Current Trends in Steroidal 17α-ethynylestradiol (EE2) Removal from the Environment: A Review

Wasiu Abibu[1,*], Gafar Bamigbade[2], Amos Kolawole[3], Taiwo Ajayi[4], Abdulwasiu Sakariyau[2]

[1] Department of Biotechnology, Fen Bilimleri Enstitüsü, Dokuz Eylül Üniversitesi, İzmir, Turkey
[2] Department of Biological Sciences, Crescent University, Abeokuta, Nigeria
[3] Department of Microbiology, Federal University of Agriculture, Abeokuta, Nigeria
[4] Department of Environmental Management and Toxicology, Federal University of Agriculture, Abeokuta, Nigeria
* Corresponding author: wasiuayodele.abibu@ogr.deu.edu.tr

Abstract

Emerging contaminants have posed major environmental and health challenges to human and aquatic lives. They include pharmaceuticals, endocrine disrupting compounds (EDCs), persistent environmental pollutants and many more. EE2 is an example of EDCs increasingly gaining acceptance and used to augment the deficiencies of other reproductive hormones. EE2 constitutes environmental nuisance via discharge into aquatic bodies, thus, threatening aquatic lives and resulting in health defects in human. It is worthy of note that previous researchers have channeled their studies to identifying ways of expelling EE2 from the environment. However, they remain persistent in the environment. The current review examined biological, chemical, physical and nanotechnological approaches in expelling EE2 from the environment. All methods discussed have been efficient in EE2 removal. From the review, both independent and combinatorial approaches in EE2 removal has yielded efficient results.

Abbreviations: E1 (Estrone), EE2 (17α-Ethynylestradiol), E2 (17β-Estradiol), E3 (17β-Estriol), NP (Nonylphenol), OP (Octylphenol), THN (Take Home Naloxone), LNG (Levonorgestrel), BPA (Bisphenol A), EDC (Endocrine Disrupting Compounds), TCS (Triclosan), SAL (Salbutamol sulfate)

Introduction

Gone are days when the inability to produce certain hormones in individuals spells doom for them. Today, several synthetic hormones are now available to augment these deficiencies. Vast majority of these manufactured hormones ends up in the environment after use [1]. Diethylstilbestrol is an estrogen which came into limelight in 1938 and endorsed to forestall undermined premature delivery in the primary trimester before its detrimental effect was discovered [2]. Antiestrogens and antiandrogens are other estrogens recommended for malignant growth treatment [3]. Manufactured glucocorticoids are recommended generally as anti – inflammatory agents [4]. Stanczyk et al. (2013) expressed the importance of synthetic estrogens (especially EE2) usage in contraceptive and hormone replacement therapy formulations [5].

In a review on the environmental and health consequences, persistence and fate of EE2 in the environment by Laurenson et al. [6], EE2 presents most of the excreted prescription – based estrogenicity. EE2 additionally is known to be more persistent in the environment according to de Mes et al [7]. Laboratory tests for the biological impacts of EE2 applicable to aquatic environments were available on fish, amphibians, invertebrates, and algae. Untreated wastewater and low or effluent dominated stream possessed elevated levels. Adeela et al. opined that estrogens at contamination levels have been connected with breast cancer in women and prostate disease in men [8]. Fenske et al. reported that EE2 had estrogenic impact on zebrafish [9]. It was responsible for male gonad development arrest in zebrafish exposed to man-made EE2 at an environmentally relevant concentration of 3 ng L^{-1} despite the initial reports from published works that EE2 is harmless at low concentration levels. The increasing levels of EE2 and other EDCs in surface water exposes human and animals to toxic effects of these biological compounds which may be symptomatic or asymptomatic.

EE2 has been found to exist in the environment via excretion by man as detailed by Paulwels et al. [10] as well as industrial effluents from companies synthesizing this compound for commercial purposes [11]. According to de Mes et al. [7] prior to excretion in urine, EE2 is metabolized by humans to become a biologically inactive, water-soluble sulphate or glucuronide conjugate. In addition, feaces contain enteric bacteria present in the gut. The bacteria are able to deconjugate EE2 metabolites due to its β-glucuronidase and sulfatase activity as reported by Atkinson et al [12]. However, EE2 persists in the environment for a long period of time although at tolerable concentrations.

EE2 is an estrogenic drug widely used as an anti-conception medication pills in combination with Progestin. Initially, EE2 was generally utilized as a segment of menopausal hormone treatment [13]. In contrast with E2 (estradiol), EE2 had enormously improved bioavailability when taken orally as it is progressively impervious to digestion, and shows moderately expanded impacts in specific parts of the body like the liver and uterus. Evans and Sutton (2015) opined that EE2 is found in practically all combined forms of birth control pills and is nearly the exclusive estrogen utilized for this purpose, making it one of the most generally used estrogens [14]. Figure 1 shows the 3D chemical structure of EE2.
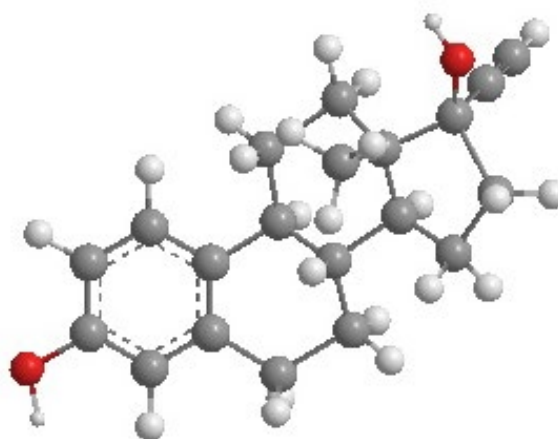

Figure 1 3D structure of EE2.

There are numerous uses for EE2 as reported by Takei et al. [15]. These include sex determination alteration, delay in sexual maturity and decrease in secondary sexual characteristics [15]. According to Regidor, "EE2 halts ovulation by smothering gonadotrophic hormone, thickening cervical mucus to prevent the movement of sperm, and suppressing changes in the endometrium required for implantation of a fertilized egg" [16]. EE2 has additionally been utilized in Hormone Replacement therapy (HRT) to diminish luteinizing hormone and vascularity in the endometrium. However, EE2 increases sex hormone binding globulin [17]. Hamoda et al. detailed that EE2 is also utilized as "menopausal hormone therapy" [18]. The fundamental purpose behind utilizing HRT in menopausal women as reported by Hamoda et al. [18] "is to mitigate basic vasomotor manifestations, for example, hot flashes, night sweats, and flushing". In addition, EE2 has been utilized as a component of feminizing hormone therapy for transgender women [19]. EE2 is also used in the treatment of hypogonadism and prevention of osteoporosis in women and has been utilized as palliative consideration for prostate cancer in men and breast cancer in women [20]. Evans regarded EE2 as one of the most powerful endocrine disrupting compounds (EDCs) [21]. Estrogen components of EE2 can cause breast tenderness and fullness with severity depending on the dosage and administration route [22].

It is worthy of note that "Health" refers not only to the state of wellbeing of the body, but also includes the wellbeing of the environment. Health, Safety and Environment (HSE) as a discipline evolved from concerns regarding environmental health and safety of the 3 major biospheric components (air, water and soil). The greatest environmental consequence of EE2 is felt by the aquatic bodies. Its presence in water bodies requires expensive expenditure to combat and most times efficient removal are not achieved. Environmental and health consequences of EE2

are numerous. To human health, general side effects of EE2 according to Aronson include" headache, fluid retention (bloating), nausea, dizziness, and weight gain" [23]. In men, this may include "gynecomastia (breast development), feminization, hypogonadism, infertility, and sexual dysfunction". However, in men who received dosage as high as 200 μg daily for 3–4 months, gynecomastia was observed in 98% of the patients studied [5]. Other side effects include: "Venous thromboembolism (VTE) which refers to blood clot in veins, and includes Deep Vein Thrombosis (DVT) and Pneumonic Embolism (PE)" [23]. EE2 conveys a more serious danger of blood clump arrangement and VTE than E2 (estradiol). This arose from the structural differences between E2 and EE2 and susceptibility difference to liver inactivation [13]. In addition, it has been commonly detailed that high doses of EE2 significantly increase risk of endometrial cancer in specific arrangements, for example those containing the progestogen dimethisterone [24]. In an examination by Blaustein, "unopposed estrogens like EE2 appeared to be carcinogenic in the endometrium while progestogens is believed to lower the carcinogenic role of EE2 [25].

Aquatic flora and fauna are not left from the environmental and health consequences of EE2 presence. The feminization of male fishes is a major reported effect of EE2 on aquatic lives. This has a deleterious effect on male fish's population. In addition, consumption of aquatic lives obtained from EE2 polluted water bodies exposes man to health consequences [19]. EE2 is highly resistant to natural degradation, its xenobiotic and organic nature confers on it this property thereby making water unfit for domestic and recreational purposes. Usually, they are not completely removed by wastewater treatment plants.

EE2 is a contaminant of emerging concern because its toxicity and persistence significantly alter the metabolism of living organisms [26]. Li classified EE2 and other pharmaceutical wastes as CECs (Contaminants of Environmental

App. Envi. Res. 43(2) (2021): 130-158

133

Concern) due to their global use (in human and veterinary medicine) and biological effects on target and non-target organisms in aquatic environments [27]. According to de Rudder et al. [28], "the most important compounds present in municipal wastewaters that possess estrogenic activity are the endogenous hormones E1, E2, E3, EE2, NP and OP".

EE2 is a synthetic hormone with high estrogenic potency and was added to the Watch List adopted by the European Commission stating the priority substances to be monitored. Essentially, this estrogenic compound, even in trace concentrations, was found to have accumulated in wild and laboratory exposed bivalves. The most common effects reported were changes on the reproductive function and energy metabolism [29]. Also, Directives stated that the contamination of water with pharmaceutical residues is now an emerging environmental concern in the field of water policy [30].

Indisputably, EE2 possess extraordinary advantage in the field of medicine, however, it has few cons which need to be satisfactorily monitored. This review thus took a look at current state of EE2 research together and various measures by which it can be expelled from the environment. This review work has classified EE2 removal methods into four (4) namely: Biological, Physical, Chemical and Nano-technological.

Biological methods for EE2 removal
1) Bacteria

Bacterial degradation of EE2 can be aerobic or anaerobic. The possibility for anaerobic degradation of EE2 via microorganisms isolated from water bodies was done by Czajka and Londry [31]. The outcome later proved unsuccessful. However, Sarmah and Northcott reported biodegradation of four EDCs which included EE2 present in waste water [32]. Czakja and Londry in their study reported that anaerobic degradation of EE2 (added at 5 mg L^{-1}) was not observed in multiple trials over long incubation periods (over three years). They also reported E2 (added at 5 mg L^{-1}) was transformed to estrone (E1) under all four anaerobic conditions (99–176 μg L^{-1} d^{-1}), but the extent of conversion was different for each electron acceptor. However, Sarmah and Northcott reported 90% degradation effectiveness via aerobic conditions was achieved in 22–68 h. However, under anaerobic conditions, it exceeded 1,000 d. Sarmah and Northcott ascribed anaerobic removal of EE2 to sulfate, nitrate and iron-reducing conditions. It was additionally hypothesized that overall degradation of the compounds was influenced by abiotic factors like hydrolysis, chemical reduction, photolysis, irreversible sorption or volatilization representing up to 40% degradation. Ying et al. accomplished a faster degradation of EE2 under aerobic conditions in effluent supplemented aquifer material [33]. However, under anoxic condition, biodegradation was not achieved. In another study conducted by Ying and Kookana which focused on the aerobic and anaerobic degradation of five EDCs (EE2 and others) in seawater within 56 d of degradation, EE2 was found to be degraded in the marine sediment under aerobic conditions ($t_{1/2} > 20$ d) while under anaerobic conditions. Thus, the failure to achieve EE2 degradation under anaerobic conditions may be attributed to the half-life (occurring in years) when compared to that under aerobic conditions [34]. However, not all EDCs degrading bacteria has been reported to successfully degrade EE2. In another investigation conducted by Ke et al., three EDCs were degraded aerobically and anaerobically by *Acinetobacter, Agromyces*, and *Sphingomonas* but could not degrade EE2 [35]. Also, the function of dissolved organic matter in anaerobic biodegradation of EE2 was researched by He et al., *Shewanella oneidensis* MR-1 and another microorganism from an activated sludge were the microbial strains used in the study. Dissolved organic matter were prepared from Humic Acid (HA), Fulvic Acid (FA) and Sigma humic acid (SHA).

0.5 mg L^{-1} EE2 degradation was explored under anaerobic conditions at pH 5.5 for 90 min in three different experimental set up namely: (i) Electrochemical degradation of EE2 alone; (ii) Electrochemical degradation in the presence of the domesticated micro-organisms (E+M) or of *S. oneidensis* MR-1 (E+S); and (iii) Electroche-mical and microbial degradation in the presence of 5.0 mg L^{-1} of the DOM (containing SHA, HA and FA). The anaerobic degradation experiment was conducted in an anaerobic incubator and lasted for 3 d. From the results, in the presence of *S. oneidensis* MR-1, FA improved removal effi-ciency while the domesticated micro-organisms aided EE2 removal by FA and SHA. The authors concluded that FA functions basically to ensure EE2 biodegradation and mineralization efficiency by *S. oneidensis* MR-1 and domesticated micro-organisms [36].

Research conducted by Yoshimoto et al. with *Rhodococcus zopfii* and *Rhodococcus equi* obtained from activated sludge of Japanese wastewater treatment plants were shown to de-grade EE2 [37]. Highest removal efficiency was recorded in *R. zopfii* Y50158 removing completely 100 mg L^{-1} of EE2 in 24 h. *Sphingobacterium sp.* JCR5 is another EE2-degrading bacterium as detailed by Ren et al. [38]. It utilizes EE2 as the sole source of carbon and energy and degrades 87% of the EE2 (30 mg L^{-1}) within 10 d. Review of EE2 biodegradation reveals that the first step is characterized by oxidation to E1 with a subsequent ring cleavage to 2-hydroxy-2, 4-dienevaleric acid and 2-hydroxy-2, 4-diene-1, 6-dioic acid, which were the main catabolic intermediates. Effective EE2 degradation by bacterial is achieved under aerobic conditions.

As indicated by Hamid and Eskicioglu, elect-ron donors by heterotrophs or via cometabolism by the ammonium monooxygenase (AMO) enzyme of ammonia oxidizing bacteria (AOB) could expel estrogens in EDCs [39]. In the same vein, higher removal efficiency of EDCs under higher nitrification rates have been reported by

Dytczak et al. and Yi et al. [40–41]. Khunjar et al. and Ren et al. like-wise asserted that high elimination is achieved by the interplay of heterotrophs and AOBs [42, 38]. Kassotaki et al. researched on the comparative removal of EE2 and other EDCs via nitrification rates increase using NAS (Nitrifying Activated Sludge) and AOB (Ammonia Oxidizing Bacteria) with CAS (Conventional Activated Sludge) in studying nitrifying and heterotrophic bacteria involvement in EDCs removal [43]. The research stemmed up from the conclusion of Yi and Harper that a direct proportionality existed between EE2 removal and NH4 abundance in enriched nitrifying cultures [41]. The result recorded low removals (<14%) for NAS and AOB. Also, heterotrophic component of CAS was highly productive in EE2 removal compared to NAS and AOB. 100% and 78% removals for E2 and E3 respectively were recorded, but, EE2 and BPA yielded lower removals of 10% to 39% respectively.

Larcher et al. accessed EE2 removal abilities of seven (7) bacteria found in Activated sludge. *Bacillus subtilis* (6051), *Pseudomonas aeruginosa* (PA01), *Pseudomonas putida* (12633), *Rhodococcus equi* (13557), *Rhodococcus erythropolis* (4277), *Rhodococcus rhodochrous* (13808), and *Rhodo-coccus zopfii* (51349) were the bacteria utilized in the study [44]. All bacteria were able to utilize EE2 as a nutritional and growth source. *Rhodococcus genera* (*R. zopfii*, *R. erythropolis*, *R. equi*) resulted in removals ranging from 38% to 61% after 12 d. However, *R. rhodochrous* achieved 100% removal efficiency with no traces of EE2 after 48 h. However, the authors never concluded that *R. rhodochrous* solely achieved this biodegradation power due to the fact that *R. rhodochrous* might have used ethanol as an additional carbon source thereby enabling EE2 degradation through *cometabolism*. *P. putida*, *B. subtilis*, *P.* aeruginosa recorded lower removals within 21% to 34%. Larkin et al. and Martínková et al. supported *Rhodococcus* removal efficiency

because it has a history of successfully degrading xenobiotics and other persistent pollutants of environmental concern [45-46]. Also, the idea of mixing the heterotrophic bacteria together to determine the possibility of an increased removal efficiency was conducted by Larcher and Yargeau [44]. Two groups were made: Group 1 (*Pseudomonas aeruginosa*, *Pseudomonas putida*, *Rhodococcus equi*, *Rhodococcus erythropolis* and *Rhodococcus rhodochrous*) and Group 2 (*Bacillus subtilis*, *Pseudomonas putida*, *Rhodococcus equi*, *Rhodococcus erythropolis* and *Rhodococcus rhodochrous*). The outcome revealed that EE2 removal efficiency is best achieved with individual bacteria than mixed consortia. In a related study by Ma et al., *β-Proteobacteria*, *Clostridia*, *α-proteobacteria*, Acidobacteria-6, *δ-proteobacteria*, *Chloracidobacteria* and *γ-proteobacteria* were identified as the bacterial classes needed to achieve high removal efficiency of EE2 [47]. Also, *Candidatus*, *Nitrososphaera* and *Escherichia* were listed amongst bacteria genera favoring easy and efficient degradation of EE2.

2) Fungi

As for fungi involvement in EE2 biodegradation, Suzuki et al. studied biodegradation of E2 and EE2 with manganese peroxidase (MnP) by the laccase-mediator system with 1-hydroxy benzotriazole prepared from *Phanerochaete chrysosporium* ME-446 and *Trametes versicolor* IFO-6482 cultures [48]. As reported by Solomon et al., Laccase enzymes are involved in oxidation-reduction dynamics of substrates eventually yielding H_2O from O_2 [49]. It also plays a major role in degradation of polymeric components of lignin in plants. It achieves this via non phenolic components oxidation resulting in hydrogen atom removal and hence, lignin degradation. Suzuki et al. found that 10^{-5} Mol dm^{-3} E2 and EE2 were completely transformed within 1 h [48]. Blanquez and Guieysse credited degradation activity of *T. versicolor* to laccase enzyme present in lignocellulolytic fungi [50]. Non-

lignocellulolytic fungi has likewise been reported to possess EE2 removal potential. Norethisterone and EE2 are common EDCs biotransformed by *Buchnera aphidicola* and *Cunninghamella elegans* as reported by Choudhary et al. [51]. Biotransformation was attributed to several hydroxylations of the parent substrate (EE2) and a resulting methoxyla-tion of the hydroxyl derivative. Shi et al. additionally reported *Fusarium proliferatum* potential to use EE2 as the sole source of carbon [52]. In 15 d, a 97% removal efficiency of 25 mg L^{-1} of EE2 was achieved by this fungus.

Nicotra et al. and Auriol et al. studied the removal of EDCs by the laccase enzymes present in *Trametes* and *Phanerochaete* genera [53-54]. Likewise, Beck et al. catalyzed the degradation of some known estrogens including EE2, and E2 by incubating with pure laccase enzyme from *T. versicolor* and achieved an excellent removal efficiency [55]. According to Lloret et al., the dynamics of EE2 degradation via laccase enzymes is credited to radical presence at the hydroxyl component of phenolic structures of EE2 [56]. This is followed by radical re-distribution at C2 and C4 positions in the EE2 structure leading to formation of oligomers via radical linkage.

3) Microalgae

Financial implication and effectiveness are two considerations of an Environmentalist while embarking on pollutants removal and waste water treatments. The fast development rate, improved photosynthesis effectiveness and proficient versatile capacity are a portion of characteristic features which make microalgae a good choice in waste water treatment. Microalgae can take-up and utilize pollutants in aquatic environments as a nutritional source, thus, lowering metallic and organic contaminants present in polluted water bodies [57–59]. de Godos et al. reported the removal of veterinary antibiotics from wastewater by alga [60]. According to Zhang et al., photodegradation, biodegra-

dation and biosorption are the means of action used by alga in pharmaceutical wastes removal from water bodies [61]. For EE2 removal via photodegradation, initial concentration, pH, water complexity, light condition, and temperature are significant components that must be considered according to Gmurek et al. [62]. Bai et al. studied mechanisms for EDCs removal from wastewater effluents using freshwater green algae [63]. E2 E1 and EE2 were the EDCs studied in the research. *Nannochloris sp.* (a typical freshwater green alga with little scientific reviews regarding estrogen removal) was used in the research. Upon 7 d of alga cultivation in ultrafiltration effluent, 60–62% removal efficiencies of E1, E2 and EE2 were recorded. *Nannochloris sp.* removal potential for E2 and EE2 were only possible in ultrafiltration effluent. According to Bai et al. [63], algae mediated photo and bio-degradation were the essential pathways for the removal of E2 and EE2.

Sole and Matamoros accomplished 97% EE2 removal from waste water with *Chlorella sp* [64]. Cheng et al. researched on the removal efficiencies of EE2 uptake from wastewater by the mutant *Chlorella* PY-ZU1 under a limited CO_2 supply [65]. *Chlorella* PY-ZU1 was able to use EE2 as a nutritional opportunity. In a further research, concentration range of 0.1–5 mg L^{-1} was observed to reduce EE2 molecular weight and hence, biodegradation. This is corroborated by Balina et al. who discovered the potential of 8 µg L^{-1} EE2 to reduce algal growth by 10% [66]. Low concentrations of EE2 promoted micro algal growth, and this phenomenon is known as "hormesis" in toxicology as detailed by Calabrese and Baldwin [67]. Increased EE2 concentration repressed micro algal development resulting in cell damage in the long run. From the outcome, an appreciable and acceptable removal surfaced after 9 d with *Chlorella* PY-ZU1 culture yielding 80% removal efficiency. Increasing concentration of EE2 resulted in further removals. 0.01 to 5 mg L^{-1} resulted in 83% to 94% removals. The

maximum EE2 removal efficiency of 94% by microalgae was obtained at 5 mg L^{-1} EE2. As indicated by Della Greca et al., EE2 is probably biodegraded into three less toxic bio-products through glucosylation process: ethinylestradiol glucoside, 3-β-D-glucopyranosyl-2-hydroxyethinylestradiol, and 3- β -D-glucopyranosyl-6 β – hydroxy-ethinylestradiol [68].

Hom–Diaz and co-authors researched on the microalgae cultivation on wastewater digestate and its impact on E2 and EE2 de-gradation [69]. *Selenastrum capricornutum* and *Rhapidocelis subcapitata* were the cultivated microalgae in the study while *Chlamydomonas reinhardtii* was used to study E2 and EE2 degradation on anaerobic digestate centrate (ADC). Previous authors like Abreu et al., Li et al. and Singh et al. have revealed wastewater as a significant nutrient hotspot for microalgae cultivation due to its abundant nitrogen and phosphorous reserve [70–72]. The study was conducted for 10 d with 100 mg L^{-1} dry weight of *Selenastrum capricornutum* and *Rhapidocelis subcapitata*. E2 and EE2 were later added to the culture. From the outcome, 24 h cultivation of the microalgae resulted in 89% removal of E2 from the *S. Capricornutum* culture. Upon 7 d completion, removals recorded were in the range of 88–100% when treated with *S. capricornutum* and between 76–100% when treated with *C. reinhardtii*. E2 and EE2 were completely removed in the experiments performed with *C. reinhardtii*, except for EE2 in the presence of ADC which decreased to 76%. *C. reinhardtii* presented higher adsorption percentages: 86% and 71% after 7 d for E2 and EE2 respectively.

Wang et alstudied the biotransformation of EDCs (E1, E2 and EE2) in a 40 d study by four species of microalgae namely: *Haematococcus pluvialis*, *Selenastrum capricornutum*, *Scenedesmus quadricauda*, and *Chlorella vulgaris* [73]. Transformation products of EDCs degradation by microalgae were achieved via ultra-high-performance liquid chromatography coupled

with electrospray ionization high-resolution mass spectrometry (UHPLC-ESI-HRMS) and EAWAG-BBD prediction system as reported by Wang et al. [73]. The outcome recorded 97%, 80%, and 97% removals for *H. pluvialis*, *S. capricornutum*, and *S. quadricauda* respectively. Also, all microalgae species tested yielded 100% removal for E2. However, only *H. pluvialis* and *S. quadricauda* could reach 85% removals in EE2. This result was corroborated by Layton et al. (2000) that recalcitrance of EE2 to biodegradation arose from ethinyl component of its structure. In EE2 degradation as studied by Wang et al. [73], the degradation process was in 4 steps namely: (i) hydroxylation of EE2 at C2 or C4 (ii) a second hydroxylation at C9 (iii) hydration of the C4–C5 double bond and (iv) aldolytic cleavage of the C3–C4 bond.

Shah et al. studied the biotransformation of EE2 with microorganisms and plant cell cultures. It was discovered that hydroxylation and methoxylation at C-1, C-3, C-4, C-6, C-7, C-10, C-11, C-12, C-15 positions in the structural orientation of EE2 or oxidation and reduction of C-3 alcohols, ketones and C=C bond

at C-4 and C-5 positions were responsible for the biotransformation. These modified EE2 substituted steroidal drugs are currently favored when compared to their natural counterparts due to some therapeutic advantages. Biotransformation transforms hazardous chemicals most especially pharmaceutical ones into none or less lethal ones. Shah et al. reported fungi-mediated stereo- and regio-selective hydroxylation process as profoundly effective for EE2 biodegradation [75]. Kresinova et al. also used *Pleurotus ostreatus* to investigate the metabolism of EE2. Reported bio-transformed products are shown in Figure 2 [76].

Microbial fuel cells (MFCs) and microbial electrolysis cells (MECs) have been utilized in wastewater remediation with ease. Gao et al., Zeng et al. and Hou et al. have successfully used this method for biodegradation of xenobiotic hydrocarbons like furans, phenolics and azo dyes respectively [77–79]. They are characterized by low energy consumption and degrades pollutants effectively. The electrochemical modification of dissolved organic matter also aids the xenobiotic EE2 biodegradation [80].
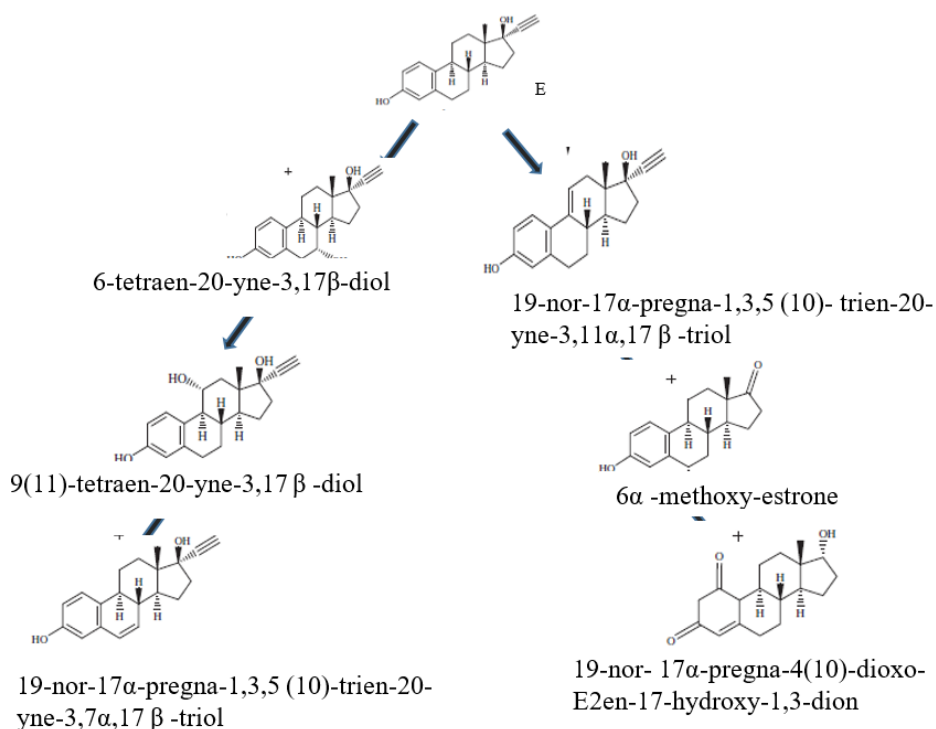

Figure 2 Biotransformed products of EE2 by *Pleurotus ostreatus* as reported by Krˇesinova et al. [76].

Use of constructed wetlands (CW)

Campos et al. studied the removal efficiencies of EE2, LNG, and BPA from water by utilizing four (4) laboratory scale Constructed wetlands (CW): "one cultivated with *Cyperus isocladus* (WL1), other with *Eichhornia crassipes* (WL3), and one without macrophyte (WL2)" [81]. "The fourth unit contained gravel and bamboo charcoal as support medium and cultivated with *Cyperus isocladus* (WLC)". Hydraulic retention times of 2–4 d were tested. LNG is known to have "masculinization effect in fish" as reported by Lin et al. and Harris et al. [82–83]. According to ITRC, (2003), "Constructed wetlands (CW) are improvised wastewater treatment frameworks with the function of a characteristic wetlands and achieving phytoremediation via reduction of microbial population in wastewater" [84]. From the outcome, normal removals were within the range of 9.0–95.6% for EE2, 29.5–91.2% for BPA and 39.1–100.0% for LNG. The authors concluded that "the most proficient CW for evacuation of EE2 and BPA was WLC and for LNG removal was WL3". In addition, "a 2 d HRT was statistically more efficient in removing EE2 and the 4 d HRT was more efficient in the LNG removal". This outcome is corroborated by Ávila et al. who detected a reverse association between hydraulic retention time and removal rates [85].

Chemical methods for EE2 removal
1) Adsorption

Adsorption is one of the most regularly utilized strategies to expel EE2 in water. In order to investigate EE2 removal by sorption, numerous sorbents have been investigated. As reported by Gupta et al. "Activated carbon (AC) is the most famous sorbent in water treatment forms with various structures such as powdered AC (PAC) and granular AC (GAC) which are relevant to water treatment process [86]. AC is characterized by a rich surface territory, porosity, and high adsorption limit with respect to EE2. It was discovered that "the removal of pharmaceuticals and EE2 by AC was excellent as indicated by Nam et al. [87]. Mailler et al. observed that PAC acts as an adsorbent in pollutants removal when the organic matter in water grips the dynamic site of PAC and contend with pollutants for adsorption [88]. The limitations of AC are the response time issue to achieve removal and the recovery cost issue warranting the need to consider minimal effort adsorbents [89]. Taking into account the constraints of AC as a powerful sorbent, de Rudder et al. [28] directed analyses in which the evacuation of EE2 from water was checked in three upstream bioreactors (UBRs) and loaded individually with sand, granulated activated carbon (GAC) and MnO_2 granules. The outcome indicated that "the removal of EE2 in the sand, GAC and MnO_2 reactors were 17.3%, >99.8% and 81.7% respectively. The researchers observed that "In spite of the fact that GAC had the most noteworthy EE2 removal ability because of adsorption, the MnO_2 reactor, nonetheless, expelled fundamentally more EE2 than could be anticipated from its adsorption limit and synergist properties". Thus, these properties could make it a cost-productive method for the removal of EE2. Recently, numerous investigations found that graphene and graphene oxide are potential viable sorbents for expelling EE2. This is corroborated by Sophia et al. laboratory scale investigation of EE2 adsorption by graphene and graphene oxide which yielded an appreciable result [90].

Table 1 Summary of biological conditions in EE2 removal

Microbial type	Source of organism	Initial concentration of EE2 (mg L^{-1})	EE2 degrading efficiency (%)	Degrading condition of EE2	Duration of disintegration (days)	Ref
Bacteria						
Methanogenic bacteria	Lake water and sediment	5	10	Anaerobic	3–5	[31]
microcosms	Groundwater	5	30–46.5	Aerobic	15–26	[33]
microcosms	Groundwater	0.001		Aerobic	81	[34]
Rhodococcus	Activated sludge		70–80	Aerobic	1	[37]
Ammonia oxidizing bacteria	Nitrifying activated sludge	5		Aerobic		[38]
Ammonia oxidizing bacteria	Nitrifying activated sludge		10–39	Aerobic		[43]
Rhodococcus		5	21–61	Aerobic	2	[44]
Fungi						
Trametes versicolor		10	97	Aerobic	1	[50]
Fusarium proliferatum strain HNS-1	Wastewater	25	97	Aerobic	15	[52]
Trametes versicolor	Wastewater	0.000001	91	Aerobic	0.042	[54]
Myceliophthora thermophila	Wastewater	4	84–95	Aerobic	4	[56]
Pleurotus ostreatus	Wastewater	0.00100	90	Aerobic	1	[76]
Microalgae						
Scenedesmus dimorphus	Wastewater	100	85	Aerobic	4	[61]
Nannochloris sp	Wastewater		60	Aerobic	7	[63]
Chlorella sp. and Nitzschia acicularis	wastewater	10	97	Aerobic	10	[64]
Chlorella PY-ZU1	Wastewater	5	94	Aerobic		[65]
Desmodesmus communis	Wastewater	0.001	50	Aerobic	3	[66]
Selenastrum capricornutum	Wastewater	10	92	Aerobic	4	[68]
Selenastrum capricornutum and Chlamydomonas reinhardtii		5	60–95	Aerobic	7	[69]
S. oneidensis MR-1	Dissolved organic matter	0.2–1	41.6	Anaerobic	5	[80]

EDCs inspire estrogenic reactions in vertebrates with presence in treated sewage effluent and receiving natural waters [91–92]. The Australian Water Regulatory Authority prescribes a constraint of 0.0015–0.175 µg L^{-1} for characteristic manufactured EE2 in consumables while the World Health Organization (WHO) regarded 30–50 ng daily dosage per person as an overdose [93]. Various researchers have used different chemical methods for EE2 advanced oxidation processes removal from water bodies. A portion of these strategies incorporate activated carbon and nanostructured materials for adsorption, propelled oxidation procedures and membrane reactors [94–95]. Han et al. utilized three kinds of aliphatic polyamides in particular PA6, PA612 and PA12 to consider EE2 removal in water by means of adsorption [96]. PA612 and PA12 displayed essentially higher adsorption capacities with respect to EE2 compared to PA6 particles which showed generally low adsorption capacities with respect to EE2 in water. Hydrophobicity of PA612 and PA12 enhanced degradation of EE2. This is characterized by its high octanol water partition coefficient (log Kow ¼ 3.67) as asserted by Yamamoto and Liljestrand [97]. PA612 recorded an excellent EE2 degradation and its adsorption limit was compared and XAD4 for the removal of EE2 from water. XAD4 (was utilized as the standard and benchmark polymeric adsorbent in the research) because of its polymeric adsorption potential and ability to be used in aqueous and non-aqueous conditions. PA612 and XAD4 exhibited high adsorption capacities of 24.8 mg g^{-1} and 35.6 mg g^{-1} respectively for EE2 in water. According to Han et al. [96], "the binding affinity observed between PA612 and EE2 is attributed to Lewis acid-base interactions in which each carbonyl oxygen atom in PA612 amide group possesses one or two lone electron pairs reacting with the phenolic hydroxyl and alkylene moieties on EE2 molecule acting as proton donors and binding to the electronegative

carbonyl oxygen atoms via intermolecular hydrogen bonds". Accordingly, hydrophobic aliphatic PAs (PA612 and PA12) showed a lot higher adsorption limits than PA6 particles since hydrophobicity is a significant determinant of adsorption amongst aliphatic PAs in EE2 removal.

Szabo et al. investigated the adsorption of EE2 on soils with organic matter in different degradation stages and with various quality dependent on redox status [98]. The sorption of EE2 in soils and sediments has been previously reported by Sun et al. and Oliveira et al. [99-100]. Examination was done to quantify the sorption of EE2 on the soils investigated and on intrinsic features of organic matter responsible for the differences in sorption by characterizing soil organic matter quality utilizing FTIR. Five soils (H20, H80, A20, G40, and G20) were gathered from various soil profundities at three distinct areas. From the outcome, the adsorption of EE2 on the soils increased in the order H80 < A20 < G40 < H20 < G20. Organic matter content of soils is the most important factor responsible for adsorption of hydrophobic pollutants as reported by Bielsk et al. [101–102]. This is corroborated by the Q_{max} values in the experiment (10.7–83.6 mg g^{-1}) in the order G20 > H20 > G40 > A20 > H80 indicating the organic matter content of the soils. The researchers later concluded that the organic matter content was the most important property of the soils with regard to the capacity and strength of sorption. Hydromorphic soils, in which organic matter accumulation occurred, were found to have high adsorption capacity for EE2.

2) Electrocoagulation

Maher et al. examined the impact of operation parameters on EDCs degradation via iron electrocoagulation [103]. "Current density, conductivity, stir rate, and polarity reversal time were the parameters tested" as reported by the authors. Westerhoff et al. had prior considered coagulation /flocculation using alum and ferric chloride as

coagulants in the removal of EDCs (E1, E2, and EE2) with 5%, 2%, and 0% removal individually recorded [104]. Electrocoagulation (EC) stands apart as a superior choice for estrogen removal than ordinary coagulation/flocculation because EC drives direct coagulation in association with redox potential [105–106]. Pan et al. revealed the capability of EC to expel "pollutants, turbidity, chemical oxygen demand, biochemical oxygen demand, phosphate, and color in wastewaters" [107]. From Maher et al. [103] study, three stir rates (50, 120, 500 rpm) were explored in the study. "The result indicated that a solid relationship between current density and percent removal for E1, E2, and E3 with Pearson r-values of 0.95, 0.96, and 0.93, respectively existed". Conductivity had no impact on estrogen removal. The best removal was accomplished with a mix rate of 500 rpm. Thus, oxidation responses from higher mix rate had a superior favorable position over adsorption for the estrogens removal. Increasing stir rates aids velocity, thus, resulting in an increased electron transfer flux between the electrode surface and the mixture and influencing estrogen removal. The 30 s polarity reversal time resulted in the most noteworthy removal for E1, E2, and E3. Thus, to achieve the greatest EDCs removal, the authors suggested "16.7 mAcm^{-2}, 1000 µS cm^{-1}, 30 s polarity reversal time, and a stir rate of 500 rpm which yielded average removal efficiencies 81%, 87%, 85%, and 97% for E1, E2, E3, and EE2 respectively". Expanding the conductivity gave no critical increment in estrogen removal.

3) Magnetic agglomeration

Magnetic agglomeration effect and increased surface area (allowing rapid adsorption) are the main features of magnetic ion exchange resin (MIEX) as reported by Ding et al. and Boyer et al. [108–109]. According to Mastrup (2001) and co-author "MIEX is a strong base anion exchange resin with a macro-porous polyacrylic matrix in the chloride form that can be used to adsorb

negatively charged aquatic contaminants through exchange of anions" [110]. The removal efficiencies of environmental and aquatic pollutants by MIEX from water bodies has been recorded [111]. Mastrup and Schäfer and Schäfer et al. examined EE2 removal via MIEX and concluded that MIEX potential for EE2 removal is pH and ionic strength dependent. At pH < 11, MIEX expelled 30% of E1 from solution [110, 112]. Wang et al. likewise examined the removal efficiency of EE2 via MIEX by a "multi-cycle adsorption-regeneration experiments" [113]. The experiment was done with three initial EE2 concentrations (20, 50 and 100 µg L^{-1}). The removal efficiency of EE2 had a direct correlation with increasing MIEX doses. However, a decline was observed at MIEX dosage of 10 ml L^{-1} but yielded 50% EE2 removal. [112] also reported that "EE2 removal increased as initial EE2 concentration decreased because of limited surface area (exchange sites) on MIEX while a maximum removal of 75.3% for EE2 was obtained at the initial EE2 concentration of 20 µg·L^{-1}". In addition, EE2 removal by MIEX as functions of pH recorded the highest removal of 100% at pH 12. Also, at acidic pH range, a higher removal efficiency was recorded. This can be concluded that, at extremely low and high pH, there is high tendency for EE2 removal by MIEX. A schematic chart of the expected structural modification of the effect of extremely low and high pH on EE2 by MIEX is shown in Figure 3.
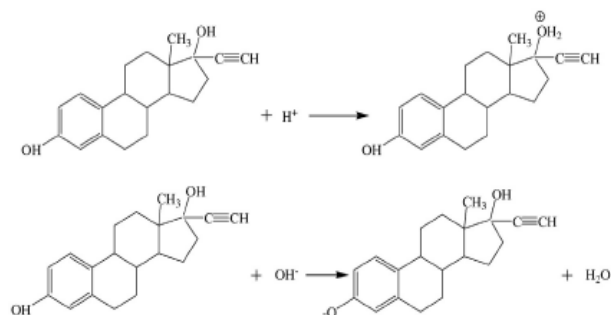

Figure 3 EE2 alteration by acid and alkali.

In the same vein, Wang et al. [113] described two types of mechanisms employed by MIEX for EE2 removal: ion exchange and adsorption (which can either be reversible or irreversible). The author later concluded that "the main removal mechanism of EE2 by MIEX was ion exchange instead of reversible micro-pore adsorption".

4) Use of acids

Maurıcio et al. researched on the effectiveness of peracetic acid (PAA) in the removal of EE2 in wastewater [114]. PAA is used as a substitute for chlorine in treatment plants due to its low cost, non-carcinogenic, non-mutagenic and non-residue formation when compared to chlorine [115–118]. As indicated by Bonetta et al. and Rizzo et al., no scientific work exists for PAA effectiveness in expelling EE2 [118–119]. Maurıcio et al. research was conducted "by determining the reduction in EE2 concentrations in jar tests and by measuring the estrogenic activity (vitellogenin - VTG), antioxidant enzyme activities (gluta-thione-S-transferase - GST, and catalase - CAT) and oxidative stress (lipid peroxidation - LPO) following zebra fish (Danio rerio) exposure to different concentrations of PAA" [114]. PAA concentrations and contact times were varied for EE2 removal. From Maurıcio et al. [114] findings, "the lowest contact time (10 min) did not show a dose-response relationship between PAA concentration and EE2 removal". In addition, "at the intermediate contact time (15 min), a removal efficiency of approximately 50% could be attained at a PAA concentration of 5 mg L^{-1}". Further increment in PAA concentration didn't bring about higher removal efficiencies. However, at 20 min contact time, a removal efficiency of 100% at 15 mg PAA/L was recorded. Researchers like Luukkonen et al. [120] is of the opinion that PAA ability to degrade pollutants is more related to dosage than contact time. Rizzo et al. [119] also claimed that low PAA concentration is effective in the

degradation of EE2. Maurıcio et al. [114] concluded from the investigation that EE2 removal efficiency is an element of the PAA concentration and the contact time. In this manner, "PAA has a high EE2 removal efficiency, both in terms of EE2 concentrations and decreasing the potential toxicity effects EE2 may exert". In addition to the absence of significant consequences for quality of wastewater, this may show the incredible capability of PAA to expel EE2 in Wastewater treatment plants. From the authors' final report, "total suspended solids, chemical oxygen demand and pH in PAA treatments stayed well inside levels set in European legislation for wastewater discharge. EE2 induced significant increased vitellogenin (VTG) levels in both female and male fish, indicating increased estrogenic activity, especially in males suggesting an endocrine disruption effect. With the addition of PAA (15 mg L^{-1}), however, VTG levels in both sexes returned to control values".

5) Advanced oxidation

Advanced oxidation has been successfully employed in the removal of microbial pollutants during water treatment. Advanced oxidation processes (AOPs) are modern practice employed in water treatments for the removal of EE2. As described by Pignatello et al., and Deng, "AOPs are defined as the oxidation processes related to the generation of reactive oxygen species (ROS) such as hydroxyl radicals (HO.) in enough quantity to produce reclaimed effluents and achieves degradation of pollutants and other high molecular weight organics via hydrogen abstraction, combination or addition of radicals, and electron transfer" [121–122].

The characteristic small size of EE2 also contributes to difficulty in their removal. Thus, there is need for a strong oxidation process to achieve removal. According to Nicholas (2019), the advantages of advanced oxidation as a method of EE2 removal are its rapid reaction

rates, production of non-toxic new products, excellent disinfection potential and non-production of products requiring further treatment for further treatment [123].

As reported by Shen et al., "Advanced oxidation process (AOP) is based on the production of substances with strong oxidation properties and low reaction selectivity" [124]. It achieves degradation by breaking down different pollutants into low molecular weight compounds while further removal measures is needed for the final removal of the low molecular weight compounds. Common AOPs for EDCs removal as mentioned by Shen et al. [124] include "ozonation, conventional fenton oxidation, UV oxidation processes, photocatalysis, ultrasonication, and electrochemical methods". Newer AOPs are microwaves, ionizing radiation, pulsed plasma, and the use of ferrate reagent.

6) Liquid–liquid extraction

Ben Fredj et al. reported that EE2 and other EDCs' weak solublility in water, hydrophobicity and high octanol/water distribution coefficients qualifies them for removal via a liquid–liquid extraction (LLE) [125]. It is worthy of note that the LLE removal effectiveness is determined by the solvent used in the process. "Solvents should be non-toxic, environmentally benign and possess low volatility and solubility to minimize associated losses". In a study by Ben Fredj et al. [125], "the organic solvent decamethylcyclopentasiloxane (D5) which possessed the characterristics of an appropriate solvent for the LLE process mentioned above was used to expel EDCs from the aqueous phase". In addition, D5 has proven a better result and a good solvent for LLE for EE2 removal in waste-water treatment when combined with ozone [126]. LLE was regarded to be a potent analytical method in the removal of EE2. However, factors like pH, temperature, initial aqueous concentration of EE2 and volume ratio (D5/water) must be taken

into consideration for better results. Table 2 reveals the degrading conditions employed by chemical conditions in EE2 removal.

Physical methods for EE2 removal
1) Membrane filtration

As reported by "Membrane filtration is one of the most widely used techniques for removing contaminants from water bodies and includes microfiltration, ultrafiltration (UF), nano filtration (NF), and reverse osmosis (RO) which are widely known for efficient pollutants removal from wastewater" [128]. EE2 removal via membrane filtration is achieved by "particle size exclusion, electro-static repulsion, and hydrophobic adsorption on membrane materials" as described by Wang and Rana et al. [128–129]. Thus, the structure and physicochemical properties of EE2 and membranes are important factors influencing its removal efficiency. In addition, some process parameters (such as pH and separation time) also affect the final removal efficiency. In a study by Ge et al., a composite poly-amide NF film was studied to remove 14 drugs at trace level from water, and results showed that the rejection rates increased with the increase of the sizes of EDCs studied indicating that size exclusive is one of the main determinants for EE2 removal [130].

Lin observed the adverse effect of organic matters present in water on EDCs removal efficiency by NF (NF270 and NF90) and RO (XLE) due to membrane fouling [131]. This showed that the control of natural organic matter in water is very essential before membrane filtration. Park et al. also found that "the combination of coagulation with poly aluminum chloride and membrane bioreactor process can reduce membrane fouling and thus, improving the removal efficiency of tetracycline, mefenamic acid, atenolol, furosemide, ketoprofen, and diclofenac" [132].

Table 2 Summary of chemical conditions in EE2 removal

Source of waste	Treatment Process	Initial concentration of EE2 (mg L^{-1})	EE2 degrading efficiency (%)	Duration of disintegration (days)	Ref
Wastewater	Adsorption	0.003		1	[96]
Contaminated soil	Adsorption	100	84		[98]
Contaminated soil	Adsorption	100	45		[99]
Municipal wastewater	Photo-transformation	0.0015	81.7–99.8	0.042	[127]
Wastewater	Magnetic ionic exchange resin	20	75.3		[110]
Wastewater	Use of acids	50	100	<0.0005	[114]
Wastewater	Continuous extraction	10	90		[126]

Nanotechnological methods for EE2 removal

1) Photo-catalytic degradation

Upgraded or enhanced photolysis by means of nanosized photocatalysts is another method for EE2 removal from wastewater [133–134]. "EE2 removal in water bodies is achievable by photocatalytic degradation via synergistic C/N-doped β-Bi_2O_3 nano sheets" as reported by Chen et al. [135]. Kazuhito et al. considered photocatalysis an innovative technology for wastewater treatment coupled with its ability to degrade pollutants into carbon dioxide and water completely [136]. Kazuhito et al. [136] credited "Bi_2O_3 as a nano sheet choice due to its higher photocatalytic activity, unique optic absorption in visible light region and electrical properties with a narrow band gap ranging from 2.0 to 2.9eV". Jalalah and co-authors also added that" a novel solvothermal-calcination method that systematically absorb and photocatalyse EE2 was employed in the synthesis of C/N-doped β-Bi_2O_3 nanosheet photocatalyst [137]. Chen et al. [135] later developed a removal rate equation model for EE2 removal taking into consideration Jalalah [137] argument. The model produced a mathematical guide for EE2 removal via adsorption and photocatalysis (Eq. 1–3).

However, poor separation efficiency has been reported as its major setback by Wang et al. and Wang et al. [138, 73]. The idea of using zeolites as a support for nanocrystals for wastewater treatment was suggested by Anandan and Yoon [139]. Pan et al. (2014) studied the Photocatalytic degradation of EE2 in the presence of TiO_2-doped zeolite [140]. In the study, low-silica X zeolite (LSX) was used as a support for TiO_2 in order to investigate the photocatalytic activity of the TiO_2-LSX catalyst with respect to EE2 removal. From the outcome, it was discovered that EE2 removal via photocatalysis by the TiO_2-LSX catalysts involves the photo-generation of strongly reducing electron and oxidizing hole pairs via the electronic excitation of TiO_2 in order to perform the photocatalytic function of TiO_2. Holes, as strongly oxidizing species, can also directly oxidize EE2 on the catalyst surface. Photocatalysis via of TiO_2-LSX catalysts were found to be efficient than simple UV photolysis and UV- TiO_2 oxidations (which were used as a benchmark for comparism) in the removal of EE2. Two diverse degradative path-way were proposed by Pan et al. [140] for the viable photodegradation of EE2. The first proposed pathway was photodegradation at acidic pH range while the second pathway achieved the degradation at alkaline pH range. Both pathways yielded the same photodegradative product ($C_{20}H_{24}O_3$) which is less toxic when compared with the parent compound (EE2).

$$EE2\ Removal\ (\%) = (C_o - C)/C_o\ x100\% \qquad\qquad (Eq.\ 1)$$

$$EE2\ Adsorption\ (\%) = (C_o - C_q)/C_o\ x\ 100\% \qquad\qquad (Eq.\ 2)$$

$$EE2\ Photocatalysis\ (\%) = (C_q - C)/C_0\ x\ 100\% \qquad\qquad (Eq.\ 3)$$

Where C_0 (mg L^{-1}), Cq (mg L^{-1}) and C (mg L^{-1}) represent the initial concentration of EE2, the concentration of EE2 when the adsorption/desorption equilibrium was established, and the concentration of EE2 remaining in the solution at irradiation time of t (min), respectively while t (min) is irradiation time.

However, poor separation efficiency has been reported as its major setback by Wang et al. and Wang et al. [138, 73]. The idea of using zeolites as a support for nanocrystals for wastewater treatment was suggested by Anandan and Yoon [139]. Pan et al. studied the Photo-catalytic degradation of EE2 in the presence of TiO$_2$-doped zeolite [140]. In the study, low-silica X zeolite (LSX) was used as a support for TiO$_2$ in order to investigate the photocatalytic activity of the TiO$_2$-LSX catalyst with respect to EE2 removal. From the outcome, it was discovered that EE2 removal via photocatalysis by the TiO$_2$-LSX catalysts involves the photo-generation of strongly reducing electron and oxidizing hole pairs via the electronic excitation of TiO$_2$ in order to perform the photocatalytic function of TiO$_2$. Holes, as strongly oxidizing species, can also directly oxidize EE2 on the catalyst surface. Photocatalysis via of TiO$_2$-LSX catalysts were found to be efficient than simple UV photolysis and UV- TiO$_2$ oxidations (which were used as a benchmark for comparism) in the removal of EE2. Two diverse degradative pathway were proposed by Pan et al. [140] for the viable photodegradation of EE2. The first proposed pathway was photodegradation at acidic pH range while the second pathway achieved the degradation at alkaline pH range. Both pathways yielded the same photodegradative product (C$_{20}$H$_{24}$O$_3$) which is less toxic when compared with the parent compound (EE2).

Mazellier et al. investigated the photochemical transformation of E2, EE2 and THN [141]. Light absorption of the three com-pounds is connected to the presence of the photoactive phenolic group. The three compounds were subjected to similar UV–visible absorption spectra with a broad absorption band between 240 and 330 nm. According to the authors, "presence of these pollutants in surface waters makes the overlapping zones between E2, EE2 and THN absorption spectra and the solar irradiance smaller, however, with time, photo transformation was predicted". Structures of photoproducts obtained from the study were determined via liquid-gas chromatography coupled with mass spectrometry. The photo transformation of E2 and EE2 in aqueous solution occurs with a quite low quantum yield of about 0.06 upon irradiation at 254 nm or polychromatic irra-diation. This value is extremely on the brink of previously determined for phenol.

According to Grzybowski and Szydłowski, the light absorption band of EE2 partly overlaps with the solar spectrum making degradation via direct/primary photoreactions a possible means of degradation while photo radiation with wavelength > 280 nm is capable of reducing the concentration of EE2 [142]. Indirect (sensitized) reactions initiated by light absorbers also play an important role in EE2 removal. Photo degradation of EE2 in aquatic bodies was researched by Grzybowski and Szydłowski [142]. Photo degradation end up being a viable normal mode for EE2 removal when compared with biodegradation which goes on for weeks [142].

Śliwka-Kaszyńska et al. studied the photo transformation of EE2 in water [127]. Photo transformation products and transformation pathways were reported. According to Śliwka-Kaszyńska et al., "Liquid chromatography coupled with high resolution quadrupole time-of-flight mass spectrometry (LC-QTOF-MS) provided accurate mass measurements and MS/MS experiments for structural elucidation while the photolysis experiment revealed the formation of four new transformation products of EE2 denoted by EE2-(1–4)". The structures were obtained via Target MS/MS analysis. EE2–1 (m/z 361.1789) was formed after 10 min of exposure to UV/VIS light. Tetra-hydroxylation of EE2 with an ensuing mono-hydrogenation of benzene ring yield EE2–1. Oxidation of EE2-1 produced EE2–2 (m/z 357.1707) while continuous irradiation of EE2–2 resulted into EE2–3 (m/z 363.1603). Also, EE2–3 can also be formed only by a one-step hydrogenation of EE2–1 in acidic conditions. Transformation of EE2 to EE2 (1–3) was first reported by Śliwka-Kaszyńskaa et al. [127]. Mono hydroxylation of EE2 for 80 min gave EE2–4 (m/z 311.1653). Figure 4 shows the proposed transformation pathway of EE2 and structures of the photo transformation products earlier mentioned.

In addition, Kamat and Zhao et al. were of the opinion that "Graphene-based composites with plasmonic and semiconductor NPs offer unique advantage as a photocatalyst for organic pollutants and a good adsorption sites for organic molecules" [143–144]. rGOeAg, a silver NP characterized by plasmonic property of Ag for visible light aids photolysis of colourless organic pollutants which do not absorb any visible light was developed by Bhunia et al. rGOeAg is another catalyst capable of degrading colorless organic pollutants at nano scale and has successfully been used for EE2 removal [145]. Its ability to be reused without affecting its performance makes it a choice in researches. Boas et al. researched on photolysis of Phenol using rGOeAg [146]. The result indicated that "initial concentration of phenol decreases with irradiation time and nature of the light while catalyst influenced the rate of photodegradation".
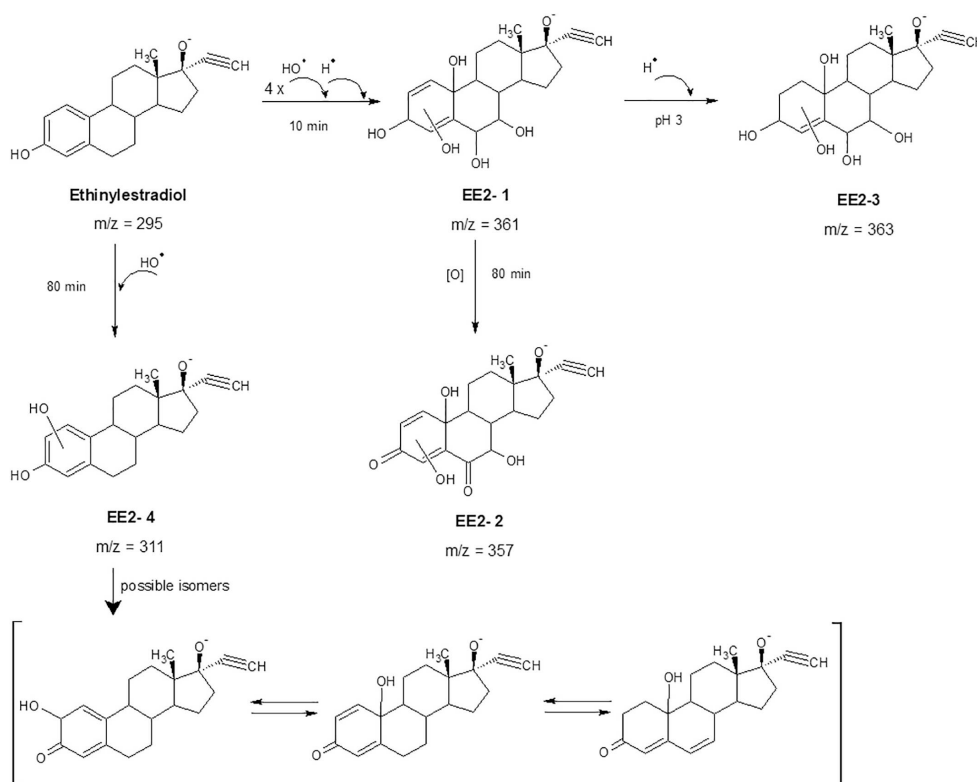

Figure 4 Proposed transformation pathway of EE2.

2) Removal using carbon nanotube electro-chemical filter (CNT)

As reported by Cunha et al., "stability, flexibility, chemical resistance, high specific surface area, and ability to form high porosity networks are the promising features of CNT" [147]. Cunha et al. [147] accessed the performance of a carbon nanotube (CNT) in EDCs removal from ultrapure water. The study methodology used was described: "preliminary experiments of sorption and electro-oxidation were investigated using breakthrough and cycle voltammetry curves to determine the CNT adsorption capacity and the electron transfer ability, then, CNT electrochemical filtration was assessed at different applied voltages (0–2.5 V) to investigate the efficacy and efficiency of the process. Scanning electron microscopy (SEM) and X-ray photoelectron spectroscopy (XPS) were completed for CNT surface analysis. YES assay was used to determine and quantify estrogenic activity before and after electrochemical filtration". From the results, CNT successfully expel E2 and EE2 with removals up to 99.1% in ultrapure water and 96.3% in urban wastewater under 2.5 V and 5 h of reaction".

3) Removal using beta- and gamma-cyclodextrin polymers (CD)

Rácz et al. defined Cyclodextrins as "macrocyclic oligosaccharides derived from starch and composed of glucose units linked by α-1, 4-glycosidic bonds in a cyclic manner" [148]. Cyclodextrin (CD) achieves EE2 removal by attracting low molecular components of EE2 to form host-guest complexes. Beta-cyclodextrin (β-CD) and gamma-cyclodextrin (γ-CD) are two types of CD with different adsorption abilities [149]. Tang et al. successfully synthesized mesoporous β-CDP and γ-CDP by crosslinking CD with rigid aromatic groups resulting in an increased surface area [150]. The two CD polymers acted as adsorbent for EE2 removal via "mesoporous adsorption and inclusion complexation" as reported by Tang et al. [143], CDPs achieved a high removal efficiency for E2 and EE2. Table 3 reveals the degrading conditions employed by physical and nanotechnological methods in EE2 removal while Table 4 shows a comparism of the methods discussed in this review for EE2 removal.

Table 3 Summary of physical and nanotechnological methods in EE2 removal

Treatment Process	Source of waste	Initial concentration of EE2 (mg L^{-1})	EE2 degrading efficiency (%)	Duration of disintegration (days)	Ref
Physical treatment					
Photocatalytic (Ultra-violet) degradation	Wastewater	50	95	<0.0005	[134]
Photocatalytic degradation / TiO$_2$-doped zeolite	Wastewater		90	0.042	[140]
	Natural water	0.000003		5–35	[142]
Nanotechnological treatment					
subsurface constructed wetlands	Water	0.002	95.6	2–4	[81]
carbon nanotube and electrochemical filter	Urban wastewater	95.3	37	0.208	[147]
beta- and gamma cyclodextrin	Wastewater	0.04	90		[150]

Table 4 Comparison of methods used in EE2 removal

Methods	Features	Advantages	Disadvantages
Physical	- Achieves degradation via photoreactions and filtration	- Cost effective and efficient	- Poor removal efficiency - Works best with combination of biological or chemical methods - Requires support (catalyst or medium) for effectiveness
Chemical	- Achieves degradation by means of adsorption	- Achieves a higher EE2 removal efficiency - Achieves removal within limited period of time	- Costly - Only achievable with strong adsorbents - pH dependent
Biological	- Achieves degradation using EE2 as a source of carbon and energy - Degradation can either be aerobic and anaerobic	- Efficient in EE2 removal Cost effective - Biotransformed products are non-toxic	- Greater disintegration is only achieved via aerobic disintegration - Individual bacterial achieves higher disintegration than microbial consortium - Only achievable with Bacteria, Fungi, Microalgae and Plant cultures - Disintegration is only achievable with low concentration of EE2 - Time consuming
Nanotechnological	- Combines nanocatalyst with physical and chemical methods to achieve degradation	- Highly efficient - Highest removal efficiency recorded - Less time consuming	- Expensive - Requires expertise for successful removal

Conclusion

Conclusively, great and efficient measures to efficiently expel EE2 (a pollutant of environmental concern) are discussed. All methods mentioned possess its merits and demerits. This guides an environmentalist in the choice of the appropriate methods in removing environmental pollutants like EE2 either by an independent or combinatorial approach. From the review, biological methods of EE2 removal has been extensively researched with aerobic degradation yielding a more efficient EE2 removal compared to anaerobic which yields unappreciable removal even after years. In addition, *Rhodococcus* genera are important consideration to the environmentalist when dealing with pollutant removals. This is backed by their established history of successfully degrading persistent pollutants of environmental concern.

Physical method achieves degradation via photoreactions and filtration and yields higher removal efficiency when supported with a catalyst while Chemical method achieves EE2 removal via adsorption. Nanotechnological approach for EE2 removal combines nanocatalyst with physical and chemical methods to achieve removal. Physical, chemical and nano technological approaches in EE2 removal had

yielded remarkable success in EE2 removal. However, the reviewers of these article had discovered that in the last few years, very few researchers have channeled their study to biological degradation of EE2 compared to chemical and nano technological approaches which had recorded some academic reviews. We therefore implore environmentalists to direct more investigations into combinatorial approach which combines two or more of the methods discussed to achieving removal of pharmaceuticals and pollutants of environmental concern.

References

[1] Darbre, P.D. What are endocrine disrupters and where are they found? Endocrine Disruption and Human Health. Elseiver Inc Publisher, 2015, 3–26.

[2] Harris, R.M., Waring, R.H. Diethylstilboestrol-a long-term legacy. Maturitas, 2012, 72, 108–112.

[3] Lonning, P.E. Endocrinology and treatment of breast cancer. Clinical Endocrinology Metabolism, 2004, 18, 1–130.

[4] Rhen, T., Cidlowski, J.A. Antiinflammatory action of glucocorticoids-new mechanisms for old drugs. New England Journal of Medicine, 2005, 353, 1711–1723.

[5] Stanczyk, F.Z., Archer, D.F., Bhavnani, B.R. Ethinyl estradiol and 17β-estradiol in combined oral contraceptives: Pharmacokinetics, pharmacodynamics and risk assessment. Contraception, 2013, 87, 706–727.

[6] Laurenson, J.P., Bloom, R.A., Page, S., Sadrieh, N. Ethinyl estradiol and other human pharmaceutical estrogens in the aquatic environment: A review of recent risk assessment data AAPS, 2014, 16(2), 299–310

[7] de Mes, T.Z.D., Zeeman, G., Lettinga, G. Occurrence and fate of estrone, 17β-estradiol and 17α-ethynylestradiol in STPs for domestic wastewater. Reviews Environmental Science and Bio/Technology, 2005, 4(4), 275–311.

[8] Adeela, M., Songa, X., Wanga, Y., Francisa, D., Yang, Y. Environmental impact of estrogens on human, animal and plant life: A critical review. Environment International, 2017, 99, 107–119.

[9] Fenske, M., Maack, G., Schäfers, C., Segner, H. An environmentally relevant concentration of estrogen induces arrest of male gonad development in zebrafish, Danio rerio, Environmental Toxicology and Chemistry, 2005, 24(5), 1088–1098.

[10] Pauwels, B., Willie, K., Noppe H., De Brabandar, H., de Wiele, T.V., Verstraete W. 17α – ethinylestradiol cometabolism by bacteria degrading estrone, 17β – estradiol and estriol. Biodegradation, 2008, 57, 330–345.

[11] Mazotto, V., Gagne, F., Marin, M.C., Ricciardi, F., Blaise, C. Vitellogenin as a biomarker of exposure to estrogenic compounds in aquatic invertebrates: A review. Environment International, 2008, 34, 531–545.

[12] Atkinson, S.K., Marlatt, V.L., Kimpe, L.E., Lean, D.R.S., Trudeau, V.L., Blais, J.M. The occurrence of steroidal estrogens in south – eastern Ontario wastewater treatment plants. Science of the Total Environment, 2012, 430, 119, 125.

[13] Kuhl, H. Pharmacology of estrogens and progestogens: Influence of different routes of administration. Climacteric, 2005, 8(1), 3–63.

[14] Evans, G., Sutton, E.L. Oral contraception". Medical Clinic of North America. 2015, 99(3), 479–503.

[15] Takei, Y., Ando, H., Tsutsui, k. Handbook of hormones. Elsevier Incorporation, 2016, 125–163.

[16] Regidor, P.A. Clinical relevance in present day hormonal contraception. Hormones

and Molecular Biological Clinical Investigation, 2018, 37, 15–28.

[17] Sahu, A., Tripathy, P., Mohanty, J., Nagy, A. Doppler analysis of ovarian stromal blood flow changes after treatment with metformin versus ethinyl estradiol-cyproterone acetate in women with polycystic ovarian syndrome: A randomized controlled trial. Journal of Gynecology, Obstettrics and Human Reproduction, 2019, 48(5), 335–339.

[18] Hamoda, H, N., Panay, R., Arya., Savvas, M. The British Menopause Society and Women's Health Concern 2016 recommendations on hormone replacement therapy in menopausal women. Post Reproductive Health. 2016, 22(4), 165–183.

[19] Unger, C.A. Hormone therapy for transgender patients. Translation Andrology and Urology, 2016, 5(6), 877–884.

[20] Oettel, M., Schillinger, E. Estrogens, Antiestrogens II: Pharmacology and clinical application of estrogens and antiestrogen. Springer Science & Business Media, 2012, 4–581.

[21] Evans, T.J. Endocrine disruption in: Reproductive and developmental toxicology. 2nd Edition. Academic Publisher. Elsevier Incorporation, 2017, 1091–1110

[22] Becker, K.L. Principles and practice of endocrinology and metabolism. Lippincott Williams & Wilkins, 2001, 1024–2153.

[23] Aronson, K. Meyler's side effects of endocrine and metabolic drugs. Elsevier, 2009, 177–242.

[24] Stein, P.D. Pulmonary embolism. Wiley Publishers, 2016, 187.

[25] Blaustein, A. Pathology of the female genital tract. Springer Science & Business Media, 2013, 291.

[26] Sauvé, S., Desrosiers, M. A review of what is an emerging contaminant. Chemistry Central Journal, 2014, 8, 15.

[27] Li, L., Guo, X.H., Fu, L., Prud`homme, R.K., Lincoln, S.F. Complexation behaviour of α-, β-, and γ-cyclodextrin in modulating and constructing polymer networks. 2014, Langmuir, 24, 8290–8296.

[28] d e Rudder, J., Van de Wiele, T., Dhooge, W., Comhaire, F., Verstraete, W. Advanced water treatment with manganese oxide for the removal of 17a-ethynylestradiol (EE2). Water Research, 2004, 38, 184–192.

[29] Almeida, Â., Silva, Mó.G., Soares, A.M. V.M., Freitas, R. Concentrations levels and effects of 17alpha-Ethinylestradiol in freshwater and marine waters and bivalves: A review. Environmental Research, 2020.

[30] Directive. Directive 2013/39/EU of the European Parliament 556 and of the Council of 12 August 2013 regarding prioritary substances in the field of water policy. Journal of European Union, 2014, L 226/1.

[31] Czajka, C.P., Londry, K.L. Anaerobic biotransformation of estrogens. Science of the Total Environment, 2006, 367, 932–941.

[32] Sarmah, A.K., Northcott, G.L. Laboratory degradation studies of four endocrine disruptors in two environmental media. Environmental Toxicology and Chemistry, 2008, 27, 819–827.

[33] Ying, G.G., Toze, S., Hanna, J., Yu, X. Y., Dillon, P.J., Kookana, R.S. Decay of endocrine-disrupting chemicals in aerobic and anoxic groundwater. Water Research, 2008, 2, 1133–1141.

[34] Ying, G.G., Kookana, R.S., Dillon, P. Sorption and degradation of selected five endocrine disrupting chemicals in aquifer material. Water Research, 2003, 37, 3785–3791.

[35] Ke, J.X., Zhuang, W.Q., Gin, K.Y.H., Reinhard, M., Hoon, L.T., Tay, J.H. Characterization of estrogen-degrading bacteria isolated from an artificial sandy

aquifer with ultrafiltered secondary effluent as the medium. Applied Microbiology and Biotechnology, 2007, 75, 1163–1171.

[36] He, H., Huang, B., Fu, G., Xiong, D., Xu, Z., Wu, X., Pan, X. Dissolved organic matter mediates in the anaerobic degradation of 17α-ethinylestradiol in a coupled electrochemical and biological system. Bioresource Technology, 2019, 292, 12, 19–24.

[37] Yoshimoto, T., Nagai, F., Fujimoto, J., Watanabe, K., Mizukoshi, H., Makino, T., Kimura, K., Saino, H., Sawada, H., Omura, H. Degradation of estrogens by Rhodococcus zopfii and Rhodococcus equi isolates from activated sludge in wastewater treatment plants. Applied and Environmental Microbiology, 2004, 70, 5283–5289.

[38] Ren, Y.X., Nakano, K., Nomura, M., Chiba, N., Nishimura, O. Effects of bacterial activity on estrogen removal in nitrifying activated sludge. Water Research, 2007, 41, 3089–3096.

[39] Hamid, H., Eskicioglu, C. Fate of estrogenic hormones in wastewater and sludge treatment: A review of properties and analytical detection techniques in sludge matrix. Water Research, 2012, 46, 5813–5833.

[40] Dytczak, M.A., Londry, K.L., Oleszkiewicz, J.A. Biotransformation of estrogens in nitrifying activated sludge under aerobic and alternating anoxic/aerobic conditions. Water and Environmental Research, 2008, 80, 47–52.

[41] Yi, T., Harper, W.F. The link between nitrification and biotransformation of 17a-ethinylestradiol. Environmental Science and Technology, 2007, 41, 4311–4316.

[42] Khunjar, W.O., MacKintosh, S.A., Skotnicka-Pitak, J., Baik, S., Aga, D.S., Love, N.G. Elucidating the relative roles of ammonia oxidizing and heterotrophic bacteria during the biotransformation of 17a-ethinylestradiol and trimethoprim. Environment, Science and Technology, 2011, 45, 3605–3612.

[43] Kassotaki, E., Pijuan, M., Joss, A., Borrego, C.M., Rodriguez-Roda, I., Buttiglieri, G. Comparative assessment of endocrine disrupting compounds removal in heterotrophic and enriched nitrifying biomass. Chemosphere, 2019, 217, 659–668.

[44] Larcher, S., Yargeau, V. Biodegradation of 17a-ethinylestradiol by heterotrophic bacteria. Environmental Pollution, 2013, 173, 17–22.

[45] Larkin, M.J., Kulakov, L.A., Allen, C.C.R. Biodegradation and rhodococcus masters of catabolic versatility. Current Opinion in Biotechnology, 2005, 16, 282–290.

[46] Martínková, L., Uhnáková, B., Pátek, M., Nesvera, J., Kren, V. Biodegradation potential of the genus Rhodococcus. Environment International, 2009, 35, 162–177

[47] Ma, W., Sun, J., Li, Y., Lun, X., Shan, D. Nie, C., Liu, M. 17α-Ethynylestradiol biodegradation in different river-based groundwater recharge modes with reclaimed water and degradation-associated community structure of bacteria and archaea. Journal of Environmental Science, 2016, 1–11.

[48] Suzuki, K., Hiraia, H., Muratab, H., Nishidaa, T. Removal of estrogenic activities of 17b-estradiol and ethinylestradiol by ligninolytic enzymes from white rot fungi. Water Research, 2003, 37, 1972–1975.

[49] Solomon, E.I., Baldwin, M.J., Lowery, M.D. Electronic structures of active sites in copper proteins: Contributions to reactivity. Chemical Revolution, 1992, 92(4), 521–542.

[50] Bla´nquez, P., Guieysse, B. Continuous biodegradation of 17b-estradiol and 17

152

App. Envi. Res. 43(2) (2021): 130-158

aethynylestradiolbyTrametes versicolor. Journal of Hazardous Materials, 2008, 150, 459–462.

[51] Choudhary, M.I., Musharraf, S.G., Ali, R.A., Atif, M., Atta-ur-Rahman. Microbial transformation of antifertility agents, norethisterone and 17-a-ethinyl estradiol. Zeitschrift für Naturforschung, 2004, 59b, 319–323.

[52] Shi, J.H., Suzuki, Y., Lee, B.D., Nakai, S., Hosomi, M.I. Isolation and characterization of the ethynylestradiol-biodegrading microorganism Fusarium proliferatum strain HNS-1. Water Science and Technology, 2002, 45, 175–179.

[53] Nicotra, S., Intra, A., Ottolina, G., Riva, S., Danieli, B. Laccase-mediated oxidation of the steroid hormone 17β-estradiol in organic solvents. Tetrahedron Asymmetry, 2004, 15(18), 2927–2931.

[54] Auriol, M., Filali-Meknassi, Y., Adams, C.D., Tyagi, R.D., Noguerol, T.N., Pina, B. Removal of estrogenic activity of natural and synthetic hormones from a municipal wastewater: Efficiency of horseradish peroxidase and laccase from Trametes versicolor. Chemosphere, 2008, 70(3), 445–452.

[55] Beck, S., Berry, E., Duke, S., Milliken, A., Patterson, H., Prewett, D.L., …, Johnson, C.M. Characterization of Trametes versicolor laccase-catalyzed degradation of estrogenic pollutants: Substrate limitation and product identification, International Biodeterioration & Biodegradation, 2018.

[56] Lloret, L., Eibes, G., Moreira, M.T., Feijoo, G., Lema, J.M. Removal of estrogenic compounds from filtered secondary wastewater effluent in a continuous enzymatic membrane reactor. Identification of biotransformation products. Environment, Science and Technology, 2013, 47(9), 4536–4543.

[57] Cheng, J., Xu, J., Huang, Y., Li, Y., Zhou, J., Cen, K. Growth optimisation of microalga mutant at high CO_2 concentration to purify undiluted anaerobic digestion effluent of swine manure. Bioresources Technology, 2015, 177, 240–246.

[58] Cheng, J., Ye, Q., Yang, Z., Yang, W., Zhou, J., Cen, K. Microstructure and antioxidative capacity of the microalgae mutant Chlorella PY-ZU1 during tilmicosin removal from wastewater under 15% CO_2. Journal of Hazardous Materials, 2017, 324, 414–419.

[59] Sun, J., Cheng, J., Yang, Z., Li, K., Zhou, J., Cen, K. Microstructures and functional groups of Nannochloropsis sp. cells with arsenic adsorption and lipid accumulation. Bioresources Technology, 2015, 194, 305–311.

[60] de Godos, I., Munoz, R., Guieysse, B. Tetracycline removal during wastewater treatment in high-rate algal ponds. Journal of Hazardous Materials, 2012, 229, 446–449.

[61] Zhang, Y., Habteselassie, M.Y., Resurreccion, E.P., Mantripragada, V., Peng, S., Bauer, S., Colosi, L.M. Evaluating removal of steroid estrogens by a model alga as a possible sustainability benefit of hypothetical integrated algae cultivation and wastewater treatment systems. ACS Sustainable and Chemical Engineering, 2014, 2, 2544–2553.

[62] Gmurek, M., Olak-Kucharczyk, M., Ledakowicz, S. Photochemical decomposition of endocrine disrupting compounds - A review. Chemical Engineering Journal, 2017, 310, 437–456.

[63] Bai, X., Acharya, K.U. Removal of seven endocrine disrupting chemicals (EDCs) from municipal wastewater effluents by a freshwater green alga. Environmental Pollution, 2019, 247, 534–540.

[64] Sole, A., Matamoros, V. Removal of endocrine disrupting compounds from wastewater by microalgae co-immobilized in alginate beads. Chemosphere, 2016, 164, 516–523.

[65] Cheng, J., Ye, Q., Yang, Z., Yang, W., Zhou, J., Cen, K. Removing ethinylestradiol from wastewater by microalgae mutant Chlorella PY-ZU1 with CO_2 fixation Bioresources Technology, 2018, 249, 284–289.

[66] Balina, K., Balode, M., Muzikante, L., Blumberga, D. Impact of synthetic hormone 17 alpha-ethinylestradiol on growth of microalgae Desmodesmus eommunis. Agronomic Resources, 2015, 13, 445–454.

[67] Calabrese, E.J., Baldwin, L.A. Hormesis: the dose-response revolution. Annual Review of Pharmacology and Toxicology, 2003, 43, 175–197.

[68] Della Greca, M., Pinto, G., Pistillo, P., Pollio, A., Previtera, L., Temussi, F. Biotransformation of ethinylestradiol by microalgae. Chemosphere, 2008, 70, 2047–2053.

[69] Hom-Diaz, A., Llorca, M., Rodríguez-Mozaz, S., Vicent, T., Barcel, D., Blanquez, P. Microalgae cultivation on wastewater digestate: b-estradiol and 17a-ethynylestradiol degradation and transformation products identification. Journal of Environmental Management, 2015, 155, 106–113

[70] Abreu, A.P., Fernandes, B., Vicente, A. A., Teixeira, J., Dragone, G. Mixotrophic cultivation of Chlorella vulgaris using industrial dairy waste as organic carbon source. Bioresources Technology, 2012, 118, 61–66.

[71] Li, Y., Chen, Y.-F., Chen, P., Min, M., Zhou, W., Martinez, B., Zhu, J., Ruan, R. Characterization of a microalga Chlorella sp. well adapted to highly concentrated municipal wastewater for nutrient removal and biodiesel production. Bioresources Technology, 2011, 102, 5138–5144.

[72] Singh, M., Reynolds, D.L., Das, K.C. Microalgal system for treatment of effluent from poultry litter anaerobic digestion. Bioresources Technology, 2011, 102, 10841–10848.

[73] Wang, Y., Suna, Q., Li, Y., Wang, H., Wu, K., Chang-Ping Y. Biotransformation of estrone, 17β-estradiol and 17α-ethinylestradiol by four species of microalgae. Ecotoxicology and Environmental Safety, 2019, 180, 723–732.

[74] Layton, A.C., Gregory, B.W., Seward, J.R., Schultz, T.W., Saylor, G.S. Mineralization of steroidal hormones by bio-solids in wastewater treatment systems in Tennessee USA. Environmental Science Technology, 2000, 34, 3925–3931.

[75] Shah, S.A.A., Sultan, S., Hassan, N., Adnan H.S. Biotransformation of 17a-ethynyl substituted steroidal drugs with microbial and plant cell cultures: A review. Steroids, 2013, 78, 1312–1324.

[76] Krˇesinova Z., Moeder M., Ezechiaš M., Svobodova K., Cajthaml T. Mechanistic study of 17a-ethynylestradiol biodegradation by Pleurotus ostreatus: Tracking of extracelullar and intracelullar degradation mechanisms. Environmental Science and Technology, 2012, 46, 13377–13385.

[77] Gao, Y., Sun, D., Dang, Y., Lei, Y., Ji, J., Lv, T., ..., Holmes, D.E. Enhancing biomethanogenic treatment of fresh incineration leachate using single chambered microbial electrolysis cells. Bioresources Technology, 2017, 231, 129–137.

[78] Zeng, X., Borole, A.P., Pavlostathis, S.G. Biotransformation of furanic and phenolic compounds with hydrogen gas production in a microbial electrolysis cell. Environmental Science and Technology, 2015, 49(22), 13667–13675.

[79] Hou, Y., Zhang, R., Yu, Z., Huang, L., Liu, Y., Zhou, Z. Accelerated azo dye degradation and concurrent hydrogen pro-

duction in the single-chamber photocatalytic microbial electrolysis cell. Bioresources Technology, 2017, 224, 63–68.

[80] He, H., Huang, B., Fu, G., Xiong, D., Xu, Z., Wu, X., Pan, X. Electrochemically modified dissolved organic matter accelerates the combining photodegradation and biodegradation of 17 alpha-ethynylestradiol in natural aquatic environment. Water Research, 2018,137, 251–261.

[81] Campos, J.M., Queiroz, S.C.N., Roston, D.M. Removal of the endocrine disruptors ethinyl estradiol, bisphenol A, and levonorgestrel by subsurface constructed wetlands. Science of the Total Environment, 2019, 693, 13–35.

[82] Lin, Y.L. Effects of organic, biological and colloidal fouling on the removal of pharmaceuticals and personal care products by nanofiltration and reverse osmosis membranes. Journal of Membrane Science, 2017, 342–351.

[83] Harris, C.A., Hamilton, P.B., Runnalls, T.J., Vinciotti, V., Henshaw, A., Hodgson, D., …, Sumpter, J.P. The consequences of feminization in breeding groups of wild fish. Environmental Health Perspectives, 2011, 119(3), 306–311.

[84] ITRC - Interstate Technology, Regulatory Council. Technical and Regulatory Guidance Document for Constructed Treatment Wetlands (Washington, D.C., USA), 2003.

[85] Ávila, C., Matamoros, V., Reyes-Contreras, C., Piña, B., Casado, M., Mita, L., …, Bayona, J.M. Attenuation of emerging organic contaminants in a hybrid constructed wetland system under different hydraulic loading rates and their associated toxicological effects in wastewater. Science of Total Environment, 2014, 470–471, 1272–1280.

[86] Gupta, V.K., Carrott, P.J., Carrott, M.M., Ribeiro, C.S. Low-cost adsorbents: Growing approach to wastewater treatment - A

review. Critical Review of Environmental Science and Technology, 2009, 39(10), 783–842.

[87] Nam, S.D., Choi, S., Kim, N., Her, K.D. Adsorption characteristics of selected hydrophilic and hydrophobic micropollutants in water using activated carbon. Journal of Hazardous Materials, 2014, 270, 144–152.

[88] Mailler R., Gasperi, J., Coquet, Y., Deshayes, S., Zedek, S., Cren-Olivé, C., …, Rocher, V. Study of a large scale powdered activated carbon pilot: removals of a wide range of emerging and priority micropollutants from wastewater treatment plant effluents. Water Research, 2015, 72, 315–330.

[89] Grassi, M.K., Gul, B., Vincenzo, L.G. Removal of emerging contaminants from water and wastewater by adsorption process. Emerging compounds removal from wastewater: Natural and solar based treatment, 2012, 15–38.

[90] Sophia, A.C., Lima, E.C., Allaudeen, N. Application of graphene based materials for adsorption of pharmaceutical traces from water and wastewater-A review. Water Treatment, 2016, 57(57), 1–14.

[91] Harris, C.A., Hamilton, P.B., Runnalls, T.J., Vinciotti, V., Henshaw, A., Hodgson, D., …, Sumpter, J.P. The consequences of feminization in breeding groups of wild fish. Environmental Health Perspectives, 2011, 119(3), 306–311.

[92] Limpiyakorn, T., Homklin, S., Ong, S.K. Fate of estrogens and estrogenic potentials in sewerage systems. Critical Reviews in Environmental Science and Technology, 2011, 41(13), 1231–1270.

[93] Middleton, H., Moore, M.R., Chapman, H., Leusch, F., Tan, B., Drew, R., …, Shaw, G. Australian guidelines for water recycling: Recycled water quality - A guide to determining, monitoring and achieving

safe concentrations of chemicals in recycled water. Environmental Protection and Heritage Council, National Water Commission, Queensland Government, Canberra, ACT, 2008.

[94] Clouzot, L., Marrot, B., Doumenq, P., Roche, N. 17 alphaethinylestradiol: An endocrine disrupter of great concern. Analytical methods and removal processes applied to water purification: A review. Environmental Progress, 2008, 27(3), 383–396.

[95] Tadkaew, N., Hai, F.I., McDonald, J.A., Khan, S.J., Nghiem, L.D. Removal of trace organics by MBR treatment: the role of molecular properties. Water Research, 2011, 45(8), 2439–2451.

[96] Han, J., Qiu, W., Meng, S., Gao, W. Removal of ethinylestradiol (EE2) from water via adsorption on aliphatic polyamides. Water Research, 2012, 46–58.

[97] Yamamoto, H., Liljestrand, H.M. Partitioning of selected estrogenic compounds between synthetic membrane vesicles and water: Effects of lipid components. Environmental Science and Technology, 2004, 38(4), 1139–1147.

[98] Szabo, L., Vancsik, A., Kiraly, C., Ringer, M., Kondor, A., Jakab, G., Szalai, Z., Filep, T. Investigation of the sorption of 17a-ethynylestradiol (EE2) on soils formed under aerobic and anaerobic conditions. Chemosphere, 2020, 240, 12–17.

[99] Sun, K., Jin, J., Gao, B., Zhang, Z., Wang, Z., Pan, Z., ..., Zhao, Y. Sorption of 17a-ethinyl estradiol, bisphenol A and phenanthrene to different size fractions of soil and sediment. Chemosphere, 2012, 88, 577–583.

[100] Oliveira, R.A. de, Tardelli, E.R., Jozala, A.F., Grotto, D. Evaluation of the 17- a - ethinyl estradiol sorption capacity in soil. Water, Air and Soil Pollution, 2019, 230, 85.

[101] Bielská, L., Skulcová, L., Neuwirthová, N., Cornelissen, G., Hale, S.E. Sorption, bioavailability and ecotoxic effects of hydrophobic organic compounds in biochar amended soils. Science and Total Environment, 2018, 624, 78–86.

[102] Wang, D.J., Shin, J.Y., Cheney, M.A., Sposito, G, Spiro, T.G. Manganese dioxide as a catalyst for oxygen-independent atrazine dealkylation. Environmental Science and Technology, 1999, 33(18), 3160–3165.

[103] Maher, K., O'Malley, K.N., Heffron, J., Huo, J., Mayer, B.K., Wang, Y., McNamara, P.J. Analysis of operational parameters, reactor kinetics, and floc characterization for the removal of estrogens via electrocoagulation. Chemosphere, 2019, 220, 1141–1149.

[104] Westerhoff, P., Yoon, Y., Snyder, S., Wert, E. Fate of endocrine-disruptor, pharmaceutical, and personal care product chemicals during simulated drinking water treatment processes. Environmental Science and Technology, 2005, 39, 6649–6663.

[105] Heidmann, I., Calmano, W. Removal of Cr(VI) from model wastewaters by electrocoagulation with Fe electrodes. Separation and Purification Technology, 2008, 61, 15–21.

[106] Liu, H., Zhao, X., Qu, J. Electrocoagulation in water treatment. *In:* Comninellis, C., Chen, G. Electrochemistry for the Environment. Springer New York, 2010, 245–262.

[107] Pan, C., Troyer, L.D., Catalano, J.G., Giammar, D.E. Dynamics of chromium (VI) removal from drinking water by iron electrocoagulation. Environmental Science and Technology, 2016, 235–245.

[108] Ding, L., Wu, C., Deng, H.P., Zhang, X.X. Adsorptive characteristics of phosphate from aqueous solutions by MIEX

resin, Journal of Colloid Interface Science, 2012, 376, 224–232.

[109] Boyer, T.H., Singer, P.C. Bench-scale testing of a magnetic ion exchange resin for removal of disinfection by-product precursors, Water Research, 2005, 39, 1265–1276.

[110] Mastrup, M., Schäfer, A.I. Removal of estrone in solution by magnetic ionic exchange resin (MIEX), Environmental Engineering Research Event, 2001, 235–243.

[111] Schwarzenbach, R.P., Escher, B.I., Fenner, K., Hofstetter, T.B., Johnson, C.A., von Gunten, U and Wehrli, B. The challenge of micropollutants in aquatic systems. Science 2006, 313, 1072–1077.

[112] Schäfer, A.I., Mastrup, M., Venkatesh, S. Trace contaminant removal using magnetic ion exchange and microfiltration, Recent Advance Water Recycle Technology, 2001, 26, 41–54.

[113] Wang, L., Liu, L., Zhang, Z., Zhao, B., Li, J., Dong, B., Liu, N. 17α-Ethinylestradiol removal from water by magnetic ion exchange resin. Chinese Journal of Chemical Engineering, 2018, 26, 864–869.

[114] Maurıcio, R., Semedo, F., Dias, R., Noronha, J.P., Amaral, L., Daam, M.A., …, Diniz, M.S. Efficacy assessment of peracetic acid in the removal of synthetic 17a-ethinyl estradiol contraceptive hormone in wastewater. Journal of Environmental Sciences, 2020, 89, 1–8.

[115] McFadden, M., Loconsole, J., Schockling, A.J., Nerenberg, R., Pavissich, J.P. Comparing peracetic acid and hypochlorite for disinfection of combined sewer overflows: Effects of suspended-solids and pH. Science of Total Environment, 2017, 599–600, 533–539.

[116] Henao, L.D., Turolla, A., Antonelli, M. Disinfection byproducts formation and ecotoxicological effects of effluents treated with peracetic acid: A review. Chemosphere, 2018, 213, 25–40.

[117] Sun, P., Zhang, T., Mejia-Tickner, B., Zhang, R., Cai, M., Huang, C.H. Rapid disinfection by peracetic acid combined with UV irradiation. Environmental Science and Technology Letters, 2018, 56, 400–404.

[118] Bonetta, S., Pignata, C., Lorenzi, E., De Ceglia, M., Meucci, L., Bonetta, S. Peracetic acid (PAA) disinfection: Inactivation of microbial indicators and pathogenic bacteria in a municipal wastewater plant. Water, 2017, 9, 427.

[119] Rizzo, L., Agovino, T., Nahim-Granados, S., Castro-Alferez, M., Fernandez-Ibanez, P., Polo-Lopez, M.I. Tertiary treatment of urban wastewater by solar and UV-C driven advanced oxidation with peracetic acid: Effect on contaminants of emerging concern and antibiotic resistance. Water Research, 2019, 149, 272–281.

[120] Luukkonen, T., Teeriniemi, J., Prokkola, H., Ramo, J., Lassi, U. Chemical aspects of peracetic acid-based wastewater disinfection. Water, 2014, 40, 73–80.

[121] Pignatello, J.J., Oliveros, E., MacKay, A. Advanced oxidation processes for organic contaminant destruction based on the fenton reaction and related chemistry. Critical Review Environmental Science Technology, 2006, 36.

[122] Deng, Y., Zhao, R. Advanced oxidation processes (AOPs) in wastewater treatment. Current Pollution Reports, 2015, 1.

[123] Genesis Water Technologies. Benefits and disadvantages of the advanced oxidation process, 2019.

[124] Shen, J., Ding, T., Zhang, M. Analytical techniques and challenges for removal of pharmaceuticals and personal care products in water. Elsevier BV, 2019.

App. Envi. Res. 43(2) (2021): 130-158

157

[125] Ben Fredj, S.J., Nobbs, B. C. Tizaoui, L. M. Removal of estrone (E1), 17b-estradiol (E2), and 17a-ethinylestradiol (EE2) from wastewater by liquid–liquid extraction. Chemical Engineering Journal, 2015, 262, 417–426.

[126] Ward, D.B., Tizaoui, C., Slater, M.J. Continuous extraction and destruction of chloroorganics in wastewater using ozone-loaded Volasil™245 solvent. Journal of Hazardous Materials, 2005, 125, 65–79.

[127] Śliwka-Kaszyńskaa, M., Jakimska-Nagorskab, A., Wasikc, A., Kot-Wasikc, A. Phototransformation of three selected pharmaceuticals, naproxen, 17α-Ethinylestradiol and tetracycline in water: Identification of photoproducts and transformation pathways Microchemical Journal, 2019,148, 673–683.

[128] Wang, H.Y.X. Mechanism of removal of pharmaceuticals and personal care products by nanofiltration membranes. Desalinated Water Treatment, 2015, 53(10), 2816–2824.

[129] Rana, D., Narbaitz, R.M., Garand-sheridan, A. Development of novel charged surface modifying macromolecule blended PES membranes to remove EDCs and PPCPs from drinking water sources. Journal of Material Chemistry, 2014, A2 (26), 10059–10072.

[130] Ge, S., Feng, L., Zhang, L., Xu, Q., Yang, Y., Wang, Z., Kim, K.H. Rejection rate and mechanisms of drugs in drinking water by nanofiltration technology. Environmental and Engineering Research, 2017, 22(3), 329–338.

[131] Lin, Y.L. Effects of organic, biological and colloidal fouling on the removal of pharmaceuticals and personal care products by nanofiltration and reverse osmosis membranes. Journal of Membrane Science, 2017, 342–351.

[132] Park, J., Park, J.H., Lee, J.Y., Kim, K.T., Joe, H.E., Cho, H.J., …, Kim, D.D.

Physostigmine-loaded liposomes for extended prophylaxis against nerve agent poisoning. International Journal of Pharmaceutics, 2018.

[133] Zhang, Z., Feng, Y., Liu, Y., Sun, Q., Gao, P., Ren, N. Kinetic degradation model andestrogenicity changes of EE2 (17 a-ethinylestradiol) in aqueous solution by UV and UV/H2O2 technology. Journal of Hazardous Materials, 2010, 181, 1127–1133.

[134] Frontistis, Z., Daskalaki, V.M., Hapeshi., E., Drosou, C., Fatta-Kassinos, D., Xekoukoulotakis, N.P., Mantzavinos, D. Photocatalytic (UV-A/TiO2) degradation of17a-ethynylestradiol in environmental matrices: experimental studies and artificial neural network modeling, Journal of Photochemistry and Photobiology, 2012, 240, 33–41.

[135] Chen, Y., Yefei, Z., Lijun, L., Yingying, S., Shan, W., Lingxin, L., …, Fengzhi, J. A novel templated synthesis of C/N-doped β-Bi2O3 nanosheets for synergistic rapid removal of 17α-ethynylestradiol by adsorption and photocatalytic degradation. Ceramics International, 2017.

[136] Kazuhito, H.I., Hiroshi, F.A. TiO2 photocatalysis: A historical overview and future prospects, Japanese Journal of Applied Physics, 2005, 44, 826–829.

[137] Jalalah M., Faisal, M., Bouzid, H., Park, J.G., Al-Sayari, S.A., Ismail, A.A. Comparative study on photocatalytic performances of crystalline α- and β-Bi2O3 nanoparticles under visible light. Journal of Industrial and Engineering Chemistry, 2015, 30(2015), 183–189.

[138] Wang, R., Ren, D., Xia, S., Zhang, Y., Zhao, J. Photocatalytic degradation of bisphenolA (BPA) using immobilized TiO2and UV illumination in a horizontal circulating bed photocatalytic reactor

(HCBPR). Journal of Hazardous Materials, 2009, 169, 926–932.

[139] Anandan, S., Yoon, M. Photocatalytic activities of the nano-sized TiO₂-supportedY-zeolites. Journal of Photochemistry and Photobiology, 2003, 4, 5–18.

[140] Pan, Z., Stemmler, E.A., Cho, H.J., Fan, W., LeBlanc, L.A., Patterson, H.H., Amirbahman, A. Photocatalytic degradation of 17 a-ethinylestradiol (EE2) in thepresence of TiO₂-doped zeolite. Journal of Hazardous Materials, 2014, 279, 17–25.

[141] Mazellier, P., Méité, L., De Laat, J. Photodegradation of the steroid hormones 17b-estradiol (E2) and 17a-ethinylestradiol (EE2) in dilute aqueous solution. Chemosphere, 2008, 73, 1216–1223.

[142] Grzybowski, W., Szydłowski, J. The impact of chromophoric dissolved organic matter on the photodegradation of 17a-ethinylestradiol (EE2in natural waters). Chemosphere 2014, 111, 13–17.

[143] Kamat, P.V. Graphene-based nano-architectures. Anchoring semiconductor and metal nanoparticles on a two-dimensional carbon support. Journal of Physical Chemistry Letters, 2010, 1, 520–527.

[144] Zhao, G., Song, S., Wang, C., Wu, Q., Wang, Z. Deatermination of triazine herbicides in environmental water samples by high-performance liquid chromatography using graphene-coated magnetic nanoparticles as adsorbent. Analytica Chimica Acta, 2011, 708, 155–159.

[145] Bhunia, S.K., Jana, N.R. Reduced graphene oxide-silver nanoparticle composite as visible light photocatalyst for degradation of colorless endocrine disruptors. ACS Applied Material Interfaces, 2014, 6, 20085–20092.

[146] Boas, M., Feldt-Rasmussen, U., Main, K.M. Thyroid effects of endocrine disrupting chemicals. Molecular and Cellular Endocrinology, 2012, 355, 240–248.

[147] Cunha, G.S., Bianca, M.S.., Daniele, M. B., João, P.B., Chad, D.V., Márcia, D. Insights into estrogenic activity removal using carbon nanotube electrochemical filter. Science of the Total Environment, 2019, 678, 448–456.

[148] Rácz, C.P, Borodi, G., Pop, M.M., Kacso, I., Sánta, S., Tomoaia-Cotisel, M. Structure of the inclusion complex of β-cyclodextrin with lipoic acid from laboratory powder diffraction data, Acta Crystallographica B., 2012, 68(Pt 2), 164–170.

[149] Chen, G.S., Jiang, M. Cyclodextrin-based inclusion complexation bridging supramolecular chemistry and macromolecular self-assembly. Chemical Society Review, 2011, 40, 2254–2266.

[150] Tang, P., Qiaomei Sun, Z., Suo, L.Z., Hongqin Yang, X.X., Hongyu Pu, N.G., Hui, L. Rapid and efficient removal of estrogenic pollutants from water by using beta- and gamma-cyclodextrin polymers, Chemical Engineering Journal, 2018, 1–30.