




Review

Adsorption Technologies for the Removal of Cytostatics in Water: A Review

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Abstract: One of the most common treatments for cancer disease requires the administration of cytostatics, which are very effective drugs in the elimination of cancerous cells, but are toxic for healthy tissues. After being administered to patients, they are excreted and frequently reach natural water bodies, due to their poor degradation in wastewater treatment plants (WWTPs), posing a global threat to the environment and human health. The study of proper treatment approaches for the effective removal of these hazardous drugs in WWTPs is thus a topic of concern and of utmost importance to ensure environmental integrity, resilience and sustainability. The aim of this work is to perform a comprehensive review of the application of adsorption-based processes for the treatment of aqueous matrices contaminated with cytostatics, which has never been addressed before. A detailed discussion on the operating conditions, type and concentrations of sorbents used, toxicity of the effluents and other relevant parameters is presented. This paper aims to help identify the most promising sorbents and conditions, the current knowledge gaps, and future challenges/perspectives on adsorption technologies (isolated or coupled with other processes) to tackle the problem of cytostatic fingerprints in water courses. Additionally, information concerning the implementation of these technologies from an environmental and economic (life cycle assessment) perspective is given.

Keywords: hazardous medicinal products; antineoplastic agents; adsorption; water treatment; life cycle assessment



Citation: Garcia-Costa, A.L.; Gouveia, T.I.A.; Alves, A.; Santos, M.S.F. Adsorption Technologies for the Removal of Cytostatics in Water: A Review. *Water* **2023**, *15*, 4005. <https://doi.org/10.3390/w15224005>

Academic Editor: Alexandre T. Paulino

Received: 18 October 2023
Revised: 13 November 2023
Accepted: 15 November 2023
Published: 17 November 2023



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1. Introduction

For the past few decades, the contamination of worldwide wastewaters and waters by several types of contaminants has been getting worse due to human activity. These contaminants can be classified into three groups: inorganic chemicals, organic chemicals and pathogenic organisms [1]. Pharmaceutical active substances are among the organic chemicals of highest relevance in terms of water cycle contamination, as they are constantly released into the sewage system (intact or metabolized), and there is a lack of specific and effective treatments at wastewater treatment facilities for their removal/elimination. Among the multiple pharmaceuticals consumed worldwide, cytostatics must be carefully considered. These are mainly used in chemotherapy to treat different types of cancer, one of the most widespread diseases and the second cause of death worldwide. To illustrate this issue, 19.3 million new cancer cases were diagnosed and 9.96 million people died in 2020, according to the International Agency for Research on Cancer (IARC) by the World Health Organization (WHO) (Lyon, France) [2]. Furthermore, this agency estimates that more than 29 million new cases per year will be detected by 2040 [2].

Cytostatics act by inhibiting cell division and cell growth, causing the death of cancerous tissues. Nonetheless, healthy cells are also sensitive to these compounds [3]. The Anatomical Therapeutic Chemical classification system of the World Health Organization classifies these drugs in the L category, also known as Antineoplastic and Immunomodulating agents. This group is divided into four subcategories: L01—antineoplastic agents; L02—endocrine therapy agents; L03—immunostimulants; and L04—immunosuppressants. Even though these drugs are used to cure cancer, some of them were proven to be carcinogenic to humans (group 1, according to IARC), such as cyclophosphamide (CYC), etoposide and tamoxifen (TAM). Others, such as cisplatin (CPT), doxorubicin (DOX), bleomycin (BLEO) and daunorubicin (DAU) have been classified as probable/possible carcinogens [4]. Given the advances in medical research and the release of new therapies every year, there is yet no information regarding the toxicity of many other cytostatics, which may also have toxic effects on both animal and human health. Therefore, the spread and accumulation of these pharmaceuticals in natural water bodies poses a great environmental and human threat.

The occurrence of cytostatics in wastewaters and environmental waters has been reported in many countries, suggesting that they are not being effectively degraded/removed by conventional wastewater treatments [5]. As an example, Gouveia and co-workers detected bicalutamide (BICA), capecitabine (CAP), cyclophosphamide (CYC), ifosfamide (IFO) and mycophenolic acid in the tertiary effluents of a Portuguese wastewater treatment plant (WWTP), operating with a tertiary treatment by UV radiation. According to Gouveia et al. [6], several cytostatics have been detected in WWTP effluents worldwide: CYC (25 ng/L), IFO (up to 2900 ng/L), TAM (up to 369 ng/L), methotrexate (68 ng/L), platinum drugs (up to 1200 ng/L), mycophenolic acid (395–874 ng/L), epirubicin (up to 24,800 ng/L), etc. This clearly highlights the inefficiency of the most conventional degradation treatments used in the WWTPs for the removal of cytostatics. The authors have concluded that most cytostatics exhibited a non-significant concentration decrease at WWTPs, even at those equipped with tertiary treatment by sand filtration, ozonation, UV radiation, chlorine disinfection, trickling filters, membrane bioreactor or oxidation ditches [7–13]. Consequently, these hazardous medicinal products are discharged into receiving water bodies, contributing to their detection in surface waters worldwide and their spread throughout the environment. In this sense, concentrations up to 1907 ng/L CYC and 578 ng/L 5-fluorouracil (5-FU) have been detected in river waters in Thailand [14].

With the aim of overcoming this issue, advanced oxidation processes (AOPs) have been taken into consideration to improve the degradation of cytostatics in WWTPs, but the formation of byproducts that are more toxic or exhibit a different toxicity profile than the parent drug is frequently reported [15]. Thus, adsorption processes emerge as a valuable pre- or post-treatment technology to improve the quality of the final effluent by reducing the residual amounts of cytostatics and also retaining undesired byproducts [16]. Other possible applications of adsorption processes for wastewater treatment can be dye removal [17], contaminant removal from biological samples [18] acting as an analog of hospital wastewaters and hard water softening [19], among many others.

For the first time, this work aims to compile and present a comprehensive review on the use of adsorption and its combination with other processes for the removal of cytostatics from aqueous streams. Additionally, critical points that should be considered in the implementation of this type of technologies are addressed from an economical and environmental (life cycle assessment) perspective. Therefore, this work aims to guide future research, bridge knowledge gaps, and contribute to the safeguarding of environmental integrity, resilience and sustainability.

2. Literature Search

Scientific documents related to this review were obtained from the SCOPUS database. For that, multiple combinations of the following keywords were applied: cytostatics (along with its synonyms antineoplastic agents, cytotoxic drugs and anticancer drugs),

adsorption, separation, carbon-based materials, wastewater treatment, sorbents and life cycle assessment. Only original articles written in English and published until July 2023 were retained. Duplicates were removed and the first selection was based on the title. Further screening was performed through abstract analysis, resulting in a total of 22 publications dealing with cytostatics' adsorption that matched our inclusion criteria.

The publications were categorized according to the type of treatment process applied to the water: adsorption as a stand-alone process (Section 3—Adsorption), or adsorption as a pre- or post-treatment process (Section 4—Hybrid Technologies).

3. Cytostatics' Adsorption

The removal of cytostatics in the aqueous phase by means of adsorption has drawn the attention of researchers over the past decades, and different commercial and tailor-made sorbents are being exploited for this purpose. The discussion of the available results is thus organized by the type of sorbent employed in the treatment process: carbon materials, bio-sorbents, Fe₃O₄-based materials and others.

3.1. Carbon Materials

Due to their low cost and versatility, carbon materials have been widely employed for adsorption of micropollutants in WWTP effluents [16,20]. Regarding cytostatics' removal, activated carbon (AC), carbon black (CB), carbon nanotubes (CNT) and graphene oxide (GO), amongst others, have been employed for this purpose, as shown in Table 1.

Macedo et al. studied the adsorption of 5-FU in ultrapure water on different commercial ACs and CBs [21]. These materials were used as a powder (particle size: 212–600 µm) using 5-FU concentrations between 1 and 10 mg/L at 30 °C for 24 h to ensure that the adsorption equilibrium was reached. Adsorption isotherms were fitted to the Langmuir, Freundlich and Temkin models, the first one being the best model to describe the system. The adsorption capacity of the studied materials varied between q_e : 18.7 mg/g (CB—Vulcan) and 111.9 mg/g (CB—BP2000). The adsorption capacity had a linear correlation with the surface area (S_{BET}) and the oxygen content of the materials, which suggests a monolayer adsorption that takes place preferentially on the surface oxygen groups of the sorbent.

Also employing commercial AC (Calgon), Chen et al. studied the removal of irinotecan (IRI), TAM and CYC in ultrapure water [22]. In their work, which used a significantly lower concentration of cytostatics (C_{cyt} : 10 µg/L) at neutral pH in NaHCO₃ buffer, they observed an increase in the cytostatic elimination when increasing the AC dose, reaching a 90% removal after 4 h using 100 mg/L of sorbent. TAM was more easily retained, followed by IRI and finally CYC. Despite the good results obtained, no sorbent characterization was provided. Furthermore, the authors stated that changes in the pH may affect the process, but since real effluents present pH values around 7, they did not test other conditions.

Folens et al., performed a comparison amongst different sorbents for Pt recovery from platinum-based cytostatics (cisplatin (CPT), carboplatin (CBP), oxaliplatin (OXA)) in synthetic urine [23]. This Pt recovery was evaluated through cytostatic adsorption and microwave-assisted acid digestion of the sorbents for Pt extraction, which was measured in an inductively coupled plasma–mass spectrometry analyzer. As carbon materials, they tested granular activated carbon (GAC) and a biochar obtained by the pyrolysis of bench wood at 550 °C in a N₂ atmosphere, finding a significantly higher Pt recovery when using the commercial GAC (45%) than with biochar (24%). These same experiments were performed for CPT in ultrapure water, reaching up to 75% CPT removal. Therefore, the effect of the matrix constituents plays a key role, which should be considered when studying these processes.

In this sense, Kovalova et al. studied the use of powdered activated carbon (PAC) and activated lignite for the removal of cytarabine (CytR) and 5-FU in ultrapure water and WWTP effluent [24]. These matrices were spiked with 200 µg/L of each cytostatic prior to the adsorption tests. Under the studied conditions, both drugs presented a neutral charge,

whereas the sorbents presented a positively charged surface, which favors the adsorption. When increasing the pH of the solution, the removal efficiency of 5-FU decreased due to a lower number of positively charged groups on the carbon surface. This effect was not as significant when using CytR, as the molecule remained neutral over the whole studied pH range. As a result, at a pseudo-equilibrium contact time of 16 h, a 70% 5-FU and CytR removal were achieved at PAC doses of 90 and 30 mg/L, respectively. When using activated lignite, the required sorbent dose rose to 200 and 140 mg/L, respectively. This latter material presents a higher particle size and a smaller surface area. In this study, it is signaled that the presence of organic matter in WWTP effluents greatly lowered the adsorption uptake of both cytostatics, as may be seen in Figure 1. This figure, which compiles the relation between surface area and 5-FU adsorption capacity for various carbon materials, shows that the adsorption capacity of AC drops down very remarkably when employing real matrices. According to Kovalova et al., the effect of the organic matter had a greater impact on the removal rate than the pH, ionic strength or temperature [24]. This is due to the competition between the background organic matter and the target pollutants for the adsorption sites. Therefore, an increase in the sorbent dose may overcome this drawback.

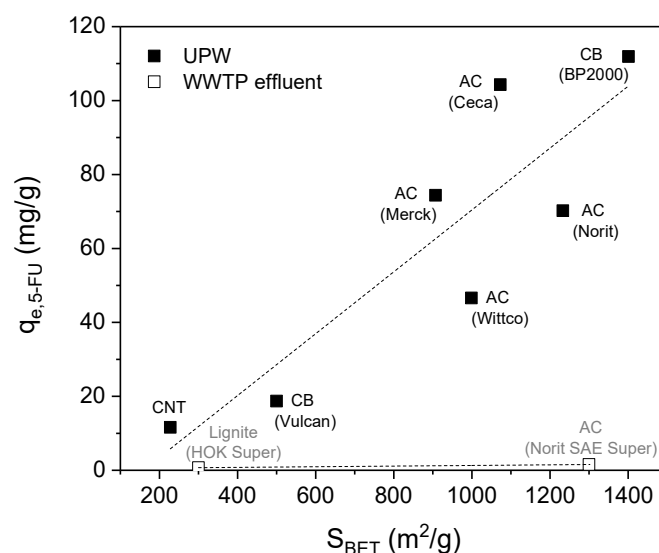


Figure 1. Relation between 5-FU adsorption capacity and the surface area of the carbon materials in ultrapure water and WWTP effluents [21,24,25]. Dotted lines = linear fitting.

Besides AC, other carbonaceous materials are gaining attention in adsorption processes. Carbon nanotubes (CNT) have been employed for the removal of CYC, IFO and 5-FU by Tonski et al. [25,26]. This kind of material presents a stable performance regardless of the employed pH with a very quick adsorption equilibrium reached in 20 min [25]. Moreover, the authors proved that no negative impact on the sorption capacity of any of the target cytostatics would be expected after five cycles of contamination–thermal regeneration [26]. Compared to AC and CB, CNT presents a significantly lower 5-FU adsorption capacity, as shown in Figure 1. Nonetheless, it seems that the adsorption capacity of cytostatics on CNT can be modulated with sorbent surface modifications. Masouleh et al., tuned the properties of multi-walled CNT by carboxylation followed by acylation with dimethyl formamide and an esterification step for imatinib (IMA) adsorption [27]. This process increased the surface oxygen groups available on the sorbent surface, which resulted in an enhancement of the adsorption capacity, with an increase from q_e : 480 mg IMA/g CNT on the carboxylated CNT to q_e : 2920 mg IMA/g CNT on the acylated and esterified CNT. However, the particle size of CNT is in the nanometer range, which limits its real application for water polishing due to the difficulties related to their separation from the aqueous phase. This drawback must also be considered when applying GO as a sorbent, despite its great adsorption capacity, as reported by Wu et al. [28]. Despite the low

surface area of GO, the agglomeration of GO sheets results in a mesoporous material that presents a quick adsorption and equilibrium time (10 min), due to the one-atom layered structure and the effect of surface oxygen groups, in which DOX is adsorbed by H-bonding.

It should be noted that most of the works presented in this section were performed in ultrapure water using unrealistic concentrations of cytostatics (most of them in the range of mg/L). Whilst the adsorption mechanisms may be studied in these conditions to understand the interactions between the target pollutants and the sorbents, these investigations are very limited towards the implantation of these technologies in WWTP. The interference of other organic and inorganic constituents present in real water matrices decreases the efficiency of these processes, diminishing the sorbent lifetime and augmenting the operating costs.

Table 1. Adsorption of cytostatics on carbon materials.

Cytostatic	Matrix	Sorbent	Sorbent Characterization	Operating Conditions	Results	Ref.
5-FU	Ultrapure water	AC (Ceca)	pH _{PZC} : 5.6, S _{BET} : 1073 m ² /g, V _p : 0.57 cm ³ /g, C: 78.9%, O: 19.6%, ash: 5.6%	Sorbent: 90 mg/L, C _{5-FU} : 1–10 mg/L, pH: not specified, V: 500 mL, V _{agit} : 88 rpm, T: 30 °C, t: 24 h	q _e : 104.3 mg/g	[21]
		AC (Merck)	pH _{PZC} : 11, S _{BET} : 907 m ² /g, V _p : 0.43 cm ³ /g, C: 89%, O: 10%, ash: 4.8%	Sorbent: 40 mg/L, C _{5-FU} : 1–10 mg/L, pH: not specified, V: 500 mL, V _{agit} : 88 rpm, T: 30 °C, t: 24 h	q _e : 74.4 mg/g	
		AC (Norit)	pH _{PZC} : 6.8, S _{BET} : 1233 m ² /g, V _p : 0.49 cm ³ /g, C: 89%, O: 9.1%, ash: 5.2%	Sorbent: 60 mg/L, C _{5-FU} : 1–10 mg/L, pH: not specified, V: 500 mL, V _{agit} : 88 rpm, T: 30 °C, t: 24 h	q _e : 70.2 mg/g	
		AC (Wittco)	pH _{PZC} : 6.9, S _{BET} : 999 m ² /g, V _p : 0.50 cm ³ /g, C: 92.6%, O: 4.2%, ash: 0.3%	Sorbent: 90 mg/L, C _{5-FU} : 1–10 mg/L, pH: not specified, V: 500 mL, V _{agit} : 88 rpm, T: 30 °C, t: 24 h	q _e : 46.6 mg/g	
		CB (BP 2000)	pH _{PZC} : 8.9, S _{BET} : 1401 m ² /g, V _p : 3.11 cm ³ /g, C: 99%, ash: <0.2%	Sorbent: 60 mg/L, C _{5-FU} : 1–10 mg/L, pH: not specified, V: 500 mL, V _{agit} : 88 rpm, T: 30 °C, t: 24 h	q _e : 111.9 mg/g	
		CB (Vulcan)	pH _{PZC} : 2.7, S _{BET} : 500 m ² /g, V _p : 1.33 cm ³ /g, C: 100%	Sorbent: 90 mg/L, C _{5-FU} : 1–10 mg/L, pH: not specified, V: 500 mL, V _{agit} : 88 rpm, T: 30 °C, t: 24 h	q _e : 18.7 mg/g	
CPT	Urine (synthetic)	Biochar	pH _{PZC} : 7.3	Sorbent: 10 g/L, C _{cyt} : 100 µgPt/L, V: 20 mL, pH: 4, t: 24 h	Pt recovery: 24% q _e : 0.664 mg Pt/g	[23]
		GAC (Merck)	pH _{PZC} : 7.1		Pt recovery: 45% q _e : 1.21 mg Pt/g	
CytR, 5-FU	Ultrapure water and WWTP effluent	Activated lignine (Hok SUPER)	pH _{PZC} : 10, S _{BET} : 300 m ² /g, dp: 24 µm	Sorbent: 0.5 g/L, C _{cyt} : 200 µg/L, pH: 7.8 (phosphate buffer), V: 400 mL, V _{agit} : 100 rpm, T: 20 °C, t: 21 h	q _e 5-FU: 0.7 mg/g, X _{5-FU} : 70% q _e CytR: 1 mg/g X _{CytR} : 70%	[24]
		PAC (Norit SAE SUPER)	pH _{PZC} : 9.8, S _{BET} : 1300 m ² /g, dp: 15 µm		q _e 5-FU: 1.56 mg/g X _{5-FU} : 70% q _e CytR: 4.67 mg/g X _{CytR} : 70%	[24]
CYC, IFO	Hospital wastewater	PAC (Norit SAE SUPER)	pH _{PZC} : 9.8, S _{BET} : 1300 m ² /g, dp: 15 µm	Sorbent: 8 ± 4, 23 ± 7 and 43 ± 14 mg/L; C _{CYC} : 185 ng/L; C _{IFO} = 10 µg/L	X _{CYC} : 41 ± 6% > 73% X _{IFO} : 24 ± 0% > 60%	[29]
CYC, IFO, 5-FU	Ultrapure water	CNT (Cheap Tubes)	pH _{PZC} : 9.5, S _{BET} : 228 m ² /g, l: 10–30 µm, d: 8 nm, C > 95%, Ashes: <1.5%	Sorbent: 0.1–10 g/L, C _{cyt} : 0.625–150 mg/L, pH: 4–10, CaCl ₂ : 0–0.1 M, V: 10 mL, T: not specified, t: 24 h	q _e CYC: 27.3 mg/g q _e IFO: 18.2 mg/g q _e 5-FU: 11.6 mg/g	[25]

Table 1. Cont.

Cytostatic	Matrix	Sorbent	Sorbent Characterization	Operating Conditions	Results	Ref.
CYC, IRI, TAM	Ultrapure water	AC (Calgon)	No characterization available	Sorbent: 0.1–100 mg/L, C_{IRI} : 10 µg/L, pH: 7.1 (4 mM NaHCO ₃), t: 4 h	$X_{CYT} > 90\%$	[22]
DOX	Ultrapure water	GO	S_{BET} : 32 m ² /g, V_p : 0.11 cm ³ /g, Negative surface charge.	Sorbent: 600 mg/L, C_{DOX} : 350 mg/L, V: 10 mL, pH: 3.4–8.5, T: 15–37 °C, t: 2 h	q_e : 1428.6 mg/g	[28]
IMA	Ultrapure water	Modified CNT	No characterization available	Sorbent: 0.1–10 g/L, C_{IMA} : 0.4–1.8 g/L, V: 5 mL, T: 25 °C, t: 6 h	X_{IMA} : 97% q_e : 2920 mg/g	[27]

3.2. Fe₃O₄-Based Materials

Despite the use of magnetite (Fe₃O₄)-based materials not yet being very extended for cytostatics' adsorption, it presents numerous advantages. First of all, the magnetic properties of Fe₃O₄ nanoparticles make them interesting for the sake of an easy recovery using a magnetic field. Furthermore, the presence of iron on the core of these materials allows an easy sorbent regeneration using H₂O₂ in Fenton-like reactions, as recently presented by Munoz et al. for the adsorption and subsequent abatement of micropollutants [30].

Nonetheless, magnetite usually presents a very low surface area (S_{BET} : 8 m²/g) [31] and, consequently, a reduced adsorption capacity, which can be practically negligible [31,32]. Hence, researchers have worked on the introduction of organic surface groups or the deposition of porous coatings to increase the adsorption capacity of these materials. The results obtained for cytostatics' removal in the aqueous phase with Fe₃O₄-based materials are collected in Table 2.

Table 2. Adsorption of cytostatics on Fe₃O₄-based materials.

Cytostatic	Matrix	Sorbent	Sorbent Characterization	Operating Conditions	Results	Ref.
DOX	Ultrapure water	Fe ₃ O ₄ /SiO ₂	S_{BET} : 130.5 m ² /g	No information available	q_e : 18.8 mg/g	[33]
DOX	Ultrapure water and WWTP effluent	Fe ₃ O ₄ nanoparticles	S_{BET} : 95.8 m ² /g, d_p : 10–30 nm	Sorbent: 0.5 g/L, C_{DOX} : 20 mg/L, V: 20 mL, T: 30 °C, pH: 3–9, t: 48 h	q_e : 32 mg/g X_{DOX} , WWTP effluent: 73.6% X_{DOX} , ultrapure water: 80.2%	[34]
DOX	0.9% NaCl solution	Fe ₃ O ₄ nanoparticles	S_{BET} : 9.57 m ² /g, d_p : 21.6 nm	C_{DOX} : 10–20 mg/L, pH: 7, t: 45–90 min	q_e : 17.5 mg/g X_{DOX} : 80%	[32]
DOX, IMA	Well water and WWTP effluent	Fe ₃ O ₄ /GO	No characterization available	Sorbent: 160 mg/L, C_{DOX} : 4 mg/L, C_{IMA} : 4 mg/L, V: 250 mL, pH: 2–10, t: 15 min	q_e : 56.4 mg/g	[35]
TAM	Ultrapure water, tap water and pharmaceutical manufacturing WW	Fe ₃ O ₄ /SiO ₂ /PAMAM-CS	pH_{PZC} : 6.0 d_p : 60 nm	Sorbent: 3–20 g/L, C_{TAM} : 20 mg/L, V: 1.5 mL, T: 25 °C, pH: 4–9, t: 45 min	q_e : 20.5 mg/g X_{TAM} , ultrapure water: 99.7% X_{TAM} , Pharmaceutical wastewater: 99.3%	[36]

Tuan et al. tried the use of different coatings on Fe₃O₄ nanoparticles using either citrate ions or SiO₂, finding in the latter a greater adsorption capacity [33]. The SiO₂-coated sorbent, which presented a surface area of S_{BET} : 130.5 m²/g, was tested against DOX, finding a monomolecular layer adsorption mechanism with q_e : 18.8 mg/g. Also to eliminate DOX, Weng et al. synthesized Fe₃O₄ nanoparticles using *Euphorbia Cochinchinensis* extract as organic media to confer superficial organic groups to the final nanoparticles [34]. This

organic coating resulted in an increased surface area of S_{BET} : 95.8 m²/g and a sorption capacity of q_e : 32.0 mg/g. Therefore, it seems that rather than the surface area, the chemistry surface of these materials plays a key role. Additionally, Weng et al. discovered that DOX removal was partially hindered when decreasing the operating pH, with a 57% DOX removal at pH 3 against up to a 87% DOX uptake at pH 7.

Arvand et al., developed a Fe₃O₄/GO composite for DOX and IMA recovery for analytical purposes [35]. They prepared various materials, modifying the GO content of the samples: when using an Fe₃O₄:GO ratio of 10, a cytostatic adsorption capacity of q_e : 56.4 mg/g was reached, which is significantly higher than the values previously presented. IMA could be efficiently retrieved regardless of the operating pH in a range of 2–10, whereas DOX hydrolyzed at pH > 8. The most interesting feature of this work is the selective retention of DOX and IMA in presence of other cytostatics such as GEM and CAP.

Ghoochian et al. produced novel sorbents using an Fe₃O₄ core covered by a SiO₂ substrate on which a polyamidoamine/chitosan (PAMAM-CS) polymer was anchored [36]. Since this polymer is thermosensitive, at temperatures lower than the lower critical solution temperature (LCST), the polymeric adsorbent is soluble in water, favoring the adsorption. Contrarily, at $T > \text{LCST}$, the polymer goes to a non-soluble state of expansion, releasing the adsorbed TAM. These researchers found a maximum adsorption at pH 8; at higher pH values, a complexation between TAM and the sorbent diminished the process efficiency. This material was tested using ultrapure water, tap water and pharmaceutical wastewater, reaching in all cases $X_{\text{TAM}} > 99\%$. Moreover, regeneration with MeOH + NaOH (0.1 M) combined with ultrasound allowed a 98% TAM recovery and a stable performance over 10 adsorption–desorption cycles.

3.3. Biological Adsorbents

The removal of pollutants by biological adsorbents can be performed either with living or non-living biomass. Biosorption is an adsorption process where the adsorbent is deactivated (non-living) biomass, such as agricultural residues, wood sawdust, deactivated microorganisms, deactivated algae, fruit wastes and other plant biomasses. If the biomass is active (or living), the process is defined as bioaccumulation [37,38]. Table 3 gathers the results found in the literature for the removal of cytostatics using biological materials.

Habibzadeh et al. studied the removal of flutamide (FLU) using living *Chlorella vulgaris* microalgae as a sorbent in ultrapure water with 20% MeOH [39]. This study evaluated the contact time between 10 and 120 min, the sorbent concentration from 0.5 to 4.1 g/L and the operation pH. The dead biomass of the freshwater microalga presented a sorption capacity of 12.5 mg/g. This value increased more than twofold (q_e : 26.8 mg/g) when working with living algae. Regarding the influence of pH, maximum FLU removal was obtained in both cases (i.e., dead and living biomass) at acidic pH. When increasing the pH, the microalgae surface becomes negatively charged, due to the deprotonation of carboxylic, phosphoric and amine groups, and FLU loses the NH group, also becoming negatively charged. Therefore, at neutral to basic pH, there is a repulsion between FLU and *Chlorella vulgaris*, which diminishes the sorption capacity. For living biomass and a starting FLU concentration of 84 µg/L, optimum conditions were found to be pH = 1.07, $t = 117$ min and a biomass concentration = 5 g/L, achieving a 98.5% FLU removal. The use of microalgae as a sorbent seems interesting due to their low cost and environmental-friendly nature. The non-living biomass is not affected by the toxicity of the pollutants, being able to treat heavily polluted streams, and requires less maintenance and space compared to living biomass. On the other hand, living cells have been found to be efficient when the pollutant concentration is low [39]. Still, there is no information on how to treat the sorbent after use, or even if dead microalgae can be regenerated and reused as sorbent.

Jureczko and Przysaś studied the biosorption of two cytostatics, BLEO and vincristine (VIN), by five white-rot fungi: *Fomes fomentarius*, *Hypholoma fasciculare*, *Phyllotopsis nidulans*, *Pleurotus ostreatus* and *Trametes versicolor* [40]. They found that among live biomass, *T. versicolor* had the greatest sorption ability for BLEO (0.1730 mg/g), whereas *P. nidulans*

worked best for VIN (0.1791 mg/g). Nevertheless, it was proven that inactive (dead) fungal biomass generally has a greater sorption ability for these two cytostatics [40].

Lenz et al. studied bioaccumulation using active sludge as a sorbent for platinum-based cytostatics (CPT, CBT and OXA) in real matrices, urban wastewaters and hospital wastewaters [41,42]. In this case, the efficiency of the process is followed by means of Pt sorption on the active sludge measured by inductively coupled plasma–mass spectrometry. The wastewater employed was spiked at cytostatic concentrations similar to those found in an oncologic ward in Vienna (1.77–144 µg/L), with the cytostatics' sorption being evaluated on suspended solids in raw wastewater and on the microorganisms in the active sludge. Suspended solids in wastewater were found at 50.5 mg/L. At pH = 7, these solids were able to remove 88% of CPT, 26% of CBT and 54% of OXA. On the other hand, active sludge at 4.2 g/L achieved higher removal rates, with 96%, 70% and 74% elimination of CPT, CBT and OXA, respectively. Different wastewaters were evaluated, finding no clear relation between the concentration of suspended solids and cytostatics' removal. Nonetheless, when testing different inoculums of active sludge, there was a good reproducibility with a stable performance regardless of the employed sludge sample [41].

A second work by this same group was developed working in a membrane bioreactor (MBR), using real hospital wastewater from an oncologic ward [42]. This work confirmed that Pt removal partially took place due to the suspended solids present in the raw wastewater and to adsorption on the active sludge. The authors found that the Pt sorption capacity increased from 7.1 µg/g in the first 30 days of operation to 175 µg/g after 365 days, demonstrating a high accumulation capacity in MBR systems.

Table 3. Biological adsorbents applied to the removal of cytostatics from waters and wastewaters.

Cytostatic	Matrix	Sorbent	Operating Conditions	Results	Ref.
BLEO, VIN	Ultrapure water	<i>F. fomentarius</i> , <i>H. fasciculare</i> , <i>P. nidulans</i> , <i>P. ostreatus</i> and <i>T. versicolor</i>	Sorbent: 10 g/L, C_{cyt} : 5–15 mg/L, t: 4 h, T: 22.5 °C, pH_{BLEO} : 4.5; pH_{VIN} : 3.6	$q_{\text{e BLEO}}$: 0.1730 mg/g $q_{\text{e VIN}}$: 0.1791 mg/g	[40]
CPT, CBT, OXA	Urban wastewater	WWTP active sludge	C_{cyt} : 5 µg/L, Act sludge: 4.2 g/L, pH: 7	X_{CPT} : 96% X_{CBT} : 70% X_{OPT} : 74%	[41]
CPT, CBT, OXA	Hospital wastewater	Active sludge (MBR)	C_{cyt} : 3–250 µg/L, Act. sludge: 12–15 g/L, pH: 7–9	X_{cyt} : 28–34% q_{e} : 175 µg Pt/g	[42]
FLU	Ultrapure water + 20%v MeOH	<i>Chlorella vulgaris</i> (microalgae)	Sorbent: 0.5–4.1 g/L; C_{FLU} : 100 mg/L; pH: 1–8; t: 10–120 min	Dead algae— q_{e} : 12.5 mg/g; Living algae— q_{e} : 26.8 mg/g	[39]

3.4. Other Sorbents

This section analyzes the use of clays and other sorbents for the removal of cytostatic drugs, collected in Table 4. Despite clays such as saponite, montmorillonite, kaolin, etc. having been widely employed for the elimination of micropollutants in the aqueous phase, there is only one work in the literature addressing the use of these materials for cytostatic drugs. Akalin et al. studied the adsorption of 5-FU on natural smectite clays (montmorillonite and saponite) [43]. Montmorillonite and saponite are clays that belong to the smectite group and are made up of stacked aluminosilicate layers. They are known for their ability to adsorb many types of compounds in their interlayer space, resulting in an intercalation type of inclusion compounds [43]. Adsorption tests were carried out, putting 5-FU in contact with the clays for two days. Afterwards, they performed Fourier-transform infrared spectroscopy analyses to see the interactions between 5-FU and Al_2O_3 . They found out that 5-FU adsorption was augmented with the basal spacing of the clays from 12 Å to

15 Å, indicating that the drug intercalation into the interlayers of the clays takes place as monolayers. 5-FU molecules adsorbed on the clays are coordinated to Lewis acidic centers directly or indirectly through water bridges. Despite this interesting and detailed view of the adsorption mechanism, the specific operating conditions and the adsorption capacities are not reported in this work.

Aghagoli et al., worked on the development of $\text{CaFe}_2\text{O}_4/\text{MoS}_2$ magnetic composites for the elimination of paclitaxel (PTX) [44]. MoS_2 is a 2D transition metal dichalcogenide that presents good adsorption properties due to its layered structure. Nonetheless, its recovery is not easy due to the low particle diameter. Hence, these authors proposed the synthesis of magnetic composites to enhance the recoverability of the sorbent. This material was tested in the adsorption of a 5 mg/L PTX aqueous solution for 20 min, evaluating the effect of pH in the range from pH = 2 to pH = 9. Results showed an increase in PTX removal, as pH rose up to pH = 7. At pH < 4, both the MoS_2 and PTX were protonated, resulting in their repulsion. At $5 < \text{pH} < 7$, the sorbent presented a positive charged surface, and the PTX was negatively charged, resulting in increased adsorption rates. Finally, at alkali pH, there was again a repulsion between the sorbent and PTX, both of them being deprotonated. After determining the adsorption capacity at 68.96 $\text{mg}_{\text{PTX}}/\text{g}$, PTX desorption was studied employing different solvents (MeOH, propanol, acetonitrile, acetone and chloroform). The best results were obtained using MeOH acidified with HNO_3 0.1 M, with a PTX recovery of 98.2%. After five adsorption–desorption cycles, the $\text{CaFe}_2\text{O}_4/\text{MoS}_2$ maintained its adsorption capacity. Furthermore, different water matrices were tested for analytical purposes. In both well water and tap water, PTX recovery was around 96–100%.

Folens et al. tested chitosan and wood ash as low-cost sorbents for the removal of CPT in synthetic urine [23]. The chitosan used was purchased and the wood ash was produced from the burning of beech wood, while dried. Despite the environmental advantage of using these types of agricultural byproducts as sorbents, their adsorption capacity was inferior to that presented in the same work for activated carbon, as seen in Table 1.

Farias et al. synthesized a macroporous cryogel by the polymerization of methacrylic acid and 2-hydroxyethyl methacrylate for the adsorption of CPT [45]. Cryogels are composed of a polymeric network with controlled microporosity ($d_{\text{pore}} = 1\text{--}100 \mu\text{m}$), which allows tuning the materials' porosity for the adsorption of specific compounds. These substantial pores within cryogels are meticulously generated through cryogelation polymerization conducted at sub-zero temperatures. This macroporous architecture retains its stability under ambient conditions. Leveraging the substantial porosity, cryogels facilitate efficient mass transfer. Furthermore, the interconnected channels, characterized by macro-metric dimensions, accommodate the flow of particulate-laden fluids, such as wastewater, at elevated rates while minimizing back pressure [45]. Batch adsorption experiments were carried out using up to 2 g/L CPT in aqueous phase and 10 g/L cryogel, with a contact time of 24 h. The adsorption capacity of this material (q_e : 250 $\text{mg}_{\text{CPT}}/\text{g}$) was notably superior to those reported for the rest of the materials considered in this review. Furthermore, this cryogel was stable for 15 cycles, using 2 mM NaOH as the desorbing agent. This seems to be one of the most promising sorbents. Still, there is no information regarding its performance in more complex water matrices.

Finally, Wilczewska et al. synthesized a novel photocatalyst, $\text{BiOCl}_n\text{Br}_m$, using the solvothermal method, varying the molar ratio of halogen ions Cl^- to Br^- ($x = 0.0\text{--}2.0$), for the removal of IMA and 5-FU [46]. The influences of the photocatalysts dose and pH of the solution during the photocatalytic processes were explored, as well as the mechanisms of degradation, the formation of intermediates and the effluents' toxicity towards *Chlorella vulgaris*. The $\text{BiOCl}_{1.3}\text{Br}_{0.7}$ combination was proven to be the best for cytostatic drugs' elimination, achieving total removal of 5-FU and IMA (both individually and mixed) at the highest rate constant, along with a reduction in the effluents' toxicity after photocatalytic degradation.

Table 4. Clays and other sorbents employed for cytostatics' removal.

Cytostatics	Matrix	Sorbent	Operating Conditions	Results	Ref.
5-FU	Unknown	Montmorillonite and saponite	Not specified	5-FU is adsorbed in monolayer onto Lewis acidic centres.	[43]
CPT	Ultrapure water	Macroporous cryogel	Sorbent: 10 g/L; C _{CPT} : 0.5–2 g/L; V, pH: not specified; t: 48 h	q _e : 250 mg/g	[45]
CPT	Urine (synthetic)	Chitosan Wood ash	Sorbent: 10 g/L, C _{cyt} : 100 µgPt/L, V: 20 mL, pH: 4, t: 24 h	Pt recovery: 36% q _e : 0.974 mgPt/g Pt recovery: 5% q _e : 0.225 mgPt/g	[23]
IMA, 5-FU	Ultrapure water	BiOCl _{1.3} Br _{0.7}	S _{BET} : 53.9 m ² /g, Sorbent: 0.2 g/L, pH _{ZPC} : 6.35, C _{cyt} : 15 mg/L, pH: 3–10.5	X _{cyt} : 100%	[46]
PTX	Well water, tap water and Ultrapure water	CaFe ₂ O ₄ /MoS ₂	Sorbent: 0.8 g/L; C _{PTX} : 5 mg/L; V: 25 mL; pH: 2–9; t: 20 min	q _e : 68.96 mg/g	[44]

4. Hybrid Technologies

The combination of two or more treatment processes (hybrid technologies) can be a promising mechanism for removing several contaminants, with different physical and chemical properties, from wastewater. The purpose of this section is to present a thorough overview of research and hybrid strategies that have been documented in the literature that combine adsorption with other treatment methods to break down cytostatics from water.

As far as the authors are aware, there has not been much research carried out on using hybrid technologies to remove cytostatics from waters, with only four papers found (information is depicted in Table 5).

Kazner et al., evaluated the impact of both ACs (PAC and lignite coke dust (LCD)) and nanofiltration (NF) membranes on the degradation of endocrine disruptors and cytostatics [47]. However, the studied cytostatics (CytR and 5-FU) showed high removals using only NF membranes, as mentioned in the previous section, and hybrid technologies were not performed for these compounds.

Another study, performed by Mendonza et al., aimed to analyze the effect of ozonation + GAC, ozonation + AC and ultrafiltration (UF) + reverse osmosis (RO) in tap water [48]. However, cytostatics were not detected in this matrix and therefore they were not considered in the analysis [48].

The effect of NF + GAC on the degradation of CYC in a process with 80% water recovery was studied by Verliefe et al. [49]. Although NF itself resulted in a 32% CYC removal, the combination of this process with GAC adsorption led to a cytostatic elimination higher than 98%. The performance of the NF before the GAC adsorption increases the capacity of the AC since the largest part of the natural organic matter is removed in the NF step [49].

Finally, Lenz et al., complemented MBR with AC and UV with AC for the degradation of cancerostatic platinum compounds (CPCs), 5-FU, DAU, DOX and epirubicin (EPI). However, 5-FU, DAU, DOX and EPI were not detected in the influent of the MBR [50]. Combining MBR + UV + AC resulted in lower degradation of CPCs (74% removal) when compared to the use of AC only (82% removal). An explanation relies on the fact that degradation products of CPCs show lower affinity to activated carbon [50].

While the studies listed above show the potential of adsorption-based hybrid technologies in cytostatic removal, it is clear that more thorough and in-depth research is

required. It is essential to recognize the gaps in this field, underscoring the need for ongoing investigation and advancement.

One promising direction for future research involves the integration of AOPs with adsorption-based processes. AOPs are renowned for their ability to generate highly reactive species capable of breaking down a wide range of organic contaminants, including cytostatics [15]. Combining AOPs with adsorption may yield synergistic effects, enhancing both removal efficiency and the degradation of cytostatics and their byproducts.

Future research should also consider the complexities introduced by different matrices, as these can significantly affect the performance of treatment strategies. In-depth studies across various water sources, from tap water to hospital wastewaters, are crucial to determine the adaptability and robustness of these processes.

Table 5. Hybrid technologies for cytostatics' abatement in waters and wastewaters.

Cytostatic	Matrix	Processes	Membrane Characterization	Sorbent Characterization	Operating Conditions	Results	Ref.
5-FU, CYT	WWTP effluent	PAC/LCD + NF	NF50 M10 from Norit X-Flow	PAC: Norit SAE Super; LCD: RWE lignite coke dust	C _{CYT} = 1.0–2.0 µg/L; [PAC] = 10–100 mg/L; [LCD] = 100–350 mg/L; Flux: 20 L/(m ² .h)	NF itself achieved high removals	[47]
CPCs	Hospital wastewater	MBR	Tubular ultrafiltration membrane: MOLSEPw, Nadir Filtration GmbH. Active area of 1 m ² and a nominal cut-off of 100 kDa	N/A	C _{Pt} : 3.24–266 µg/L, g; Q: 7.6 L/h	C _{Pt} : 3.24–266 µg/L, g; Q: 7.6 L/h	[50]
CPCs	Hospital wastewater	MBR + AC	N/A	GAC: Chemviron F200	C _{Pt} : 3.24–266 µg/L, Sorbent: 500 g; Q: 7.6 L/h	X _{Pt, CPC} : 82%	[50]
CPCs	Hospital wastewater	MBR+ UV + AC	N/A		C _{Pt} : 3.24–266 µg/L, Sorbent: 500 g; Q: 7.6 L/h, λ: 254 nm, E: 900 W/m ²	X _{Pt, CPC} : 74%	[50]
CYC	Surface water	NF + GAC	Trisep TS-80 TSF (MWCO: 200 g/mol) Desal HL (MWCO: 150–300 g/mol)	Norit Row Supra 0.8. Bed density: 345 kg/m ³	C _{CYC} : 100 µg/L, 0.2 m/s, flow: 400 L/h, concentration polarization factor: 1.02, 20 ± 1 °C.	X _{CYC} : > 98%	[49]
DOX, ERL, IMA, IRI, TAM, CYC, IFO, CAP	Tap water	Ozonation + GAC Ozonation + AC UF + RO	N/A	N/A	N/A	Cytostatic drugs were not detected in the studied matrix	[48]

5. Life Cycle Assessment

Nowadays, the sustainability issue has become a high priority for water and wastewater treatment processes. In this context, life cycle assessment (LCA) has emerged as a tool for assessing the net impact (difference between the generated and avoided impacts) on the environment due to the implementation of a certain technology for water treatment, avoiding the “problem shift”. The environmental burden includes all types of impacts to the environment (e.g., depletion of natural resources; energy consumption; pollutants emission to land, water and air) coming from any step of the process: the extraction and preparation of raw materials, manufacturing, distribution, operation/use, repair/upgrade/maintenance and final disposal or recycling.

Physical adsorption using AC is one of the most established processes for organic and inorganic pollutants' removal. In Europe, the AC used in WWTPs is usually manufactured from non-renewable resources (fossil-based materials), which have a significant environmental burden [51]. This and the rapid growth of AC demand have provided a market opportunity for renewable and low-impact biobased products, as alternatives to conventional raw materials. Given the large number of potential feedstocks (e.g., agricultural wastes, wood and herbaceous plants), it is imperative to understand the environmental implications of producing ACs from these alternatives, especially given that the production process is currently referred to as the main contributor to the generated impacts in previous LCA studies [52–54]. Agricultural byproducts and other lignocellulosic materials seem to have environmental advantages over coal-based carbons in terms of acidification potential, non-renewable energy demand and carbon footprint [55,56]. Furthermore, economic advantages were noticed due to the reduction of waste-disposal costs (landfill or incineration) and environmental-restoration costs. Joseph and co-workers found that the production of AC from residual biomasses resulted in a lower global-warming potential and cumulative energy demand in comparison to fossil-based sources [51]. For instance, the production of AC from wood waste was shown to result in a reduction in the global warming potential that was approximately 1.14 kg CO₂-eq higher than coconut shells, 11.1 kg CO₂-eq higher than olive waste and on average 9.69 kgCO₂-eq higher than coal [57]. However, large variations in the environmental burdens associated with AC production from different biomass feedstocks can be observed: energy consumption may vary between 43.4 and 277 MJ/kgAC and the emission of greenhouse gases may vary between 3.96 and 22.0 kgCO₂-eq/kgAC [58].

Notwithstanding, it should be kept in mind that both raw material properties and process parameters have a large influence on the characteristics of ACs and, consequently, on the removal efficiency of highly toxic pollutants (such as cytostatics), which should not be disregarded when attending to its strong impact to the environment. As was shown in previous sections, ACs produced from different sources have distinct performances in terms of cytotoxicity removal. In some cases, ACs produced from agricultural and wood wastes have been found to have comparable contaminant removal capacities to coal-based ACs [59], but the sustainability of the process should be studied case-by-case, ensuring more informed decision making related to biomass selection, technology investment, process design and optimization.

Regarding the adsorption process itself, the current knowledge on LCA analysis has found that PAC generates higher impacts to the environment than GAC, mostly in the climate change and (eco)toxicity categories [60]. Along with the latter, the carbon footprint of μ GAC is lower than that of GAC (c.a. 0.02–0.03 kgCO₂-eq/m³ vs. 0.25 kgCO₂-eq/m³) [60,61]. Furthermore, the fluidized bed process operated with μ GAC has shown to require a smaller amount of AC dosage while keeping the removal efficiencies of emerging pollutants at high standards [62]. The combination of the adsorption process with other advanced treatment technologies would bring benefits in terms of the removal/degradation of highly toxic micropollutants, such as cytostatics, resulting in a significant avoided impacts score [60]. Current findings have pointed out that AC has a similar impact (in most categories) to the environment to that of ozonation, and lower a impact than reverse osmosis (RO) and UV (with or without hydrogen peroxide) [63].

Another issue of concern is the proper end-of-life management of adsorbents. Currently, the most common end-of-life options are regeneration and recycling of the adsorbents, incineration for energy recovery and landfill disposal [64]. In some EU countries, many industries had to close their internal landfills by 2020, which had moved the scientific community towards the development of new technically and economically feasible end-of-life treatment alternatives for adsorption materials. Meanwhile, incineration has become increasingly attractive. To date, the study of the impact of different end-of-life treatment options for adsorbents has been neglected [65].

6. Overview and Perspectives

So far, as presented in this review, there are only a few works addressing the removal of cytostatic drugs in the aqueous phase employing adsorption technologies. The 22 works analyzed focused their attention on 18 cytostatic drugs within different water matrices. Still, the majority of these investigations were performed in ultrapure water (68%), generally employing unrealistic cytostatic concentrations, with 63% of the papers working in the range of mg/L.

Table 6 collects a more detailed overview on the performance of each material/process in terms of scalability, potential for material regeneration, material availability and process sustainability. Due to the scarcity of specific literature on the removal of cytostatics, these strengths and weaknesses should be taken into account in addition to the specific characteristics of the pollutant in consideration when evaluating their potential and limitations in addressing the challenges of removal/degradation of these contaminants in wastewater treatment.

Furthermore, based on the gaps found in the literature, there is still room for improvement in this area towards gaining a deeper understanding of the adsorption of cytostatics in relevant environmental matrices, such as hospital wastewater, pharmaceutical manufacturing wastewater and WWTP effluents, where these processes would be implemented.

In this sense, and after the revision provided, future works should address the following issues:

- Deeper adsorbent characterization before and after the adsorption tests: these can aid in understanding the mechanisms involved and how to improve the efficiency of the process, offering a deeper insight into the effects of the chemical and textural properties of the sorbents on pollutant removal;
- Influence of the water matrix: applying the adsorption process in real environmental matrices;
- Relevant cytostatic concentrations: working in the ng/L–µg/L range, which is the concentration range in which these pollutants are generally found;
- Continuous experiments: using fixed-bed adsorption columns that allow continuous flow simulation, perform analyses of the dynamic behavior with breakthrough curves and residence times, as well as the scale-up potential of the technology [66];
- Adsorbent regeneration strategies: these are key to assess the real lifetime of the adsorbents. Furthermore, some hybrid processes such as the combination of adsorption and a subsequent advanced oxidation process might help mineralize the pollutants, aiding the move towards a cleaner technology.

Table 6. Process analysis. Legend: (+) promising results, (o) improvable results, (–) unfavorable results, (*) more research is required [67–73].

Material/Process	Process Scalability	Material Regeneration	Material Availability	Process Sustainability
Carbon materials	+	+	+	+
Magnetic adsorbents	*	+	*	+
Biological adsorbents	o	–	+	o
Other adsorbents	o	o	*	o
Hybrid processes	*	+	*	+

7. Conclusions

The adsorption of residual contaminants on different materials is a promising technique with the aim of eliminating such compounds from wastewaters, avoiding their release to the environment. The main objectives of this paper were to (i) perform a comprehensive review regarding different adsorption processes of cytostatics (pharmaceuticals used in

chemotherapy) on several materials (e.g., carbonaceous materials, Fe_3O_4 and bio-sorbents), as well as hybrid strategies resulting from the combination of adsorption with other remediation processes, and (ii) offer useful clues and highlights for the effective treatment of cytostatic drugs. In total, 22 papers regarding the adsorption of 18 cytostatics were found until July 2023, nine using carbonaceous materials, five using Fe_3O_4 , four regarding biological materials, five with other sorbents such as clays, and four papers mentioning hybrid technologies.

Adsorption was shown to provide high removal efficiencies for cytostatics in general. However, the process is highly dependent on different factors: (i) the type and concentration of the pollutant; (ii) the type and state of the sorbent; (iii) the concentration of the sorbent; (iv) the temperature of the medium; (v) the pH of the solution; and (vi) the matrix. Regarding their adsorption in carbonaceous materials, nine cytostatics were studied, showing relatively high removals (up to q_e : 2920 mg/g and 97% removal for IMA), with CPT being the one with the lowest performance (Pt recovery: 24%, q_e : 0.664 mg Pt/g). The adsorption of cytostatics using Fe_3O_4 also showed promising results, achieving removals higher than 99% for TAM using $\text{Fe}_3\text{O}_4/\text{SiO}_2/\text{PAMAM-CS}$ as a sorbent. There is a lack of studies regarding the exploitation of this type of sorbents to remove cytostatics, since only the removal of DOX, IMA and TAM was evaluated in the five papers found. Furthermore, these Fe_3O_4 -based materials have numerous advantages, such as the easy recovery using a magnetic field and the easy regeneration using a Fenton-like process, using hydrogen peroxide. The use of biological sorbents, such as algae and fungi, was shown to be a reliable technique for the removal of cytostatics from aqueous matrices, since these compounds can be easily absorbed by them. Between the four papers found, six cytostatics were studied, with removals of up to 96% for CPT achieved. In this type of adsorption, other factors, such as the fact of the sorbent being alive or dead, can also interfere with the results; generally, better results were achieved for the removal of FLU using living algae rather than dead ones. Still, the main challenge associated with biological sorbents is how to treat the sorbents after use, or even if they can be regenerated and reused. Regarding the adsorption of cytostatics on other sorbents such as clays, wood ash, chitosan, cryogels, etc., interesting results were achieved. Although the removal of CPT from urine using wood ash and chitosan resulted in relatively low removals (5% and 36%, respectively), IMA and 5-FU were totally removed from ultrapure water using the $\text{BioCl}_{1.3}\text{Br}_{0.7}$ composite.

The papers found regarding hybrid technologies showed some limitations: either the target cytostatics were not detected in the initial matrix, or the application of PAC was not necessary since NF itself leads to good results in the removal of 5-FU and CYT. The combination of NF with GAC removed >98% of CYC from surface waters, and the combination of MBR with AC removed around 82% of CPCs, 5-FU, DAU, DOX and EPI from hospital wastewater.

Adsorption is an easy and economical method for the elimination of cytostatics from wastewaters, but the regeneration of adsorbents and the combination of adsorption with other processes (hybrid approaches) are targets for the optimization of the system. Thus, in order to improve cytostatic removal from aqueous matrices and simultaneously be able to degrade them afterwards, the combination of adsorption with other degradative techniques such as AOPs could be a valuable tool. This combination of technologies would likely bring benefits in terms of the removal/degradation of these hazardous medicinal products (or their byproducts, if AOP is the pre-treatment), resulting in a significant avoided impacts score in the life cycle assessment.

As a vital component of cancer treatment, cytostatics are continuously introduced into sewage systems, posing a significant challenge for removal in wastewater treatment facilities. This study emphasizes the need for advanced removal techniques, with careful consideration of their environmental impact. Moreover, the study offers a vision of the future, emphasizing the importance of a collaborative effort among research institutions, environmental agencies, and industry partners to develop effective strategies and safeguard the sustainability and integrity of water resources.

Author Contributions: All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by A.L.G.-C., T.I.A.G. and M.S.F.S. The first draft of the manuscript was written by A.L.G.-C. and M.S.F.S. All authors revised and commented on previous versions of the manuscript. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by: Project POCI-01-0145-FEDER-031297 (CytoStraTech)—funded by the FEDER funds through COMPETE2020—Programa Operacional Competitividade e Internacionalização (POCI) and by the national funds (PIDDAC) through FCT/MCTES; Base Funding—UIDB/00511/2020 of the LEPABE—Laboratory for Process Engineering, Environment, Biotechnology and Energy; UIDB/04750/2020 (EPIUnit) and LA/P/0064/2020 (ITR), funded by the national funds through the FCT—Foundation for Science and Technology. I.P. Teresa I.A. Gouveia would like to thank the Portuguese Foundation for Science and Technology (FCT) for her PhD grant (SFRH/BD/147301/2019).

Data Availability Statement: The datasets supporting the results of this article are included within the article.

Conflicts of Interest: The authors declare no conflict of interest.

Nomenclature

AC	Activated carbon
AOPs	Advanced oxidation processes
BLEO	Bleomycin
CAP	Capecitabine
CB	Carbon black
CBT	Carboplatin
CNT	Carbon nanotube
CPCs	Cancerostatic platinum compounds
CPT	Cisplatin
CYC	Cyclophosphamide
Cyt	Cytostatic
CytR	Cytarabine
DAU	Daunorubicin
DOX	Doxorubicin
EPI	Epirubicin
ERL	Erlotinib
FLU	Flutamide
5-FU	5-fluorouracil
GAC	Granular activated carbon
GEM	Gemcitabine
GO	Graphene oxide
IARC	International Agency for Research on Cancer
IFO	Ifosfamide
IMA	Imatinib
IRI	Irinotecan
LCA	Life cycle assessment
LCD	Lignite coke dust
LCST	Lower critical solution temperature
MBR	Membrane bioreactor
MWCO	Molecular weight cut off
NF	Nanofiltration
NP	Nanoparticles
OXA	Oxaliplatin
PAC	Powdered activated carbon
PAMAM-CS	Polyamidoamine/chitosan
PTX	Paclitaxel

RO	Reverse osmosis
TAM	Tamoxifen
UF	Ultrafiltration
VIN	Vincristine
WWTP	Wastewater treatment plant

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