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Adsorption of Some Pharmaceutical Drugs (Metformin, Aspirin and Ponstan) and Their Assessment from Aqueous Solution

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Annotation: Metformin, aspirin and ponstan are pharmaceutical drugs used in human and veterinary medicine that is readily transported into the environment via domestic wastewaters and through direct run off. The event of over dose will cause poisoning and kidney pains and muscle ache. Adsorption of Metformin, aspirin and ponstan from aqueous solutions has been studied in this work two adsorption isotherms equations were employed including Freundlich and Langmuir equations. The adsorption was assessed using different isotherms and kinetic models. Then, researchers explained some applications of adsorption from aqueous solutions.

1- Pollution

Pollution now a day is one of the most common environmental problems which started to appear in 20th century, due to industrial development which associated with industrial revolution, all that leads to the appearance of new classes of chemical substances that were unknown previously [1]. These pharmaceuticals enter the worlds water systems through various sources such as hospital effluents human sewage, and discharge from industrial pharmaceutical plants [2]. Many researchers have reported that the pharmaceuticals are generally not eliminated during the wastewater treatment process [3,4] .In general many procedure were used for processing and removal organic pollutants and most commonly is adsorption. Adsorption had been found to be superior to other techniques for water treatment in term of initial cost, simplicity of design and subsequently the adsorbent can be regenerated [5-6].Environment pollution is a burning topic of the day. Air, water and soil are being polluted alike. Soil being a "universal sink" bears the greatest burden of environmental pollution [7]. It is getting polluted in a number of ways. There is urgency in controlling the soil pollution in order to preserve the soil fertility and increase the productivity. Pollution may be defined as an undesirable change in the physical, chemical and biological characteristics of air, water and soil which affect human life, lives of other useful living plants and animals, industrial progress, living conditions and cultural assets [8,9]. A pollutant is something which adversely interfere with health, comfort, property or environment of the people. Generally, most pollutants are introduced in the environment by sewage, waste, accidental discharge or else they are by-products or residues from the production of something useful. Due to this our precious natural resources like air, water and soil are getting polluted [10]. Metformin (C4H11N5) (MF) belongs to the biguanide family, which can play an effective role in the first-line pharmacological therapy of type 2 diabetes mellitus (T2DM) [11]. Earlier studies have shown that metformin has immunomodulatory activity by influencing anti-inflammatory action on collagen-induced arthritis through the inhibition of (Th17) cells differentiation and the up-regulation of Treg cell differentiation along with the suppression of osteoclast differentiation [12]. On the other hand, nanoscience has revealed a unique and effective treatment behavior in medicine, specifically for the treatment of cancer cells and especially with the application of the promising nanomaterials such as boron nitride nanotubes in bone and soft tissue engineering [13]. Aspirin (acetylsalicylic acid, ASA), which is a common over-the-counter drug to reduce fever and to relieve pain. The available studies related to removal of aspirin from wastewater focused on decomposition of the compound through photo degradation, advanced oxidation process and microalga–bacterial system.

Adsorption of aspirin from wastewater is considered another potential strategy, due to its economic viability in process design and operation [14]A poorly water-soluble drug, (ponstan) mefenamic acid (MA), in powder or granule forms was formulated in capsule dosage form.. The adsorption reactions temperature plays a crucial role. According to the adsorption theory, adsorption decreases with increase in temperature and molecules adsorbed earlier on a surface tend to desorb from the surface at elevated temperatures[15].

1-2 Soil pollution

Soil pollution is defined as contamination of soil at higher than normal concentrations by waste materials of human origin that have adverse effects on human and ecosystem health [16]. Soil pollutants include heavy metals and toxic organic chemicals such as pesticides, biological pathogens, and plastic waste[17]. Air pollution is the most visible and best-studied form of pollution, and images of smoke puffing out of train engines and fumes coming out of exhaust pipes are common and easily recognizable[18]. In contrast, soil pollution is not so easily observable, and

the adverse effects of soil pollution on human health are much less well characterized and are not adequately quantified [19].

1-3 Water Pollution

Water pollution refers to release of unwanted substances into subsurface groundwater or into water bodies like lakes, streams, rivers, estuaries, and oceans to a level which negatively impacts the beneficial use of the water or natural functioning of ecosystems .When harmful chemicals or microorganisms contaminate a stream, river, lake, ocean, aquifer, or other body of water, the water's quality deteriorates and it becomes toxic for both humans and the environment[20].

2- Adsorption

Adsorption is a surface process that leads to transfer of a molecule from a fluid bulk to solid surface. This can occur because of physical forces or by chemical bonds [21]. Usually it is reversible the reverse process is called desorption) [22]; then it is responsible not only for a subtraction of substances but also for release. In most of the cases, this process is described at the equilibrium by means of some equations that quantify the amount of substance attached on the surface given the concentration in the fluid [23]. These equations are called isotherms (the most famous are the Langmuir and the Freundlich equations) because of the dependence of their parameters on the temperature, which is one of the most important environmental factors affecting adsorption[24]. Adsorption has a fundamental role in ecology: it regulates the exchanges between geosphere and hydrosphere and atmosphere, accounts for the transport of substances in the ecosystems, and triggers other important processes like ionic exchange and enzymatic processes [25], figure (1).

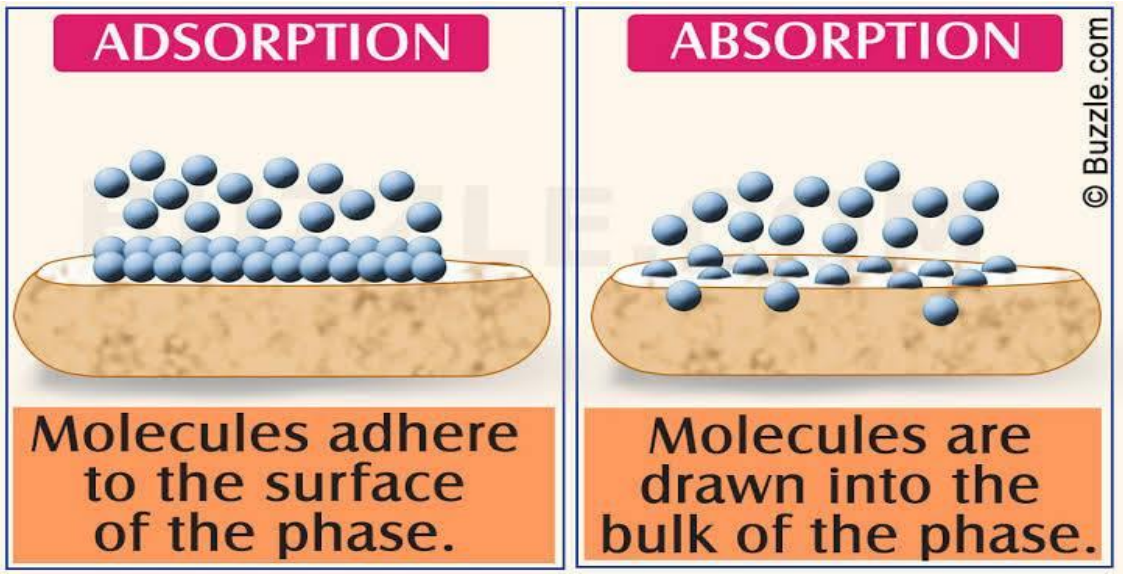


Figure (1): Adsorption v/s absorption.

2-1 Types of Adsorptions

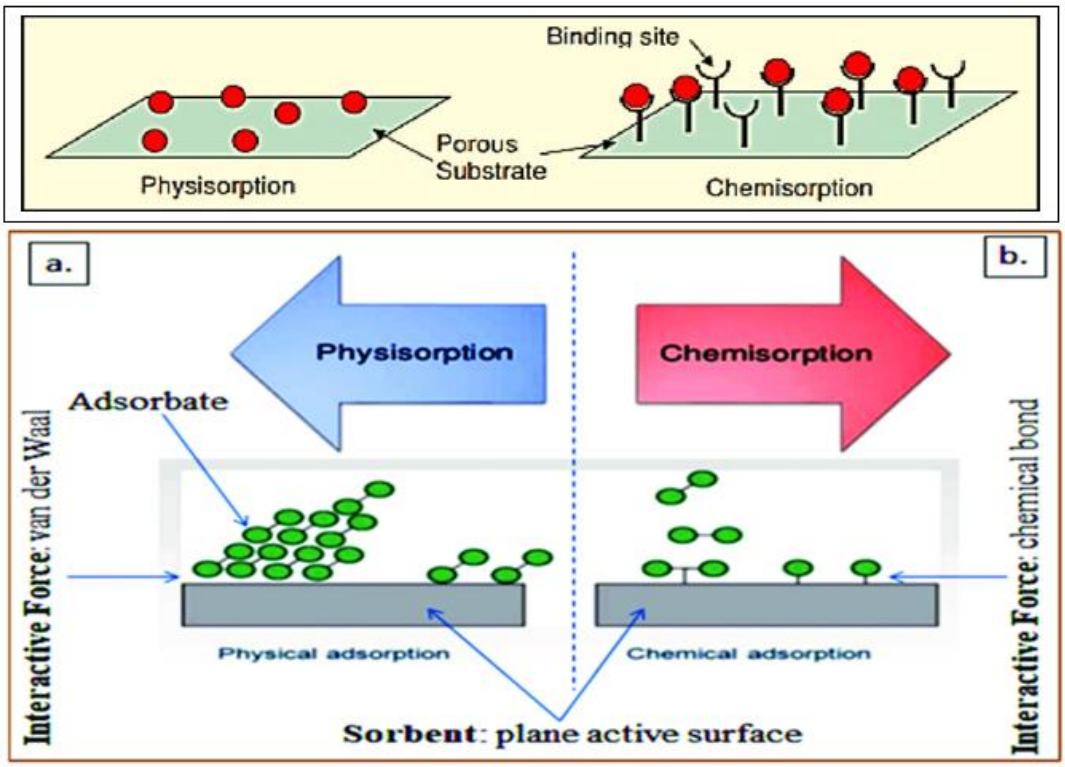
There are two types of Adsorptions:

- **Physical Adsorption**: also called physisorption, the bonding between substrate and adsorbent is a weak Van der Waals forces, no changes of chemical structure for both substrate and sorbent. [26]
- **Chemical Adsorption**: also called chemisorption, the chemical bonding formation between substrate and adsorbent, by rearrangement of electron density between the adsorbent and substrate, the nature of this bond is ionic bond or covalent bond[27], table (1).Table 1 Differences between physical and chemical adsorption.[28]

Table.1 Physical Adsorption v/s Chemical Adsorption

Parameter	Physical Adsorption	Chemical Adsorption
Specificity	Non-specific.	Highly-specific
Nature of adsorption	Depend on nature of adsorbent.	Depend on nature of adsorbent.
Reversibility	Reversible process.	ainly irreversible
Enthalpy	Low (20-40 kJ/mol).	Higher than physical adsorption (40-300 kJ/mol).
Activation energy	Does not require high activation energy.	Require high activation energy.
Layer of adsorption of interfacial region (saturation)	Multi layers.	Mono layer.
Bonding	Week Van der Waals, London forces, and dipole-dipole attraction This attraction has longer range than chemical type, and there is no chemical composition change for substrate.	Strong ionic bond, or covalent bond formed between substrate and adsorbent, there is a chemical composition change. This attraction has shorter range than the physical type.

Adsorption is the mechanism in which a molecule or ion present in a gaseous or liquid bulk phase remains on a solid surface. Here molecule or ion is an adsorbate and solid used for adsorption is known as adsorbents [29]. Quite occasionally liquid used as adsorbents. Adsorption is a surface phenomenon, in which only the adsorbent surface is concerned, and adsorbate should not penetrate inside the structure of adsorbent.



(b) chemisorption [28]

2-3 Factor Influencing on Adsorption Process

(2-3-1) PH Effect

The pH of the solution is one of the most important factors affecting the adsorption and ionic

exchange processes in clay minerals[30] .In the case of surfaces containing polarized or charged locations, the amount of adsorption increases if the surface acquires a charge that exceeds the charge of the minutes absorbed by the effect of acidity. Conversely, the amount of adsorption decreases if the surface and the evaporated minutes acquire a similar charge [31]

(2-3-2) Temperature Effect

As mentioned previously, adsorption is a heat-generating process while absorption is a heat-absorbing process (Andothermic). Absorption is through adsorption, which is often accompanied by energy emission. As is evident, the increase in temperature caused a decrease in adsorption due to increased desorption. While the adsorption process, which is accompanied by the process of absorption or spread inside the pores, is absorbent to the heat and thus the kinetic energy of the molecules absorbed increases the ability to enter the pores of the steel phase and increase the speed of spread in it, so increase the adsorption process by increasing the temperature [32-33]

(2-3-3) Nature of adsorbate

The size of the ion plays an important role in the adsorption process, affecting the amount of adsorption of a certain ion on the surface of the atom with the presence of more than one ion of different size in the solution [34]. Altine et al. has shown that under certain conditions lead ion is twice as dense as the ion of cadmium because of the large lead ion volume. The solubility of the adsorbent in the solvent also has an effect on the adsorption process where the amount of the adsorbent is reduced by increasing its solubility in the solvent. The soluble solubility is increased and the adsorption of the solvent. [35]

(2-3-4) Surface Area Effect

Adsorption is significantly affected by the rate of granularity of the material because adsorption occurs mainly on the outside of the granules and slightly inside the granules because only a few of the internal effective sites allow the element ion to propagate within. Therefore, the decrease in grain size increases the surface area of adsorption, which increases the availability of suitable sites for adsorption.[36-37].

3- Kinetic adsorption

Previous studies describe the kinetic adsorption process in two steps [38]. The first step assumes the transfer of the adsorbate from the bulk solution to the surface of the adsorbent. The second step diffuses of the adsorbate and arranges it inside the sorbent pores. The rate-limiting step of adsorption process elucidates the adsorption mechanism [39].

(3-1) Pseudo-first -order reaction kinetic

The adsorption rate constant assume to be first order reaction kinetic([40]

$$\frac{dq_t}{dt} = k_1(q_e - q_t) \quad \text{.....(1).}$$

Where k_1 is the adsorption rate constant for the first order adsorption, qt is the amount of substrate adsorbed at time t (mg/g) and q_e is the amount of substrate adsorbed at saturation (mg/g).

The integration of Eq. (1) gives the following expression:

$$\ln (q_e - q_t) = -k_1 * t + C_1 \quad \text{..... (2).}$$

Where C_1 is the integration constant for the first order reaction kinetic, Integrating Equation (2) for the boundary conditions t = 0 to t = t and $q_t = 0$ to $q_t = q_e$ where qt reaches plateau, gives the following expression:

$$\ln (q_e - q_t) = \ln q_e - k_1 t \quad \text{.....(3)}$$

The value of k_1 and ln q_e can be obtained from the slope and intercept respectively of the linear plot of ln ($q_e - q_t$) versus t. Comparing qe values obtained from the intercepts of the plots with those obtained experimentally, prove the adsorption process is first-order kinetic reaction.

(3-2) Pseudo-second-order reaction kinetic

If adsorption process obeys Pseudo-second-order reaction kinetic, it is manipulated by the following mathematical equations [3][41-42]:

$$\frac{dq_t}{dt} = k_2 (q_e - q_t)^2 \quad \ldots\ldots (4)$$

Where k_2 is the adsorption rate constant for the second order adsorption, qt is the amount of substrate adsorbed (mg/g) at time t and q_e is the amount of substrate adsorbed at saturation (mg/g).

If eq (4) is integrated, the following expression is obtained:

$$(1/q_e - qt) = k_2 * t + C_2 \quad \ldots\ldots (5).$$

Where k2 is the second order reaction constant (g mg^{-1} min^{-1}), qe and qt are the amount of metal ions adsorbed per unit weight at equilibrium and time t, respectively. Integrating equation (5) for the boundary conditions t = 0 to t = t and qt = 0 to qt = qe gives eq (6):

$$\frac{t}{q_t} = \frac{1}{k_2 q_e^2} + \frac{t}{q_e} \quad \ldots\ldots (6).$$

The values of q_e and k_2 are calculated by plotting of t / q_t vs. t. gives a straight line, experimental q_e values comparing by the calculated value.

4- **Adsorption Isotherms**

A relationship between the amount of adsorbate adsorbed on a given surface at constant temperature and the equilibrium concentration of the substrate in contact with the adsorbent is known as adsorption isotherm. Freundlich adsorption Isotherm It is an empirical relation between the amount of an adsorbate adsorbed per unit weight (qe , mg/g) of adsorbent and the adsorbate equilibrium concentration[43] .

4-1 Freundlich Adsorption Isotherm

6. It is an empirical relation between the amount of an adsorbate adsorbed per unit weight (qe,mg g-1) of adsorbent and the adsorbate equilibrium concentration (Ce,moles.l-1) in the fluid as follows :

qe = K Ce$^{(1\backslash n)}$

Where, K and n are Freundlich coefficients

qe = amount of adsorbate adsorbed on amount of adsorbent

Ce = equilibrium concentration of adsorbate

log(qe) = logK + 1\n logCe

The coefficients K and n can be determined from the intercept and slope of a plot of log(qe) versus logCe , The value of $1<n<10$ suggest the effectiveness of the adsorbent [44-45].

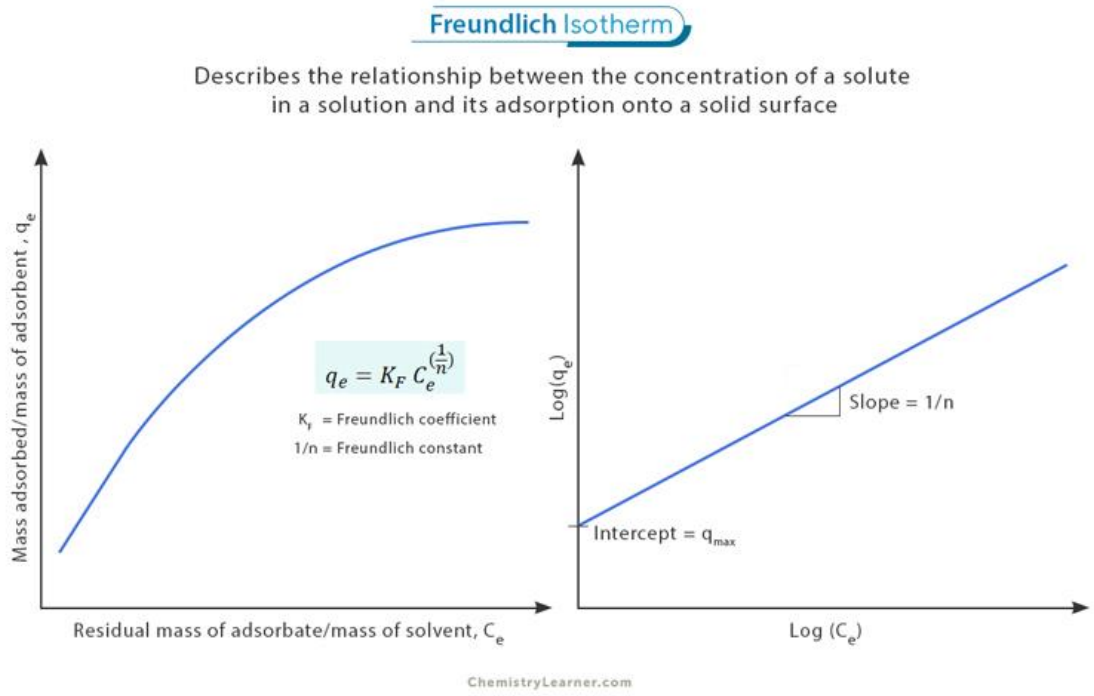


Figure (3): Freundlich equation for the adsorption

4-2 Langmuir Adsorption Isotherm

In the Langmuir model the adsorbent surface is considered to possess a number of active interaction sites for adsorption. Langmuir derived a relation between adsorbed material and its equilibrium concentration

qe = k_L Ce / 1+ k_L Ce

Where qe (mg\g) is the amount adsorbed per unit mass of adsorbent corresponding to complete coverage of sites, Ce (mg\l) is the equilibrium concentration of M.B in solution, KL(L\mg) is the adsorption energy[46-47].

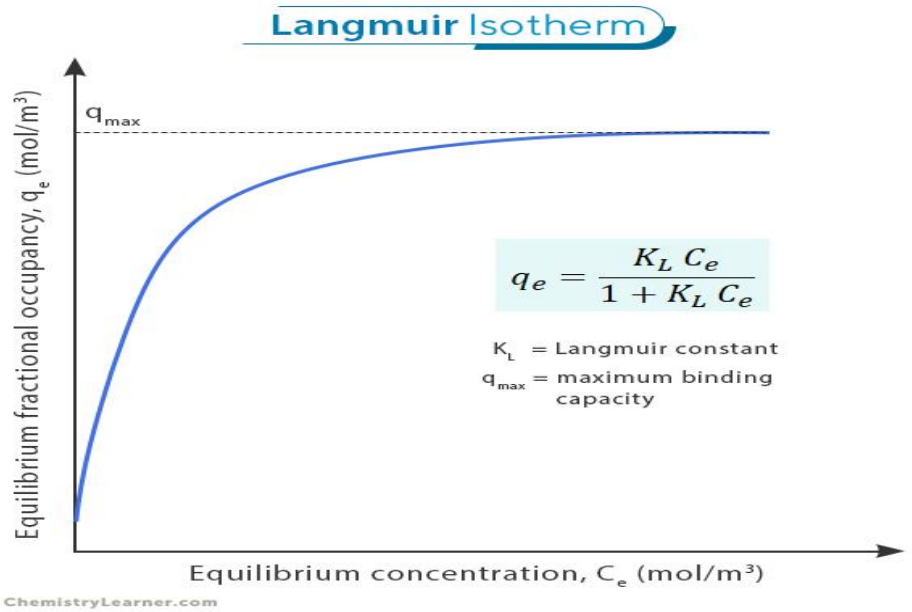


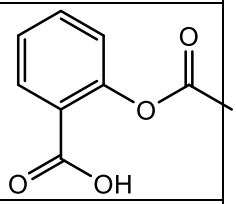
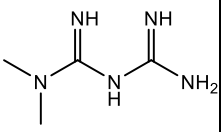
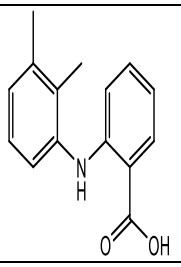
Figure. 4 Langmuir equation for the adsorption

5- Medicines used to treat soil pollution

Pharmaceuticals are biologically active substances used in both human and veterinary medicine.

Primarily, they are applied for therapeutic and preventive purposes, but not solely, since they are widely used in animal husbandry and food production, and as the so-called growth stimulants. In the past, the antibiotic growth stimulants, now banned from using, and other veterinary medicines, were commonly applied for breeding purposes. This was because the priority was to ensure the increased gain of live weight, while totally neglecting the issues of food quality as well as safety of raw materials and food items of animal origin[48].

Table 2. Charictztion of Aspirin , metoformin and ponstan[49-50]

Medicines	scientific name	Chemical Formula	M.wt g/mole	Maximum. wavelength nm	Melting point C°	Structure
Aspirin	2-acetyloxybenzoic acid	$C_9H_8O_4$	180.16	270	136	
Metformin	3-(diaminomethylidene)-1,1-dimethylguanidine	$C_4H_{11}N_5$	129.17	234	225	
ponstan	2-[(2,3-dimethylphenyl) aminobenzoic acid	$C_{15}H_{15}NO_2$	241.290	533	231	

5-1 Aspirin

Aspirin, a nonsteroidal anti-inflammatory agent, is used clinically for its anti-inflammatory, analgesic, and antipyretic properties. It is often employed for the treatment of rheumatoid arthritis and osteoarthritis, and as an antiplatelet drug for treating intravascular thrombosis. Low-dose aspirin is effective in reducing the risk of a first myocardial infarction. Aspirin is a more potent inhibitor of prostaglandin synthesis and platelet aggregation than other salicylic acid derivatives. The differences in activity are thought to be due to the acetyl group on aspirin, which is responsible for the irreversible inactivation of cyclooxygenase. The effects of aspirin are due to the actions of both the acetyl and the salicylate portions of the molecule, as well as to the active salicylate metabolite.[51], figure (3).

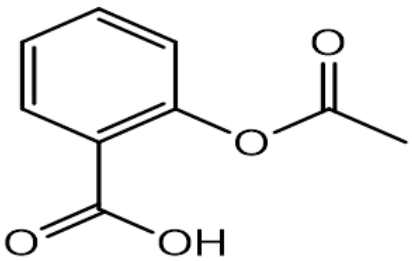


Figure 5: Aspirin structure.

5-2 Metformin

Metformin is one of the most popular oral glucose-lowering medications, widely considered to be the optimal initial therapy for patients with type 2 diabetes mellitus. Interestingly, there still remains controversy regarding the drug's precise mechanism of action, which is thought to involve a reduction in hepatic glucose production. It is now recommended as first-line treatment in various guidelines, including that of the EASD and ADA. Its favoured status lies in its efficacy, low cost, weight neutrality and good safety profile. Other benefits have also been described, including improvements in certain lipids, inflammatory markers, and a reduction in cardiovascular events, apparently independent from the drug's glucose-lowering effect.[52], figure (4).

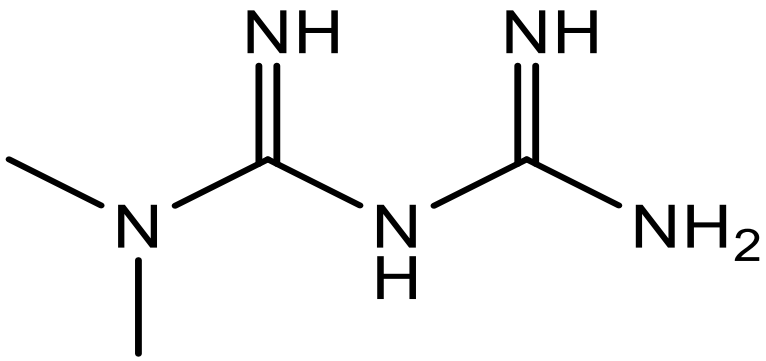


Figure 6: Metformin structure

5-3 Ponstan

Ponstan contains the active ingredient mefenamic acid. Mefenamic acid belongs to a group of medicines called non-steroidal anti-inflammatory drugs (or nsaids). These medicines work by relieving pain and inflammation. ponstan is used to relieve the symptoms of period pain and treat heavy periods.it also provides short term relief of pain in conditions such as, muscle and joint injuries such as sprains, strains and tendonitis and dental pain. Although ponstan can relieve the symptoms of pain and inflammation, it will not cure your condition.[53], figure (5).

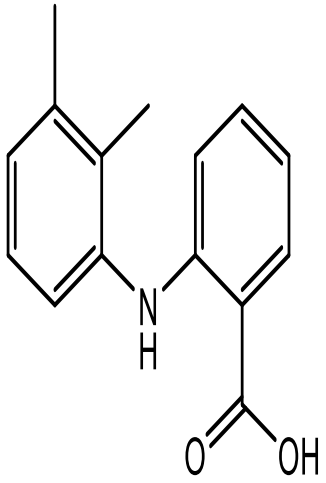


Figure 7: Ponstan structure

6- Application of Adsorbents

Standard primary and secondary treatment plants are unsuccessful at eliminating or degrading these harmful chemicals, a cost-effective tertiary treatment approach is proposed.

Adsorption is a successful approach for Contaminants removal globally, because it is low installation expense, high performance and has easy operational design [54].

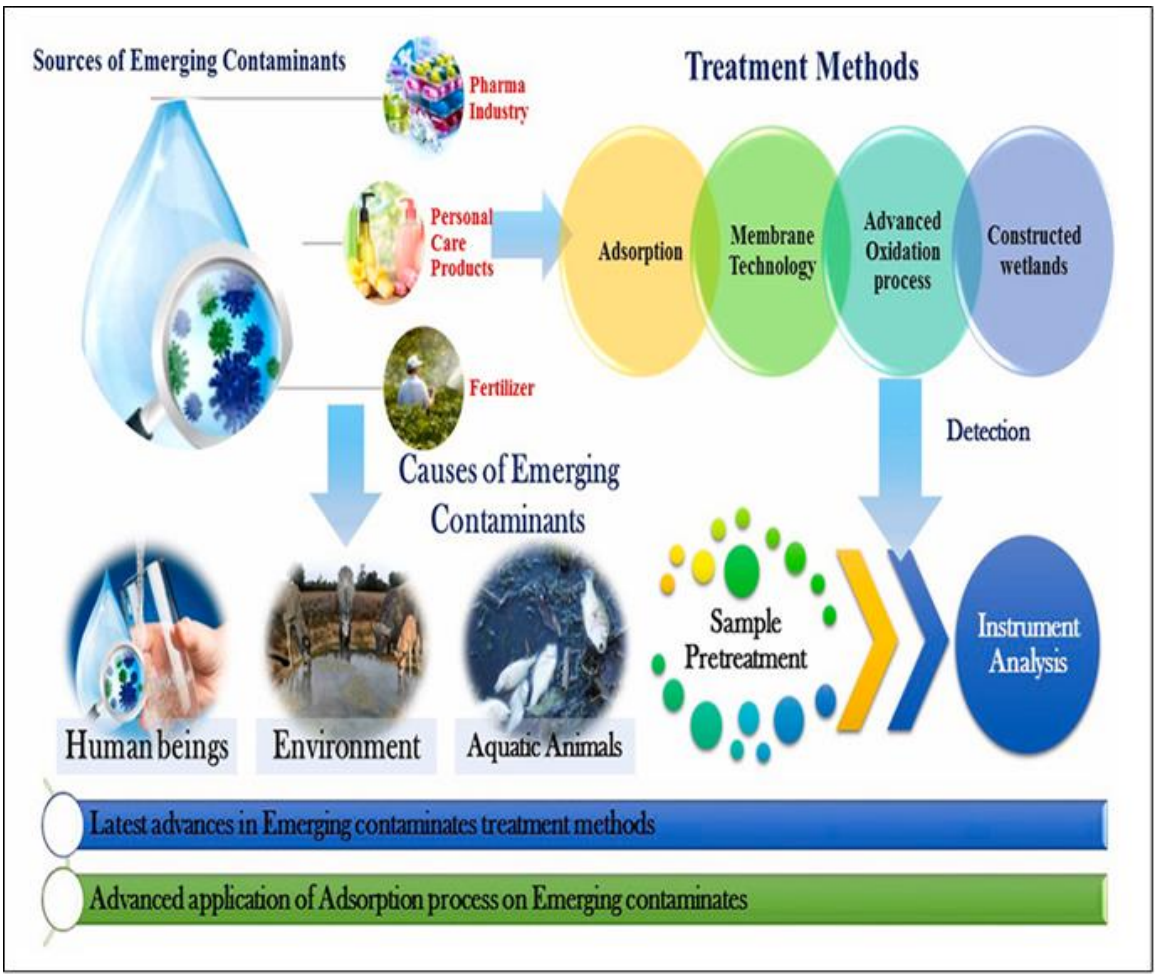


Figure (8): Application of adsorption process.

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