity than single chemicals. The use of more wonderful technologies should be taken into consideration because general DWTPs can solely partly do away with and limit the hazard of pharmaceutical residues.

As a result, the findings of the present study are massive due to the fact they offer comparative perception into the attention of pharmaceutical residues and risk assessment in water provide systems close to the Beni-suef Governorate. In addition, given the plausible for accelerated pharmaceutical consumption in the future, it is critical to emphasize the value of ongoing pharmaceutical residue monitoring in order to spot any changes in awareness that should pose even increased risks to the aquatic environment and public health.

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