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Application of graphene based materials for adsorption of pharmaceutical traces from water and wastewater- a review

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ABSTRACT

Traces of pharmaceuticals have been classified as emerging pollutants due to their persistence in the aquatic ecosystem. There has been indiscriminate disposal of pharmaceutical waste from manufacturing processes, half used, expired antibiotics as a result of which, huge quantities of bacterial resistant antibiotic wastewater have been introduced into natural ecosystems. In addition, drugs that are not fully metabolized in the body may be excreted into the sewer system. Therefore, treatment of pharmaceutical wastewater is a global concern. A wide range of treatment methodologies have been developed to treat pharmaceutical wastewater viz., chemical oxidation, biodegradation, adsorption, liquid extraction, membrane techniques, etc. However, adsorption is a promising method for the removal of micropollutants because of its simple design, low-cost, high efficiency, etc. Research has shown that graphene materials can be used as photo-catalysts, adsorbents, and as disinfectants in water treatment. They are reported to be efficient agents against a wide variety of water pollutants, including (but not limited to) organic molecules, inorganic heavy metals, and water borne pathogenic micro-organisms. This review discusses the application of graphene materials in treating pharmaceutical wastewater and explains the mechanism of adsorption. A brief perspective on the future scope of work in the area has also been examined.

Keywords: Pharmaceutical pollutants; Wastewater; Adsorption; Graphene; Graphene oxide; Graphene composites

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1. Introduction

Rapidly growing pharmaceutical industries and other activities have been discharging copious amounts of organic, inorganic, biodegradable, and non-biodegradable waste into the environment. Recently, pharmaceuticals have been identified as “emerging pollutants” greatly polluting the water streams, causing significant hazard to aquatic life systems, and human beings [1,2]. The contamination reaches the environment not only through usage and inappropriate disposal, but also by various

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pharmaceutical production facilities. Recently, pharmaceuticals have been observed in wastewaters, surface, ground, and drinking water sources. Different classes of drugs have been recognized as environmental contaminants, viz., antibiotics, anti-acids, steroids, antidepressants, analgesics, anti-inflammatories, antipyretics, beta-blockers, lipid-lowering drugs, tranquilizers, and stimulants [3].

Pharmaceuticals manufacturing process generally involves processes, namely, fermentation, extraction, purification, chemical synthesis, formulation, and packaging. Each of these processes generates solid, liquid, and gaseous wastes. The water consumption in the pharmaceutical industry depends on the process, the nature of the raw materials used, and products generated. The purification process also consumes huge quantities of water. Liquid effluents resulting from cleaning operations after batch production may also contain toxic organic residues. In addition to the manufacturing waste, drugs that are not fully metabolized in the body may be excreted into the sewer system. Numerous pharmaceutical compounds have been shown to pass through sewage treatment plants (STPs) and contaminate the aquatic environment [4].

Fig. 1 explains the various pathways of entry of pharmaceutical waste into the environment causing ground water contamination. Stringent environmental regulations have recently restricted the use of organic pollutants such as pesticides and many of them have been banned from usage [5]. However, pharmaceuticals cannot be restricted in this way, due to their beneficial human (and animal) health effects and economic importance. Indeed, their use is expected to grow with the increase in population and their increasing average age [5]. Therefore, their traces are likely to be found in the environment adjacent to any developed or developing human population.

Non-steroidal anti-inflammatory drugs (NSAIDs) like ibuprofen and diclofenac are often detected in sewage, surface, and in ground water [6]. Ibuprofen, diclofenac, acetyl salicylic acid, phenazone, and indomethacin have been detected in surface water. However, ibuprofen, diclofenac, and propy-phenazone are the most frequently detected drugs. Diclofenac has been confirmed to be lethal for vultures and cattles [7]. NSAIDs like ibuprofen, aspirin, and naproxen are very often found in municipal effluents [8].

Long-term exposure to the different classes of pharmaceutical compounds even at low concentration ranges such as μg/L to ng/L may cause endocrine disruption and inhibition of cell proliferation in humans [9]. These pharmaceutical mixtures in drinking water may result in severe and persistent chronic damages [10,11]. It’s presence in drinking water can have adverse effects on human health and ecosystem. Studies have demonstrated that fish exposed to contraceptive pharmaceutical containing wastewater can show reproductive irregularities. Extremely diluted concentrations of drug residues harm the reproductive systems of fish, frogs, and other aquatic species [12].

High solubility of most of the pharmaceutical compounds has made aquatic organisms more vulnerable to their effect. Their presence in water streams has linked to adverse effects such as feminization in fish, for example, estrogens have caused male fish to become female [12]. In addition to this, some of the unused pharmaceuticals are directly disposed in septic tanks, sewer, and landfill [12]. These drugs can easily seep through the soil during rain and pollute the ground water source too. Antibiotics can lead to a modification in microbial community composition and eventually affect the food chain [13].

However, if the receiving waters are used for potable supplies with traces of these compounds, it may represent a potential hazard to human health, especially in areas without advanced water treatment [5]. One major consequence of such pollution is that, it could generate antibiotic-resistant bacteria [14]. Wastewater treatment plants and sewage treatment plants (WTP and STP) facilities are generally not designed to treat such contaminants and thus, their pharmaceutical contaminant cannot be totally removed [15].

Currently, research is in progress for the removal of these contaminants from polluted water, such as; submerged membrane bioreactor [16] activated sludge treatment [17], constructed wetland [18], photocatalytic oxidation [19], catalytic ozonation [20], adsorption [21–23], advanced oxidation process (AOP) [24,25], nanofiltration [26], biological processes [27], reverse osmosis [28], ultra filtration [26], etc. but they cannot be used effectively and economically to remove pharmaceutical pollutants from water effluents [29]. Fig. 2 shows some of the treatment technologies in practice for pharmaceutical effluents.

Although the application of various treatment methods has been investigated, not many of them are found to be techno-economically attractive. However, the drawbacks of most of the above methods are: (i) the methods are complex, (ii) high investment and necessary maintenance cost, (iii) generation of secondary pollutant (toxic sludge), and (iv) generation of byproducts with higher toxicity than the original pollutant [30]. Therefore, effective treatment is needed for this emerging class of pollutants. Of the above-mentioned methods, adsorption is one of the most promising treatment methods. This process has been frequently applied for removing natural or synthetic

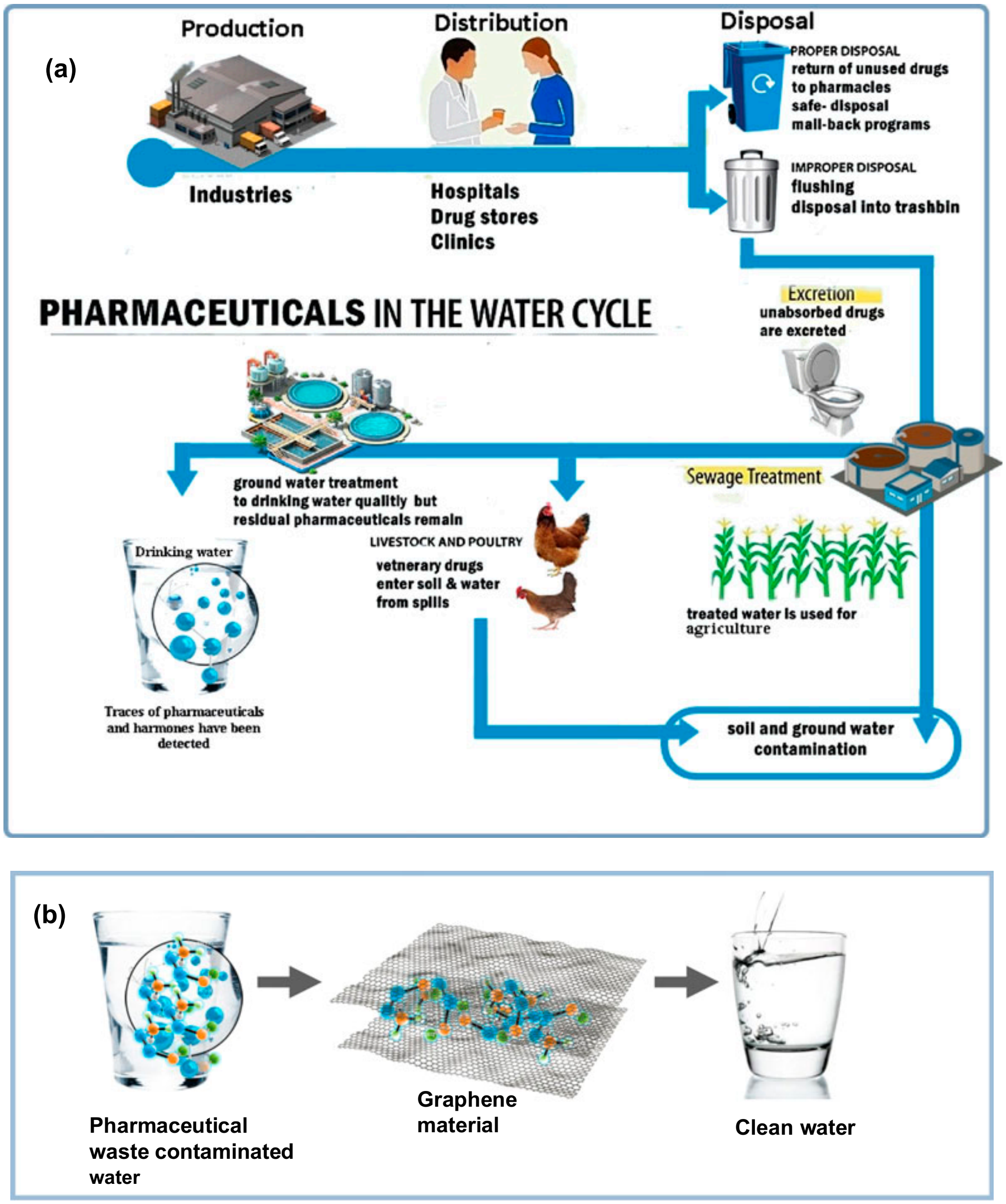

Fig. 1. (a) Pharmaceutical wastes generation sources and (b) Adsorption of pharmaceutical waste on graphene-based materials [5].

organic compounds during drinking water treatment [21–23,31]. It has numerous advantages: (i) adsorption can handle trace levels of pollutants, (ii) efficient, (iii) simple to design or easy to operate, (vi) unaffected by toxicity, (v) suitable for batch and continuous processes, (vi) adsorbent can be regenerated and reused several times, and (vii) low initial capital cost for implementation [32]. Hence, there is an ongoing search for more efficient, robust adsorbents for the removal of this type of pollutant.

Graphene is the new miracle material that has attracted the attention of scientist in recent years. It is one atom-thick and two-dimensional (2D) layer of sp^2-hybridized carbon. The interest in graphene has grown due to its extraordinary physicochemical properties such as high specific surface area, unique morphology, chemical structure, electrical, thermal properties, and mechanical strength. Graphene has been used as an expeditious adsorbent for various pollutants [33–39] due to its large, delocalized π-electron

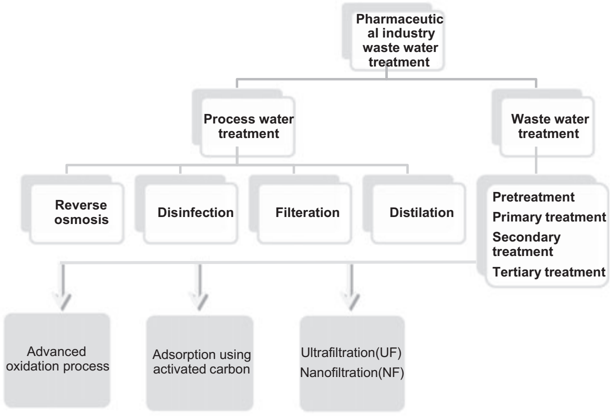

Fig. 2. Various treatment technologies of pharmaceutical effluents [21–26,28].

system, which can form strong interactions with other pollutants.

In this paper, we will briefly discuss the synthesis, characterization and the recent advances in application of graphene-based materials, for remediation of pharmaceutical wastewater.

2. Properties of graphene

In the family of carbon, graphene is the most recent member with a theoretical surface area of ~2,630 $m^2\ g^{-1}$ [40], optical transparency [41], electron-rich π system [42], exceptional mechanical strength (0.4–2.4 TPa) [43], and highly hydrophobic surface [44,45]. Graphene, in its perfect form, is composed of a single layer of sp^2-hybridized carbon atoms arranged in a 2D honeycomb structure (Fig. 3).

Moreover, when compared with carbon nanotubes, graphene still proves to be better filler. Graphene offers an exceptional support to anchor oxygen-containing functional groups such as, hydroxyl, carboxyl, and epoxy group and forms graphene oxide (GO) or reduced graphene oxide (rGO). Graphene has an improved nanosorbent design owing to its enormously higher specific surface area, abundant sorption sites, short intra-particle diffusion path-length, low temperature modification, better regeneration capacity, and reusability properties than conventional, commercial adsorbents. Furthermore, graphene has relatively large and delocalized π-electron system which may possess binding attributes for target pollutants [46]. Therefore, graphene and graphene-based materials belongs to a new class of fascinating carbon nanomaterials. This material has garnered a great interest as nanoadsorbent for pollution control applications in recent years [47].

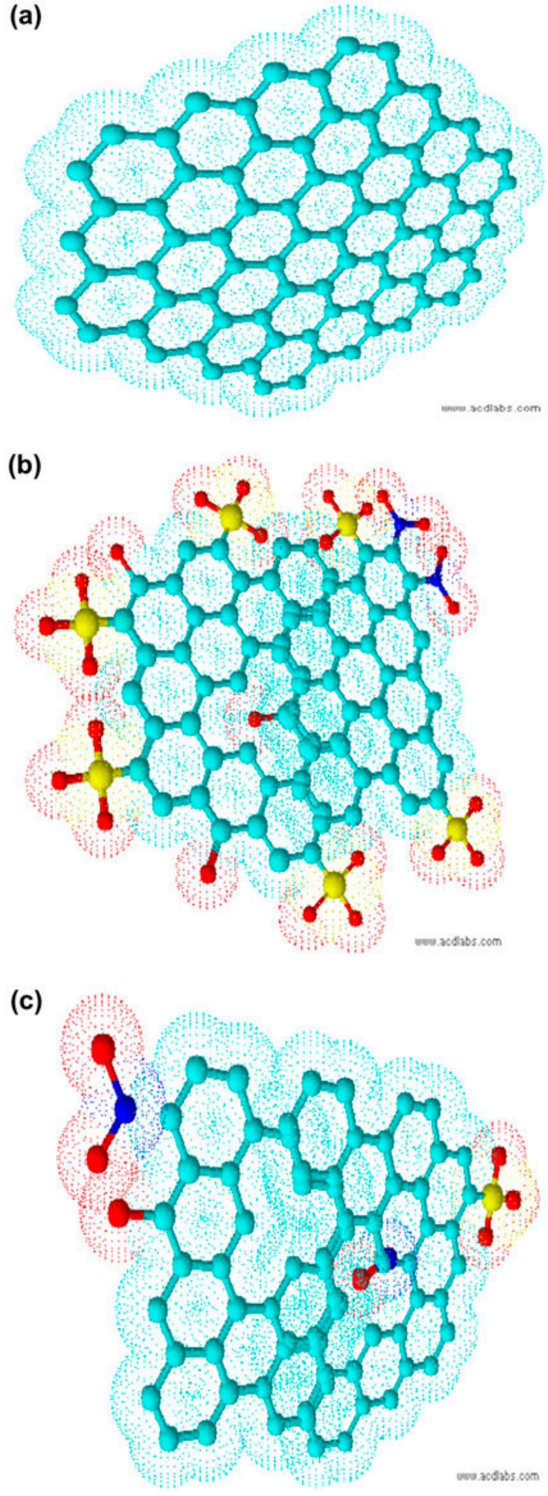

Fig. 3. (a) Two-dimensional honeycomb structure of graphene, (b) graphene oxide, and (c) reduced graphene oxide. (Light blue—CH_3, red—O functional group, yellow—OH group, and dark blue—COOH).

3. Synthesis of graphene

Properties and applications of graphene are related to its shape, size, and morphology. Hence, it is important to have synthesis procedures to control shape, size, and morphology. While considering commercial applications, scientists need to develop chemical routes which can give high-yield of graphene with good control over morphology. Graphite oxide chemistry is quite old [48]. Brodie [48] was the first to discover the oxidizing mixture ($KClO_4$ with conc. HNO_3) could form GO only with carbons that contain graphitic structure. Later, several others like Staudenmaier, Hofmann and Frenzels, Hamdi and Hummers reported synthesis of graphite oxide from graphite in the presence of oxidants, with modifications in reaction conditions [49]. Staudenmaier et al. [50] reported the formation of GO, when graphite was heated with H_2SO_4, HNO_3, and $KClO_4$. Hummers and Offeman [49] later found an easy procedure to prepare GO using H_2SO_4 and $KMnO_4$. Novoselov et al. [51] were the first to discover monolayer graphene film by exfoliation of highly oriented pyrolytic graphite. In the literature, there are various methods reported on the synthesis of graphene sheets and their derivatives, viz., mechanical cleavage of graphite, unzipping carbon nanotubes [52], chemical exfoliation of graphite, solvothermal synthesis, chemical vapor deposition (CVD), electric-arc discharge method, sonochemical approach, reduction in GO and aqueous and environment-friendly greener reduction methods.

The micromechanical exfoliation method generates flakes of size 5–100 μm. It is possible to produce high-quality graphene using this methodology. Similarly, epitaxial growth on SiC also produces graphene of thin film, which gives high-quality graphene. Carbon nanotubes unzipping usually produces high-quality graphene nanoribbons of few micron size. CVD produces thin film of less than or equal to 75 cm size. Liquid phase exfoliation produces nanosheets from nm to few μm in size and has only moderate quality with low yield. Graphene can be synthesized through the chemical reduction of graphite oxide. This method produces nanoflakes or powder of nm size. GO contains clusters of oxygen functional groups (such as epoxy, –COOH, –OH, >C=O) in the carbon lattice [53] (Fig. 3). This surface functional group of graphene governs the adsorption sites [54,55] and dispersive capacity of the graphene nanosheets in water. These groups render the material a good candidate for application in diverse field including water purification. Moreover, the combined effect of high surface area, functional group, and hydrophilic nature of GO allows a range of chemical functionalization to be carried out on the material. Thus, GO is known as a building block for graphene-based materials [47,53].

rGO is produced by reducing GO using thermal annealing, chemical reducing agents such as NaBH4, photo-reduction, microwave-assisted reduction, etc. [56,57]. This reduction process can remove oxygen to a large content (Fig. 3), with the ratio of C:O increasing from 2:1 to 246:1. Complete reduction is an exigent task to accomplish [57]. However, reduction of GO leads to alteration in chemical properties with carbon vacancies and residual oxygen, clustered pentagons and heptagons carbon structure [58,59]. Table 1 represents various properties of Graphene, GO, and rGO relevant for environmental application. It can be seen from the table, GO and rGO are hydrophilic and contains functional groups such as epoxy, carboxylic, phenol, hence support greater adsorption than pure graphene. Molecular level interactions between GO, rGO, and contaminant may be expected. In the conversion of GO to graphene, strong chemical reducing agents like N_2H_4 and $NaBH_4$ are used. These strong reducing agents are toxic and hence tough to handle during bulk production. Thus, scientists have been developing other aqueous and environment-friendly reduction methodologies for the synthesis of graphene. To overcome these problems, many green synthesis procedures are being developed in the recent past 2–3 years.

Fan et al. [66] investigated a facile green method for the deoxygenation of exfoliated graphite oxide by strong alkali. The graphene obtained had good dispersibility in water. Platinum nanoparticle-expandable graphene film (Pt/EGS) on conductive indium tin oxide by green electrochemical route was reported by Liu et al. [67]. Glucose is known for its biological importance and is a mild reducing agent. Zhu et al. [68] developed a one-pot method for the effective synthesis of chemically reduced graphene nanosheets from exfoliated graphite oxide using glucose in the presence of ammonia. This study also compared the reactivity of glucose with fructose and sucrose, where similar results were obtained. Shah et al. [69] reported an easy and efficient one-step synthesis (green) of TiO_2–graphene composite and investigated its performance in photo-catalytic applications. The catalysts exhibited improved photo-catalytic activity toward the remediation of rhodamine B dye and benzoic acid using visible light irradiation. Gupta et al. [70] reported the synthesis of graphene from cane sugar (green route). Graphenic material from cane sugar was immobilized on the sand to make graphene sand composite. Liu et al. [71] have studied graphene incorporation with silica exhibiting better removal of pollutants from wastewater. Moreover, SiO_2 is an ideal

Table 1
Various properties of Graphene, GO, and rGO relevant for environmental application [60–65]

Properties	Graphene	Graphene oxide (GO)	Reduced graphene oxide (rGO)
C:O ratio	No oxygen	2–4	8–246
Electron mobility	10,000–50,000	Insulator	0.05–200
Nature	Hydrophobic	Hydrophilic	Hydrophilic
Synthesis	Chemical vapor deposition, thermal decomposition SiC, graphite exfoliation	Oxidation and exfoliation of graphene	Reduction of graphene oxide
Functional group	No functional group	Epoxy, carboxylic, phenol	Epoxy, carboxylic, phenol
Production cost	High	Low	Low
Young's modulus	1	0.2	0.25
Color	Black	Brownish	Black

template material for mitigating aggregation of graphene. SiO_2 is an inexpensive, safe, and abundantly available material on earth. The adsorption capabilities and mechanism of graphene composite should be investigated well to understand this novel material.

4. Characterization of graphene materials

The most important part of graphene research is its characterization. It includes measurements using different microscopic and spectroscopic techniques. Characterization of graphene and graphene composites explores the number of layers and purity of the sample (presence or absence of defects). The number of layers in graphene is identified using optical contrast of layers on different substrates. This is a simple and effective method. In this method, there is interference of the reflected light beams causing contrast [72]. Scanning electron microscopy (SEM) is another simple way to elucidate the number of layers [73]. Another simple, direct method to observe the number of layers is by viewing the edges of the images from a transmission electron microscopy (TEM). In a TEM image, each layer corresponds to a dark line. Electron diffraction can be used for differentiating single layer from multiple layers of graphene using relative intensity patterns [74]. Atomic force microscopy (AFM) in tapping mode determines the thickness of graphene. Structural and electronic characteristics of graphene can be investigated using Raman spectroscopy [75]. Three major bands are exhibited by the Raman spectrum of graphene: (i) the defect-induced band is the D-band, (1,300 cm^{-1}), (ii) the in-plane vibrations of the sp^2 carbon atoms are the reason for G-band (1,580 cm^{-1}), (iii) the second-order process results in the 2D-band (2,700 cm^{-1}). The double resonance causes the appearance of the D and 2D bands in the Raman scattering process [76]. As the number of layers increases, the 2D band gets widened and blue shifted. The X-ray diffraction (XRD) is the most widely used technique for general crystalline material characterization [77]. XRD of graphene and its composites are done to qualitatively analyze their internal structure [71]. It is also used to measure the average spacings between layers and rows of atoms, determining the orientation of a single crystal or grain [77]. The XRD pattern for synthesized GO and rGO by chemical reduction of exfoliated and intercalated graphite oxide has two peaks. The strong peak at $2\theta = 11.6^\circ$ corresponds to an interlayer spacing of about 0.76 nm, indicating the presence of oxygen functional group, which can facilitate the hydration and exfoliation of graphene sheet in aqueous media. Chemical reduction of GO leads to formation of rGO with a broad peak at $2\theta = 25.8^\circ$. This broad peak corresponds to (0 0 2) plane of graphite with interlayer spacing of 0.34 nm which is due to the removal of oxygen atom during intercalation process, thus confirming reduction process of GO to graphene [60]. Functional group characterization of the graphene is done using FTIR. Moreover, functional group can aid in determining the type interaction taking place between adsorbate–adsorbent. Surface area and porosity measurements can be performed using Brunauer, Emmett and Teller technique.

5. Remediation of pharmaceutical contaminants by graphene and graphene-based materials

Over the last decade, research on graphene has increased many folds due to its outstanding properties for environmental remediation and reclamation. They can be used to reduce pollution load by adsorption, decompose organic pollutants, and persistent organic pollutants. This section presents how graphene and graphene-based materials have been successfully used for remediation of pharmaceutical waste.

In a recent study carried out by Al-Khateeb et al. [3] reporting the removal of aspirin, acetaminophen, and caffeine using graphene, nanoplatelets was investigated. Characterization of the graphene used, showed a transparent, layered structure with a surface area 635.2 $m^2 g^{-1}$. The effect of adsorption time, graphene dose, initial solution pH, and temperature of adsorption was studied. The experimental data were found to fit pseudo-second-order kinetic model. The adsorption thermodynamics revealed that enthalpy change (ΔH°) was negative at all temperatures indicating the spontaneity of the adsorption of aspirin, acetaminophen, and caffeine by graphene. The results indicated graphene nanoplatelets that showed great adsorption efficiency.

Another example of the use of graphene adsorbents for the removal of pharmaceuticals is explained by Kyzas et al. [78]. They synthesized graphite oxide/poly (acrylic acid) grafted chitosan nanocomposite (GO/CSA). This material was used for the removal of dorzolamide (dorzo), a pharmaceutical component generally found in biomedical effluents. The adsorption isotherms were plotted and the results exhibited higher adsorption capacity of GO/CSA at 25°C ($Q_{\max} = 334$ mg g^{-1}). The study revealed that the adsorption was due to a complex combination of forces, bond formation, electrostatic interactions, etc.

Yuan et al. [79] demonstrated adsorption and remediation of tetracycline using GO. GO was synthesized using modified Hummers method. AFM study indicated that the adsorbent was close to single-layered with a topographic height of 1.198 nm. TEM results showed flake-like structure, while FT-IR result revealed the presence of O–H, C=O, C–OH, C–O functional groups. This functional group suggests the existence of oxygen-containing functional group into the graphene. In this research, tetracycline was found to be strongly bonded to GO surface by means of π–π and cation–π interaction. The adsorption isotherms were plotted and the results were found to well fit in the Langmuir and Temkin models. The theoretical maximum of adsorption capacity was 313 mg g^{-1} as calculated by Langmuir model. The kinetics of adsorption perfectly fitted pseudo-second-order model. The adsorption capacities of tetracycline on GO decreased with the increase in pH or Na^+ concentration. This study also compares the adsorption isotherms of oxytetracycline and doxycycline.

Ji et al. [80] studied the adsorptive properties of graphene nanosheets and GO for removal of three organic compounds viz., naphthalene, 2-naphthol, and 1-naphthylamine and one pharmaceutical compound, tylosin. GO surface area was determined to be 3.5 $m^2 g^{-1}$, whereas graphene nanosheets had a higher surface area of 387.9 $m^2 g^{-1}$. Further characterization of graphene nanosheets and GO showed that the later had a considerably greater amount of oxygen than graphene nanosheets. TEM images were compared and the results indicated that graphite oxide was partially exfoliated, whereas the graphene nanosheets were highly exfoliated. Graphene nanosheets and graphite oxide exhibited comparable adsorption efficiencies. The adsorption efficacy followed the order, 1-naphthylamine > 2-naphthol > tylosin > naphthalene. It was proposed that the main reason for strong adsorption was due to π–π electron donor-acceptor interactions. Additionally, it was suggested that Lewis acid–base bond could have been an important factor contributing to the adsorption of 1-naphthylamine and tylosin, in the oxygen-rich graphite oxide.

Recently, the adsorption of ciprofloxacin (CIP) and norfloxacin (NOR), by reduced graphene oxide/magnetite (RGO–M) composites have been investigated by Tang et al. [81]. The adsorbents were characterized using scanning electron microscope (SEM), transmission electron microscope (TEM), Energy dispersive X-ray, vibrating sample magnetometer, and XRD. The results of batch equilibrium tests indicated that CIP and NOR adsorption on RGO–M is strongly dependent on initial pH. Both π–π interactions as well as electrostatic repulsions were responsible for adsorption. The adsorption data were fitted in adsorption isotherms and the equilibrium data fitted the Langmuir and Temkin models well. The maximum monolayer uptake of CIP and NOR onto the graphene adsorbent showed 18.22–22.20 mg g^{-1}, respectively. Both the adsorbates followed pseudo-second-order model.

GO, a potential adsorbent for the removal of tetracycline (TC) was investigated by Ghadim et al. [82].Variation of pH, sorption time, and temperature was studied to analyze adsorption efficiency of GO. The result shows that π–π interaction and cation–π bonding are responsible for adsorption of tetracycline on to GO surface. Adsorption kinetics of TC reported that within 15 min, equilibrium was reached. The experimental data were in good agreement with pseudo-second-order kinetics with rate constants derived was $k_2 = 0.2742–0.5362$ g mg^{-1} min^{-1} at different temperatures. The sorption data better fitted the Langmuir model, with the maximum adsorption of 323 mg g^{-1} at 298 K. Moreover, the thermodynamic study revealed that the sorption process was endothermic and spontaneous.

Liu et al. [83] have studied adsorption of selected organic compounds such as ketoprofen (KEP), carbamazepine (CBZ), and bisphenol A (BPA) by rGO and graphene. Single-walled carbon nanotubes, multi-walled carbon nanotubes, and commercial graphene were also investigated for comparison. The interactions of graphene with the PPCPs were shown to benon-hydrophobic. Adsorption capacities of the three organic compounds onto graphene were lower than adsorption onto graphite. The reason suggested was incomplete occupation of active sites due to aggregation of graphene sheets and the presence of oxygen-containing functional groups. Hydrogen bonding, π–π interactions that favor adsorption was predicted between the adsorbate–adsorbent.

In another recent study, Fei Yu et al. [84] synthesized an activated graphene adsorbent by a one-step KOH activation method due to which the specific surface area of the final product increased to ~512.6 m^2 g^{-1} from ~138.20 m^2 g^{-1}. This activated graphene was used as an adsorbent for the removal of CIP. FT-IR analyses of the adsorbent shows reduction in functional groups due to activation process. Raman spectroscopy analyzed the structure, quality of graphene, and its defects. The determined maximum adsorption capacity was ~194.6 mg g^{-1}. This indicated that alkali activation increased the adsorption capacity of the adsorbent and the pharmaceutical contaminant was effectively removed. The research study suggests that activated graphene may be efficient adsorbent nanomaterials for organic pollutants from aqueous solutions.

Removal of beta-blockers from aqueous media by adsorption onto GO was investigated by George et al. [85]. Atenolol (ATL) and propanolol (PRO) were used as model drug molecules for conducting lab scale experiment. Characterization of the adsorbent material was performed using SEM and FT-IR analysis. The model drug molecules were tested for their adsorptive behavior optimizing GO dosage, contact time, temperature, and pH. Adsorption mechanisms and the pH-effect curves after adsorption were discussed in this research article. Depending on the pK_a value, ionizable compounds interact through electrostatic attraction or repulsion. The surface properties of the graphene materials, such as surface charge, and the protonation–deprotonation transition of functional groups (such as carboxylic (–COOH), hydroxyl (–OH), and epoxy (–C–O–C–) on the active sites of the GO played a crucial role in the adsorption of organic pollutant. Electrostatic forces acted between the positively charged drug (mainly the protonated amino groups $-NH_3^+$) and the negative-charged group (–COO$^-$) of GO.

In addition, surface bridging via H–bonding of the organic molecules was reported. The adsorption mechanism was influenced by hydrogen bonds between: the hydrogen atoms of hydroxyl groups in GO and some nitrogen atoms of amino groups of drug molecules, the oxygen atoms of hydroxyl groups of GO and hydrogen atoms of amino groups of drug molecules. Other interaction, such as π–π interaction between the localized π electrons in the conjugated aromatic rings of the GO and the drug molecules played effective role in adsorption mechanism. Moreover, it was observed that adsorption of atenolol on GO was stronger than propranolol. The reason may be the structure of the drug molecule. Further, adsorption kinetics was calculated and isotherms were plotted. Desorption studies were also performed. Hence, the research study concluded that GO-based nanomaterials proved to be a promising, robust, and efficient adsorbent for the remediation of beta-blockers from aqueous solutions.

Nam et al. [86] conducted lab scale adsorption study with GO as adsorbent for the removal of diclofenac (DCF) and sulfamethoxazole (SMX) solution. Further, the effect of sonication was also examined. Adsorption on GO was found to involve functional groups containing oxygen, such as carbolylate, which exhibit negative charges over 3–11 pH range (COO$^-$). The removal of the compounds was greater under acidic conditions ($pH < pK_a$) than at basic pH ($pH > pK_a$). The removal under acidic pH conditions was affected mainly by attraction, such as hydrophobic effects and π–π interactions. The adsorption capacities were found to be –18.8 and –15.9 kcal mol^{-1} for DCF and SMX, respectively. This was attributed to the greater surface area exposure to the GO, which resulted in increased π–π interactions and dispersion forces between the adsorbent and diclofenac. Optimization of GO dosage, contact time, and pH was also done. Removal of diclofenac ($\log K_{ow} = 4.26$) was greater than that of sulfamethoxazole ($\log K_{ow} = 0.79$) regardless of pH. Approximately, 35% removal of diclofenac and 12% removal of sulfamethoxazole were reported by Freundlich's model. Sulfamethoxazole exhibited a slightly linear trend in the isotherm study, which was assumed to be due to the hydrophobicity of the micropollutants on carbonaceous material. Further, sonication of GO considerably enhanced the remediation of target compounds.

Table 2 summarizes the adsorption capacities of the different graphene-based materials in comparison to recent activated carbon adsorption studies reported [87] in literature for the remediation of pharmaceuticals. It also compares the efficiency of graphene-based materials with one recent research article that uses single-walled carbon nanotubes (SWCNTs), multi-walled carbon nanotubes (MWCNTs) [83]. It is obvious from the table that graphene-based adsorbents show superior adsorption capacities for pharmaceuticals depending on the synthesis method and functionalization of the surface of the adsorbent. The electrostatic forces,

Table 2
Summary of various pharmaceutical residue removal by graphene and activated carbon-based adsorbents

Adsorbent	Adsorbent synthesis method	Sample type	Adsorbate	Adsorption capacity/order of adsorption	Refs.
Graphene nanoplatelets	Stock solution prepared by NaOH, HNO_3	Synthetic sample	Aspirin, acetaminophen and caffeine	13.02, 19.72, and 18.76 mg g^{-1}	[3]
GO/CSA (Graphite oxide/carboxyl grafted chitosan nanocomposites)	GO by modified Hummers method, CSA prepared with acetic acid, NaOH and acetone	Synthetic sample	Dorzalamide	334 mg g^{-1}	[78]
Graphene oxide (GO)	Modified hummers method, oxidation of graphite by H_2SO_4 by $KMnO_4$	Synthetic sample	Tetracycline	313 mg g^{-1}	[79]
Graphene nanosheets and graphene oxide	Splitting graphite oxide [88] filtration functionalized graphene sheets [89]	Synthetic sample	Naphthalene, 2-naphthol, and 1-naphthylamine and one pharmaceutical compound (tylosin)	1-naphthylamine > 2-naphthol > tylosin > naphthalene	[80]
Reduced graphene oxide/magnetite(RGO-M) composite	RGO prepared from GO	Synthetic sample	Ciprofloxacin (CIP) and norfloxacin (NOR)	18.22–22.20 mg g^{-1}	[81]
Graphene oxide (GO)	Hummers method	Synthetic sample	Tetracycline	323 mg g^{-1}	[82]
Reduced graphene oxide and graphene. Single-walled carbon nanotubes (SWCNTs), multi-walled carbon nanotubes (MWCNTs) and powdered graphite	rGO prepared by improved hummers' method for, graphite powder and flakes	Synthetic sample	Ketoprofen, carbamazepine and bisphenol A	SWCNTs > rGO_1 > rGO_2 >MWCNTs > graphene > graphite	[83]
Activated carbon	One-step alkali activated method	Synthetic sample	Ciprofloxacin (CIP)	194.6 mg g^{-1}	[84]
Graphene oxide	Hummers method	Synthetic sample	Atenolol (ATL) and propanolol (PRO)	67 mg g^{-1} (PRO) and 116 mg g^{-1} (ATL)	[85]
Graphene oxide	Oxidation from graphite using modified Hummer's method	Synthetic sample	Diclofenac and sulfamethoxazole	−18.8 and −15.9 kcal mol^{-1}	[86]
Activated carbon from cocoa shell	Microwave-induced synthesis	Synthetic sample	Sodium diclofenac (DFC) and nimesulide (NS)	63.47 mg g^{-1} (DFC) and 74.81 mg g^{-1} (NS)	[87]

H–bonding, or π–π interactions may play a critical role in the whole adsorption process. From the above discussion, it can be concluded that GO and rGO could prove to be a promising and effective adsorbent for the removal of pharmaceutical residues from aqueous solutions. All the above research on adsorption characteristics of graphene and related materials reported is limited to batch adsorption studies. More efficient utilization of graphene materials can be obtained using column studies and the authors recommend the same for future studies.

5.1. Mechanisms of adsorption

Most of the pharmaceutical pollutants are organic in nature and possess adverse impact on environment and human beings. The organic pollutants usually have a high oxygen demand and low biodegradability, and also have a high bio-accumulation rate along the food chain due to their lipophilicity [90].

Jauris et al. [91] studied the adsorption of sodium diclofenac (s-DCF) with pristine graphene, graphene with a vacancy, rGO, and functionalized graphene nanoribbons with an aim of understanding the adsorption mechanism of this molecule on the carbon lattice. The computer simulations showed that the interactions between pristine graphene and s-DCF could be a physical adsorption process, but for pristine graphene and graphene plus a single vacancy, the results showed π−π interactions. In the case of adsorption of the s-DCF molecule onto functionalized graphene or nanoribbons, binding energies were found to increase as the number of functional groups increased. These results proved the mechanism of adsorption of s-DCF on graphene.

The adsorption mechanism of organic pollutant on graphene is dependent on π-electron system of organic molecules and π electron of the aromatic ring of graphene. In general, five possible interactions including hydrophobic effect, π–π bonds, hydrogen bonds, and covalent and electrostatic interactions have been observed in carbon materials and believed to be responsible for the adsorption of organic chemicals on the surface of carbon nanosized particles [92]. All of the above literature suggests that adsorption of pharmaceutical waste on to graphene or other graphene materials occur due to π−π interaction. Most of the pharmaceutical formulations such as tetracycline, ibuprofen, diclofenac, paracetamol, aspirin, etc., consists of one or more aromatic rings and hence π electrons. The above studies suggest that the main inter-molecular force between the adsorbent and adsorbate could be π−π interaction. Besides π−π interaction, the above research articles also suggest electrostatic forces and H–bonding to have an effective role in the adsorption mechanism for the pharmaceutical compounds [85].

Hence, these are the major mechanisms that can take place during adsorption process to facilitate pollutant removal using graphene and graphene-based materials. A schematic diagram of the mechanism of adsorption of drug molecule on graphene is shown in Fig. 4.

6. Summary and future scope of work

This review article summarizes the effective use of graphene as adsorbent material for treatment of pharmaceutical wastewaters. Prolonged exposure to pharmaceutical contaminants makes it toxic not only to aquatic life, but to human being and environment. The various conventional treatment methods available may not be suitable to completely remove pharmaceutical waste. Adsorption using graphene materials can be considered simple and low-cost technique [93] especially to treat special wastes such as pharmaceutical, which may be only present in trace levels ($\mu g\ L^{-1}$ to $ng\ L^{-1}$); toxic if not removed completely. This review presents the recent progress on the use graphene and graphene-based materials for the removal of pharmaceutical pollutants. It is evident that graphene materials are a promising substitute to activated carbon and other adsorbent materials that are presently used. Graphene materials have been shown to have the potential to be one of the most reliable and versatile materials for future wastewater treatment. However, it is important to note that graphene materials' adsorptive capacity depends on the experimental conditions. Though touted as a miracle material, there are many difficulties and short comings that have to be overcome before we realize all the potential of graphene for field applications. Here, we would like to highlight some of those important issues that might help future research.

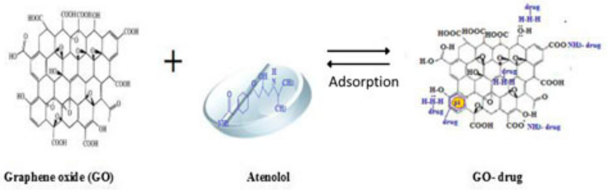

Fig. 4. Schematic representation of adsorption of drug molecule on graphene oxide.

(1) Research on adsorption characteristics of graphene and related materials reported in literature is mostly limited to batch adsorption studies. More efficient utilization of graphene materials can be obtained using column studies, hence recommended.
(2) There is very limited adsorbent regeneration studies reported. Regeneration studies should therefore be performed as they help determine the reusability of an adsorbent which in turn contributes in evaluating the cost effectiveness of the adsorbent.
(3) Most of the research papers deal with simulated wastewaters and lab scale experiments, while it is recommended to test graphene in the field with real pharmaceutical industry effluents.
(4) Adsorbent disposal after complete saturation needs to be studied.
(5) The evaluation and analysis of graphene materials life cycle, impacts, toxicity and distribution in the different ecosystem should also be understood well.

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