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Occurrence and distribution of pharmaceuticals and personal care products (PPCPs) detected in lakes around the world - A review

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ABSTRACT

This review presents a compilation of pharmaceuticals and personal care products (PPCPs) that have been detected in waters, sediments and biota of lakes throughout the world by various researchers, over a 26-year time period (1996–2021). Numerous studies published in the literature reported that 286 pharmaceuticals and 70 personal care products (PCPs) were present in waters, 101 pharmaceuticals and 50 PCPs were present in sediments, and 63 pharmaceuticals and 19 PCPs were present in biota of lakes throughout the world. Among the pharmaceuticals present in lake waters, 194 had concentrations of over 5 ng/L, 173 were present in only one continent, whereas several (e.g. caffeine, carbamazepine and sulfamethoxazole) were detected in lake waters of almost every continent (6/7). Among the PCPs present in lake waters, 56 had concentrations of over 5 ng/L, whereas 41 were present in only one continent. PPCPs were found in 260 lakes, located within 44 countries, the majority of them present in Asian, European and North American lakes. Lakes with high pharmaceutical concentrations were affected by either controlled or uncontrolled wastewater originated from various types of sources. Based on this study, of high concern is the Asian continent, where PPCP pollution should be strictly controlled in order to prevent possible serious health threats to humans and living organisms.

1. Introduction

During the last few decades, the continuous technological developments, overpopulation, global urbanization trends, and climate change, contributed to the observed depletion of drinking water and contamination of most of the available water resources throughout the world (Hena and Znad, 2018; Rabiet et al., 2006; Stewart et al., 2014; Monteiro and Boxall, 2010; Brausch and Rand, 2011; aus der Beek et al., 2016; Kaczala and Blum, 2016; Fang et al., 2019; Petrie et al., 2015). Lakes, one of the principal sources of fresh water, are often polluted by a variety of contaminants due to human activities (Chen et al., 2019). Also, numerous studies published in the scientific literature suggested that pharmaceuticals and personal care products (PPCPs) could be significant sources of contamination to surface waters, such as lakes ponds, rivers, and streams (Lyndall et al., 2017; Pal et al., 2014; González-Plaza et al., 2019; Kumar et al., 2019b; Manzetti and Ghisi, 2014; Li et al., 2020; Kandie et al., 2020; Zhang et al., 2017b; Kahle et al., 2008; Ferrey, 2013; Ferrey et al., 2015; Whitacre, 2011). The pharmaceuticals include mainly drugs administered to humans or animals, such as antibiotics, anti-inflammatories, their metabolites as well as transformation products, which are either excreted in faeces and urine, originated from wastewater treatment plants (WWTPs), clinics, hospitals, industrial effluents, aquaculture wastewaters (Katsikaros and Chrysikopoulos, 2020; Li et al., 2020; Servadio et al., 2021; Jiang et al., 2021; Li et al., 2021; Yang et al., 2021). Personal care products (PCPs) include diverse types of products such as lotions, sunscreen creams, soaps, cosmetics, perfumes, toothpastes. Many health issues can possibly arise when such contaminants finally enter the available water resources(Liu et Wong, 2013). Due to insufficient removal in WWTPs and direct disposal into the aquatic environment, PPCPs have been detected in lakes throughout the world in concentrations ranging from ng/L to μg/L (Gros et al., 2010; Petri, 2006; Wojcieszyńska and Guzik, 2020; K`oreje et al., 2016; Wombacher and Hornbuckle, 2009; Lahti and Oikari, 2012; Hu et al., 2018b; Tran et al., 2014b; Vieno, 2007; Ebele et al, 2017). It should be noted that pharmaceuticals are able to accumulate to lake biota, adversely affect and be harmful to them, even when their concentrations are similar to those detected in lake waters (Liu et al., 2015; Pascoe et al., 2003; Kidd et al., 2007; Cooper et al., 2008).

In this study, various PPCPs detected in natural aquatic environments associated with lakes throughout the world were determined,

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compiled and evaluated, based on information reported in the literature. The collected data were classified according to respective environmental media: waters, sediments, and biota. The reported range of maximum and mean concentrations of the various PPCPs were tabulated. Based on the occurrence and the detected concentration levels, the potential human health risk as well as the ecological risk imposed by PPCPs were discussed.

2. Procedures and data compilation

All available published literature were systematically surveyed in order to collect desired information about the presence of PPCPs in the waters, sediments and biota of lakes throughout the world. Several literature databases (Scopus, Springer, PubMed® and Google® Scholar) were searched, using 23 pertinent key words/phrases (pharmaceuticals, personal care products, PPCPs, antibiotics, drugs, lake, water, aquatic, water bodies, freshwater, surface, reservoir, fish, biota, environment, natural, sediment, receiving water, water pathway, receiving environment, sewage, wastewater, effluents), creating 80 combinations used separately in each database. The literature search yielded numerous publications, which were carefully screened. The majority of the literature reported PPCPs concentrations detected within lake waters, and from immediate receiving waters.

The locations (country, continent) of the various lakes where numerous PPCPs substances were detected, together with their corresponding concentrations (in units of ng/L for chemicals in lake waters and ng/g for chemicals in sediments and biota) are listed in Tables S1 (for pharmaceuticals) and S2 (for PCPs) of the Supplementary Information (SI) file. For each PPCP reported in the literature, its minimum, maximum and mean/median concentrations where compiled. Subsequently, the average of the reported values for each pharmaceutical and PCP were calculated and registered as mean concentrations, whereas the maximum of the reported values were registered as maximum concentrations (see Tables S1, S2). When more than one concentration values for a certain PPCP were reported, then only the maximum of the minimum value, mean/median value and maximum value were compiled. Furthermore, when more than one published study reported PPCP concentrations at a certain location, over different chronological periods, only the most recent studies were considered.

3. Analysis and discussion of the compiled data

3.1. Literature on PPCPs

From the available published literature, 271 studies examining the presence of PPCPs in the waters, sediments, and biota of lakes throughout the world were identified. These studies were presented in a graphical form in Fig. 1, where it is evident that the number of pertinent publications increased progressively over the years, with a peak number of publications (33 publications) in 2018. It should be noted that over the time period from 1996 to 2012 the average publication rate was 5 studies per year, while over the time period from 2013 to 2021 the average publication rate was 22 studies per year. This rate of publication growth reflects the growing concern for the concentrations of PPCPs detected in lakes throughout the world. In many lake waters there is a trend of increasing average concentrations with time. Lakes Baiyangdian and Taihu in Asia, Mead in North America, and Haapajarvi in Europe presented the widest range of concentrations, so were chosen to show that trend graphically in Fig. 2. It is worth noticing that the distribution of studies presented in Fig. 1 were published in 95 different scientific journals, with the highest activity occurring in 2014, as shown in Fig. 3. Furthermore, the identified studies published over the 26-year time period (1996-2021) were also shown graphically in Fig. 4, as a function of the continent where the study lake was located. Clearly, the majority of the published studies concern Asian lakes (see Figs. 1 and 4), where the production and consumption of PPCPs is highest globally and continuously increasing (Su et al., 2020).

Some of the early studies include the detection of PPCPs in the water of lake Zurich (Europe) (Buser et al., 1998), in the sediments of lake Greifensee (Europe) (Singer et al., 2002), and in the biota of lake Mead (North America) (Bevans et al., 1996). The studies focused in African, Antarctican and Oceanian lakes, reported concentrations of PPCPs only in water. The majority of the studies focused in South American lakes (10/11), reported concentrations of PPCPs in waters, with only one study reporting in sediments (1/11). Among the 162 studies focused on Asian lakes, 108 reported concentrations of PPCPs in waters, 39 in sediments, and 15 in biota. Among the 94 studies focused in European lakes, 69 reported concentrations of PPCPs in waters, 10 in sediments, and 15 in biota. Finally, among the 61 studies focused in North American lakes, 40 reported concentrations of PPCPs in waters, 12 in sediments, and 9 in biota.

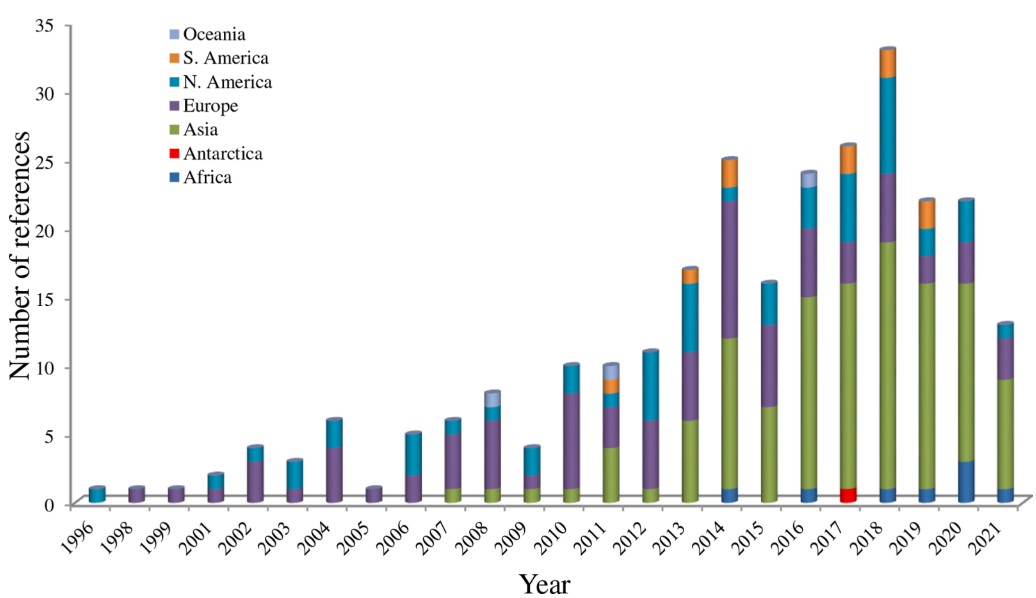

Fig. 1. Distribution of studies reporting PPCPs in waters, sediments, and biota of lakes in the various continents the world over the time period 1996 to May of 2021.

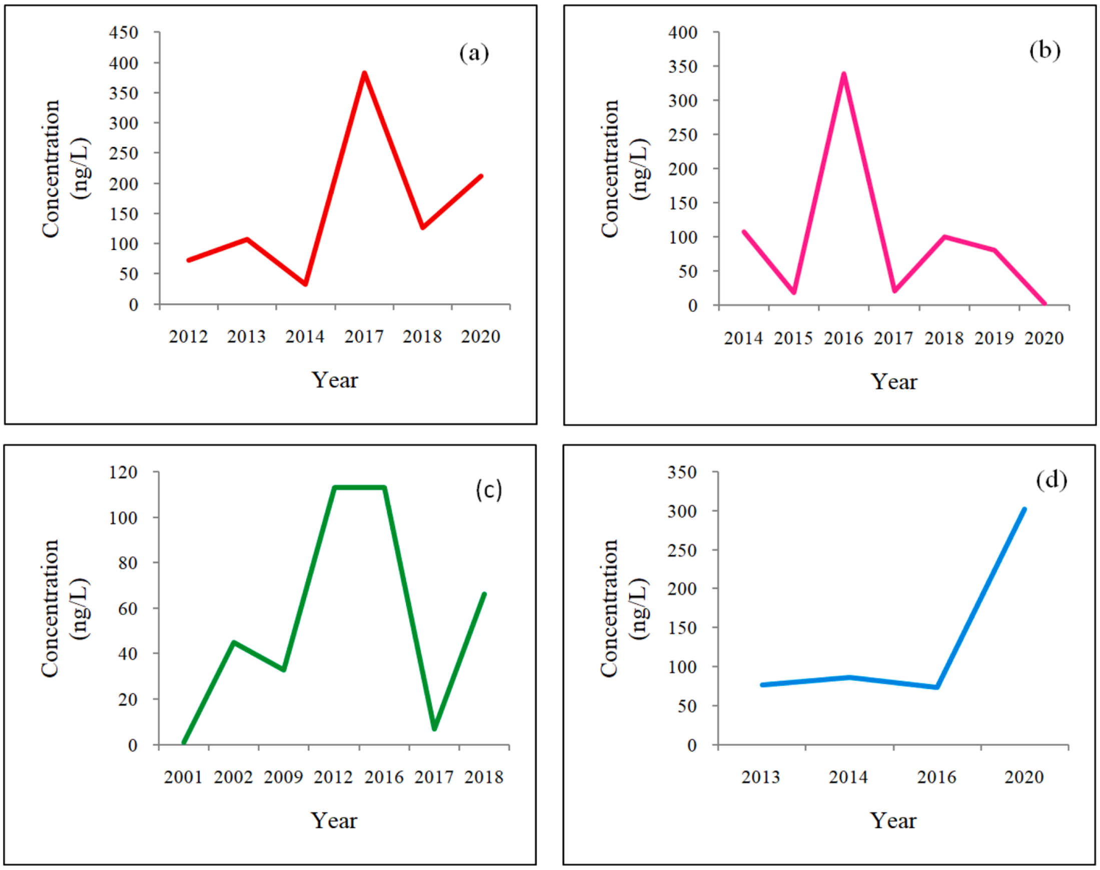

Fig. 2. Mean concentration trends of pharmaceuticals in the water of lakes: (a) Baiyangdian, (b) Taihu, (c) Mead, and (d) Haapajarvi.

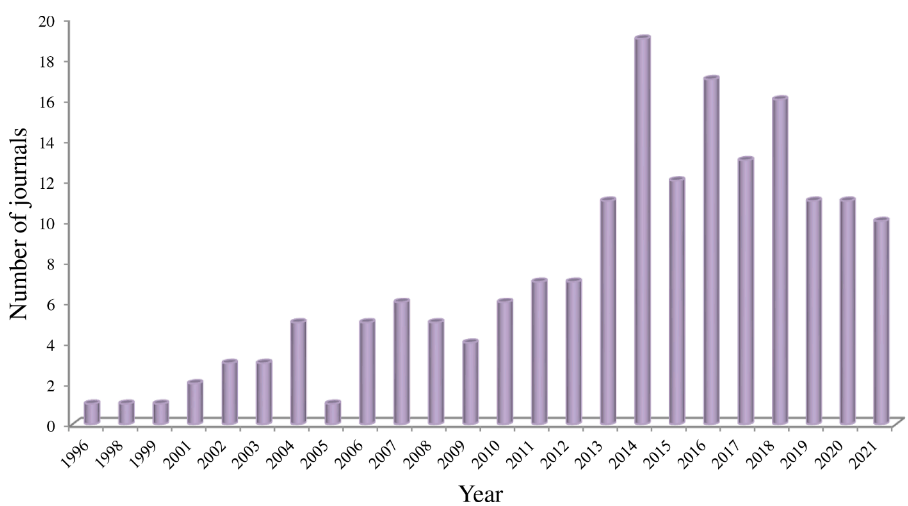

Fig. 3. Number of journals publishing research articles related to PPCPs in waters, sediments, and biota of lakes throughout the world over the time period 1996 to May of 2021.

3.2. PPCPs in lake waters

The African lakes with the highest concentrations of pharmaceuticals were located in Kenya, Uganda, South Africa, and Cameroon; whereas, Victoria and Hartbeespoort were two lakes with the heaviest PPCP contamination (see Tables S1, S2). Among the 29 pharmaceuticals reported present in waters of African lakes, the majority of them (24) were present in lake Victoria. Pharmaceuticals such as efavirenz and nevirapine were detected only in African lakes, whereas carbamazepine and sulfamethoxazole were also present in waters of numerous lakes located in several other continents. It should be noted that the waters of African lakes are not thoroughly analysed for PPCPs and more research is needed (Table S2; Dalahmeh et al., 2020).

In Antarctican lake waters the maximum concentration of pharmaceuticals ranged from <0.66 to 70 ng/L (see Table S1). In lake waters of the northern Antarctic Peninsula region 6 pharmaceuticals were detected (González-Alonso et al., 2017); whereas, in Oceanian lake waters 8 pharmaceuticals and 4 PCPs were detected. In Oceanian lake waters the maximum concentration of pharmaceuticals ranged from <10 to 135.9 ng/L; whereas, the maximum concentration of PCPs ranged from <10 to

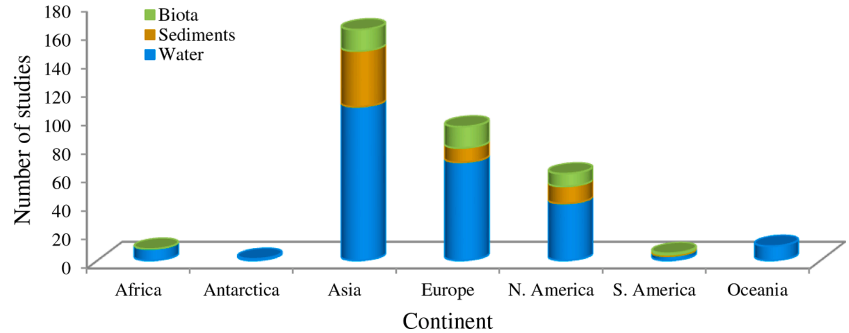

Fig. 4. Published studies from 1996 to May of 2021 reporting the presence of PPCPs in waters, sediments and biota of lakes throughout the world.

69 ng/L (Fisher and Scott, 2008; Hawker et al., 2011; Roberts et al., 2016). It should be noted that no PPCPs were detected in waters of other lakes, probably due to insufficient testing (Schallenberg and Krebsbach, 2002; Schallenberg and Armstrong, 2004).

In Asian lake waters, 179 pharmaceuticals and 39 PCPs were detected. It should be noted that among the PPCPs detected, 86 pharmaceuticals and 19 PCPs were present only in this continent. The maximum concentration of the pharmaceuticals ranged from 0.027 to 6.5×10^6 ng/L, with an average concentration of 1.14×10^5 ng/L, and the maximum concentrations of PCPs ranged from <0.35 to 7.31×10^5 ng/L, with an average concentration of 7.08×10^3 ng/L (see Tables S1, S2; Figs. 5, 6).

In European lake waters, 133 pharmaceuticals and 35 PCPs were detected. It should be noted that among the PPCPs detected, 57 pharmaceuticals and 13 PCPs were present only in this continent. The maximum concentration of the pharmaceuticals ranged from <0.02 to 1.36×10^4 ng/L, with an average concentration of 102 ng/L, and the maximum concentrations of PCPs ranged from 0.05 to 3.0×10^3 ng/L, with an average concentration of 85 ng/L (see Tables S1, S2; Figs. 5, 6).

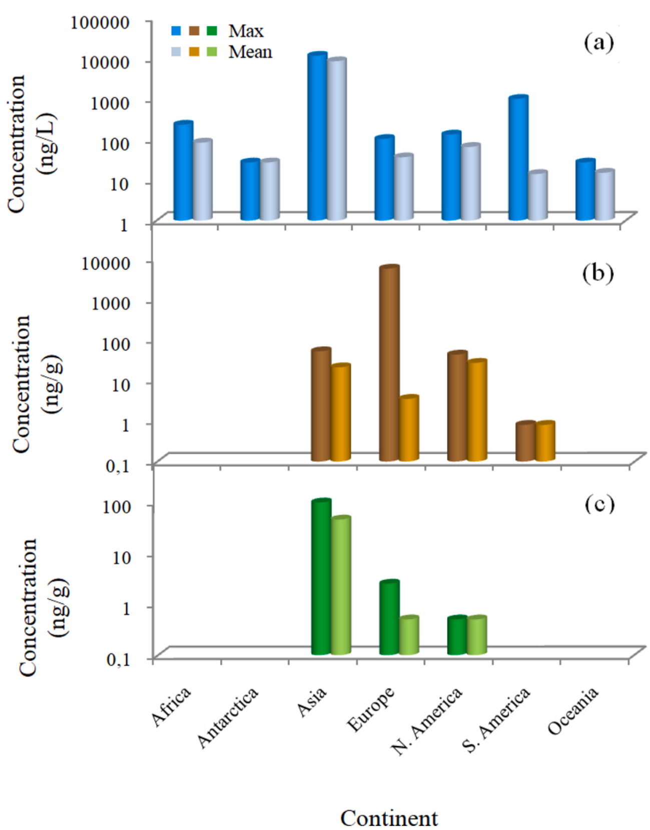

Fig. 5. Average maximum and mean concentrations of pharmaceuticals reported present in (a) waters, (b) sediments, and (c) biota of lakes throughout the world over the time period 1996 to May of 2021.

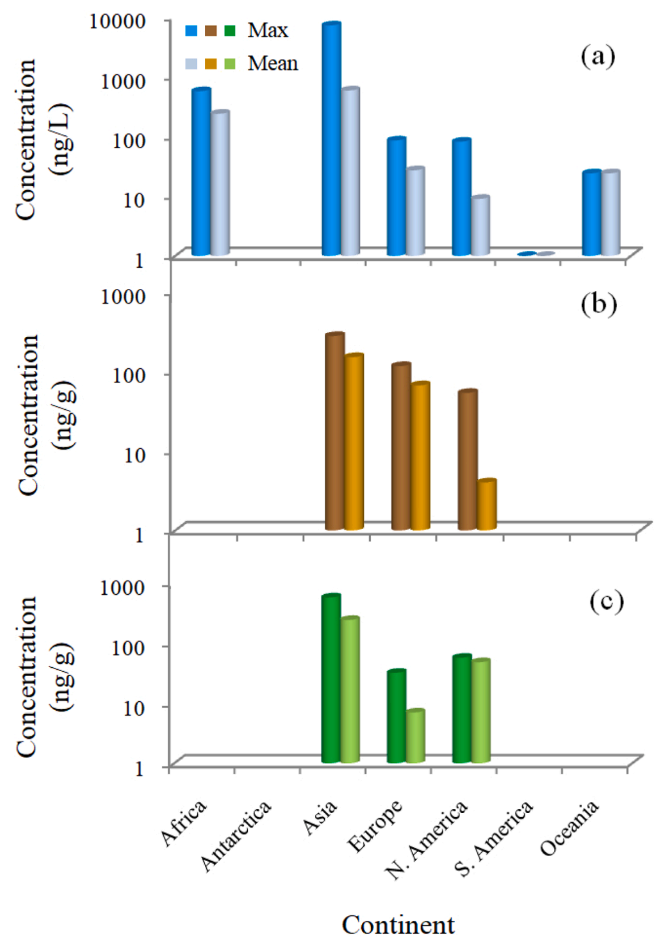

Fig. 6. Average maximum and mean concentrations of PCPs reported present in (a) waters, (b) sediments, and (c) biota of lakes throughout the world over the time period 1996 to May of 2021.

In North American lake waters, 98 pharmaceuticals were detected, which are listed in Tables S3 and S1, plus amitriptyline, benztropine, mestranol, norverapamil, tamoxifen, citalopram and paroxetine, as well as 19 PCPs, which are listed in Table S2, plus bisphenol A (Ferrey, 2013; Ferrey et al., 2015; Servadio et al., 2021). It should be noted that among the PPCPs detected, 25 pharmaceuticals and 7 PCPs were present only in this continent. The maximum concentration of the pharmaceuticals ranged from <0.1 to 9.2×10^3 ng/L, with an average concentration of 131 ng/L, and the maximum concentrations of the PCPs ranged from 0.029 to 821 ng/L, with an average concentration of 81 ng/L (see

Tables S1, S2; Figs. 5, 6).

In South American lake waters, 20 pharmaceuticals and 2 PCPs (4-MBC and Benzophenone) were detected. It should be noted that among the pharmaceuticals detected, iohexol, iopamidol, phenazone and sulfadiletoxine were present only in this continent. The maximum concentration of the pharmaceuticals ranged from 10 to 1.3×10^4 ng/L, with an average concentration of 990 ng/L (see Tables S1, S2; Fig. 5).

3.3. PPCPs in lake sediments

Pharmaceuticals and PCPs are known to sorb onto solids and to partition between lake waters and sediments (Fountouli and Chrysikopoulos, 2018; Xiang et al., 2021). Consequently, 76 pharmaceuticals and 38 PCPs were detected in Asian lake sediments. Among the PPCPs detected in Asian lake sediments, 43 pharmaceuticals and 26 PCPs were present only in this continent (see Tables S1, S2; Figs. 5, 6). The maximum concentration of the pharmaceuticals ranged from 0.01 to 1.17×10^3 ng/g, with an average concentration of 52 ng/g, and the maximum concentrations of the PCPs ranged from <0.08 to 5.76×10^3 ng/g, with an average concentration of 274 ng/g. In European lake sediments, 19 pharmaceuticals and 16 PCPs were detected. It should be noted that among the PPCPs detected, the pharmaceutical ketoprofen and 17α-estradiol, as well as and the PCPs galaxolidon, APN and B-MDM were present only in this continent. The maximum concentrations of pharmaceuticals ranged from 0.0025 to 1.35×10^5 ng/g, with an average concentration of 5.63×10^3 ng/g, and the maximum concentration of the PCPs ranged from 0.0075 to 1.2×10^3 ng/g, with average concentration 115 ng/g. In North American lake sediments, 34 pharmaceuticals were detected, which are listed in Table S1, plus clotrimazole, benztropine, gemfibrozil, paroxetine, promethazine, tamoxifen, verapamil, 17α-ethinylestradiol, atorvastatin and sertraline, as well as 10 PCPs, which are listed in Table S2, plus bisphenol A (Servadio et al., 2021). Among the PPCPs detected, 18 pharmaceuticals and 3 PCPs (4-Nonylphenol, MX, and ATII) were present only in this continent. The maximum concentration of the pharmaceuticals ranged from 0.05 to >822 ng/g, with an average concentration of 43 ng/g, and the maximum concentration of the PCPs ranged from 0.43 to 350 ng/g, with an average concentration of 53 ng/g (see Tables S1, S2; Figs. 5, 6). In South American lake sediments, only sulfamethoxazole was detected, with median maximum concentration of 0.8 ng/g (Archundia et al., 2017).

3.4. PPCPs in lake biota

In Asian lake biota, 57 pharmaceuticals and 5 PCPs were detected. Among the PPCPs detected, 54 pharmaceuticals and 5 PCPs (OP, BPS, MeP, NP, and SA) were present only in this continent. The maximum concentration of the pharmaceuticals ranged from 0.21 to 6.31×10^3 ng/g, with an average concentration of 97 ng/g, and the maximum concentration of the PCPs ranged from 0.96 to 1,952 ng/g, with an average concentration of 573 ng/g (see Tables S1, S2; Figs. 5, 6). In European lake biota, 6 pharmaceuticals and 14 PCPs were detected. Among the PPCPs detected, 3 pharmaceuticals (ethinylestradiol, malachite green and risperidone), and 5 PCPs (4-MBC, chlorophene, methyl triclosan, MK, and MX) were present only in this continent. The maximum concentration of the pharmaceuticals ranged from 0.105 to 7.7 ng/g, with an average concentration of 2.5 ng/g, and the maximum concentration of the PCPs ranged from <0.1 to 365 ng/g, with an average concentration of 32 ng/g. In North American lake biota, 5 pharmaceuticals were detected, which are listed in Table S1, plus diphenhydramine, miconazole, verapamil, azithromycin and roxithromycin, as well as 9 PCPs, which are listed in Table S2, plus DEET (Servadio et al., 2021). Among the PPCPs detected, the pharmaceuticals fluoxetine, norfluoxetine and paroxetine were present only in this continent. The maximum concentration of the pharmaceuticals ranged from 0.58 to 1.08 ng/g, with an average concentration of 0.5 ng/g, and the maximum concentration of the PCPs ranged from 0.2 to 719 ng/g, with an average concentration of 57 ng/g (see Figs. 5, 6).

3.5. Concentrations and distribution of PPCPs

The maximum and mean concentrations of the 289 pharmaceuticals and 76 different kinds of PCPs present in waters, sediments and biota of lakes throughout the world are presented in Figs. 7 and 8, respectively. Note that the maximum concentrations as well as the spread between the maximum and mean concentrations vary widely for both pharmaceuticals and PCPs (note that the vertical scale in Figs. 7 and 8 is logarithmic).

Several pharmaceuticals and PCPs were found to be simultaneously present in waters, sediments and biota of the same lake. Such PPCPs are capable of partitioning between phases and migrating easier in the environment. In the Asian lakes Baiyangdian, Dianchi, Dongting, Luoma, Taihu and al-Asfar/al-Hubail, 33 pharmaceuticals were found simultaneously present in their waters, sediments and biota, most detected in lake Taihu (16). In lake waters the maximum concentration of the pharmaceuticals ranged from 1.28 to 20.6×10^3 ng/L, with an average concentration of 310 ng/L, in lake sediments ranged from 0.56 to 1,140 ng/g, with an average concentration of 34 ng/g and in lake biota ranged from 0.21 to 6.31×10^3 ng/g, with an average concentration of 79 ng/g. Ofloxacin was detected in most of the lakes (4/6). Also, several PCPs (OP, BPS, NP and SA) were found present in water, sediments and biota of the Asian lakes Luoma, Taihu, and al-Asfar/al-Hubail. In lake waters the maximum concentration of the PCPs ranged from 5.64 to 1.76×10^3 ng/L, with an average concentration of 474 ng/L, in lake sediments ranged from 0.68 to 47.04 ng/g, with an average concentration of 15 ng/g, and in lake biota ranged from 0.96 to 1.95×10^3 ng/g, with an average concentration of 287 ng/g. In European lakes and particularly in Polish lakes Lanskie, Maroz and Rybnik, antibiotics were found simultaneously present in their waters, sediments and biota, in low concentrations. (see Tables S1, S2). The simultaneous presence of antibiotics with high concentrations in waters, sediments and biota of lakes around the world is associated with uncontrolled or insufficiently treated municipal and hospital wastewater disposal (Cheng et al., 2017; Liu et al., 2011; Ma et al., 2016; Liu et al., 2017; Bao et al., 2020; Picó et al., 2020; Gbylik-Sikorska et al., 2014).

In Fig. 9 are shown the number of PPCPs present in waters, sediments and biota of lakes within each of the seven continents. Clearly, the number of pharmaceuticals and PCPs is highest in Asian lakes and lowest in Antartican lakes. This is an expected result, which is directly proportional to the local production and consumption of PPCPs. However, it should be noted that more PPCPs were present in sediments of the North American lakes than European lakes.

The average maximum and mean concentrations of the numerous pharmaceuticals reported in the literature to be present in waters, sediments and biota of lakes within each of the seven continents are presented in Fig. 5; whereas, the corresponding concentrations of the PCPs are presented in Fig. 6. The maximum concentrations of pharmaceuticals in waters, sediments and biota were reported to be highest in Asian lakes. It should be noted that the very high extreme concentration of ketoprofen (1.35×10^5 ng/g) reported in the sediments of lake Paijanne (Finland), increased the average maximum concentration of pharmaceuticals in sediments from 23 to 5.63×10^3 ng/g, which elevated the concentration of pharmaceuticals in European lakes as the highest in the world . Throughout the world, caffeine, cetirizine, ciprofloxacin, enoxacin, enrofloxacin, iopromide, norfloxacin and oseltamivir, were reported to have the highest pharmaceutical extreme concentrations and detected in waters of nine Asian lakes (Dingshan, Ambazari, Futala, Gandhi sagar, Kazipeli, Patancheru, Biwa, al-Asfar-al-Hubail), whereas the maximum concentration ranged from 20.4×10^3 to 6.5×10^6 ng/L. Ketoprofen detected in the sediments of lake Paijanne (Finland), was the only pharmaceutical reported to have extreme concentrations (1.35×10^5 ng/g) in lake sediments throughout the world, whereas no

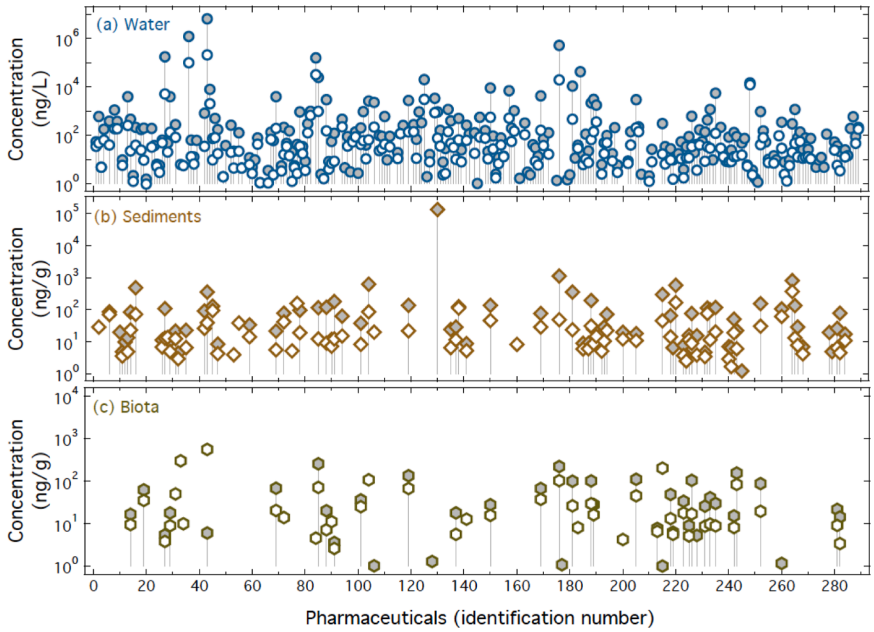

Fig. 7. Concentrations of pharmaceuticals in lake: (a) waters (circles), (b) sediments (diamonds) and (c) biota (pentagons), as reported in the literature. The names of the 289 pharmaceuticals are represented by their coresponding identification numbers, which are listed alphabetically in Table S3. The solid symbols represent maximum concentrations, whereas the open symbols represent mean concentrations.

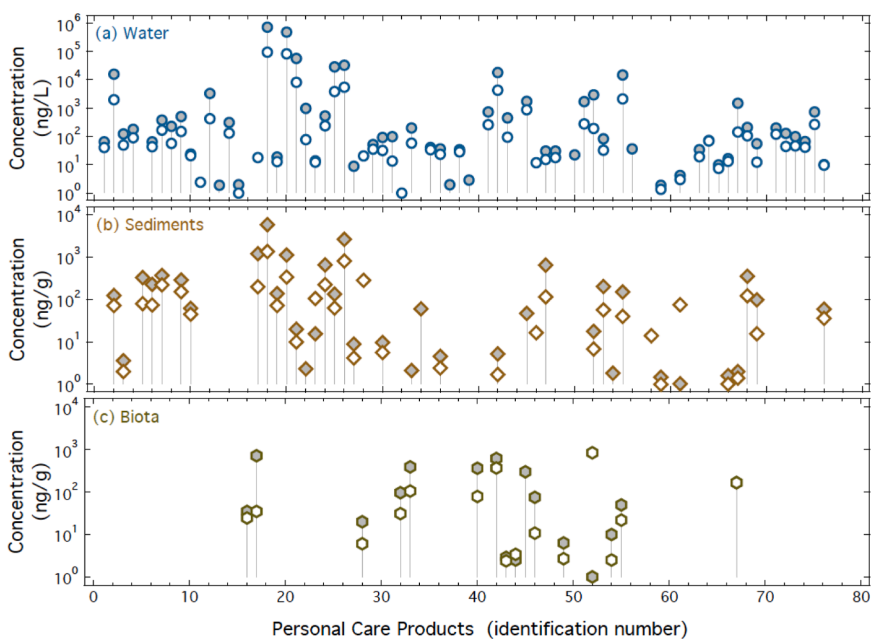

Fig. 8. Concentrations of PCPs in lake: (a) waters (circles), (b) sediments (diamonds) and (c) biota (pentagons), as reported in the literature. The names of the 76 PCPs are represented by their coresponding identification numbers, which are listed alphabetically in Table S4. The solid symbols represent maximum concentrations, whereas the open symbols represent mean concentrations.

pharmaceutical extreme concentrations reported in lake biota (Table S1; Lindholm-Lehto, et al., 2015).

Among the lakes of the world contaminated with PPCPs, lake Victoria had the highest concentrations of pharmaceuticals in Africa, which were originated from WWTPs and wastewater discharges from pharmaceutical industries (Nantaba et al., 2020). The lakes Patancheru, Kazipeli, Ambazari, Futala, Nandi Hills, Biwa, Yen So, al-Asfar, and al-Hubail were reported to have very high pharmaceutical concentrations in Asia, which were associated with insufficiently treated municipal, industrial and agricultural wastewaters, pharmaceutical industries, and intentional wastewater disposal into lakes (Fick et al., 2009; Mutiyar and Mittal, 2014; Archana et al., 2017; Gopal et al., 2020; Chen et al., 2017; Tran et al., 2019; Picó et al., 2020). The lakes Buyukcekmece, Pamvotis, Polifitos, Tegel, Paijanne, Geneva, and Mjosa exhibited the highest pharmaceutical concentrations in Europe, which were originated from controlled or uncontrolled municipal and hospital wastewater discharges (Aydin and Talinli, 2013; Nannou et al., 2015; Kosma et al., 2014; Schimmelpfennig et al., 2012; Lindholm-Lehto, et al., 2015; Morasch et al., 2010; Balmer et al., 2004; Singer et al., 2002; Borga et al., 2012; Borga et al., 2013). The lakes Michigan, Erie, Ontario,

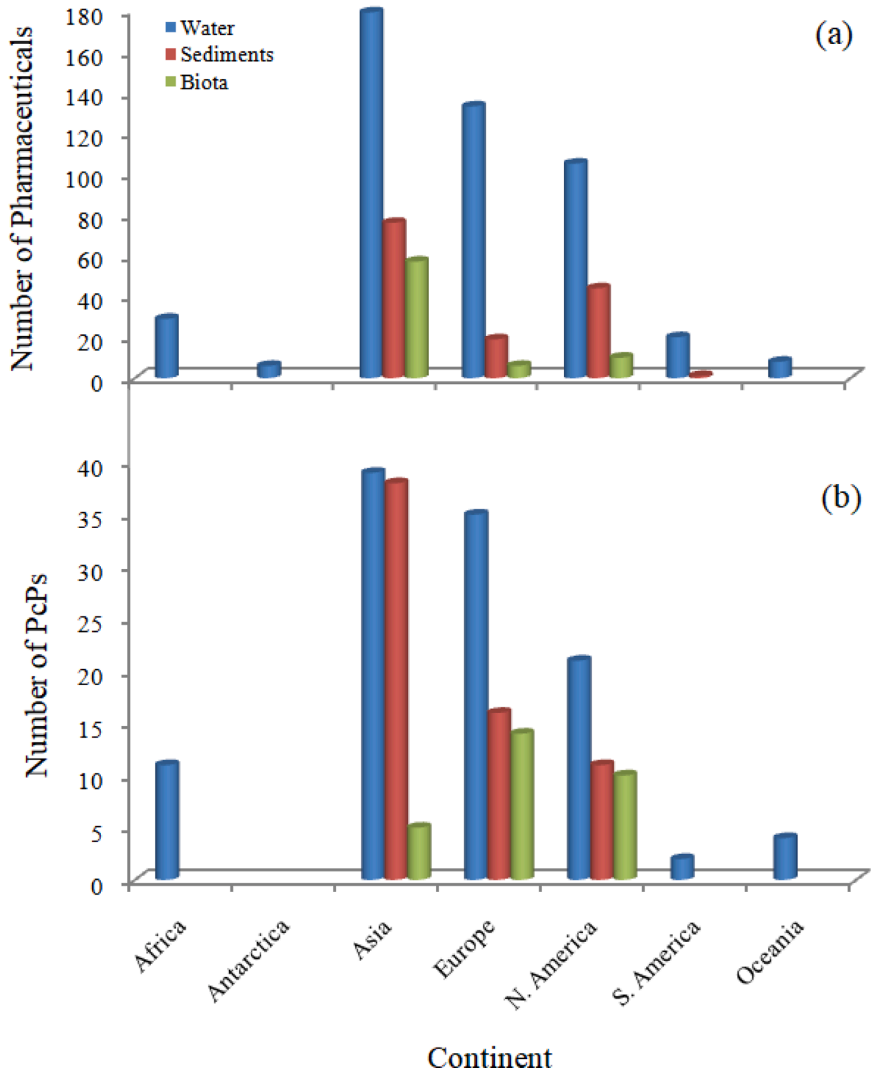

Fig. 9. Number of (a) pharmaceuticals and (b) PCPs reported present in waters, sediments and biota of lakes throughout the world over the time period 1996 to May of 2021.

Mead, and Shagawa, were reported to have the highest pharmaceutical concentrations in North America, which were directly connected to discharges from WWTPs, agricultural activities, and runoff from septic tanks (Blair et al., 2013; Wu et al., 2009; Metcalfe et al., 2003; Blunt et al., 2018; Venkatesan et al., 2012). Consequently, there is a direct connection between very high pharmaceutical concentrations in lakes and nearby municipal and industrial activities. A solution to this problem is the pharmaceutical industries and hospitals to use on-site WWTPs (Duong et al., 2008).

Anti-inflammatory drugs, sulphonamides, fluoroquinolones and antiretrovirals, were mostly detected in African lakes. Sulphonamides, anti-inflammatory drugs, macrolides, diuretics, and stimulants were detected in Antarctican lakes. Sulphonamides, fluoroquinolones, anti-inflammatory drugs, and heart and hypertension pharmaceuticals were mostly detected in Asian lakes. Anti-inflammatory drugs, heart and hypertension pharmaceuticals, and various neurological and psychiatric drugs were detected in European lakes. Anti-inflammatory drugs, sulphonamides, and various neurological and psychiatric drugs were mostly detected in North American lakes. Anti-inflammatory drugs and sulphonamides were detected in South American lakes, whereas neurological and psychiatric drugs were detected in Oceanian lakes. Certainly, all common pharmaceuticals were detected in every continent. However, groups of drugs other from the most common, were detected in each continent, which are controlled by technological developments, economy, overpopulation, urbanization, and climate of the continent. The increasing PPCP concentrations in the aquatic environment of a lake contribute to the genotoxicity and ecological risks of aquatic life; furthermore, they induce drug resistant microbes (Junaid et al., 2019; Dalahmeh et al., 2020) and accelerate the creation of antibiotic resistance genes (Cheng et al., 2017).

3.6. *Potential human health and ecological effects*

Several studies have focused on the adverse effects that pharmaceuticals impose to aquatic biota (Bean et al., 2014; Brown et al., 2004; Fong and Ford, 2014; Segner et al., 2003; Fang et al., 2019). Antidepressants present in European, North American and Oceanian lakes, are able to accumulate in fish tissues, and contribute to greater exposure risks (Schultz et al., 2010). The antidepressant venlafaxine at low concentrations (31.3 ng/L) was shown to increase foot detachment in gastropods (Fong and Ford, 2014). Note that the maximum and average lake water concentrations of venlafaxine were reported as 79 ng/L and 12.9 ng/L, respectively (see Fig. 7). Several (10) endocrine disruptors present in African, Asian, European, North American and South American lake waters, with maximum concentrations ranging from 0.5 to 124.6 ng/L and average concentration 28.5 ng/L (see Fig. 7), were reported to increase plasma vitellogenin concentrations in female rainbow trout and Xenopus laevis (Tyler et al., 2009; Mdegela et al., 2014). Estrone, with maximum concentration of 124.6 ng/L and average concentration of 106.5 ng/L in lake Pontchartrain (see Table S1), was reported to have adverse effects on fish at concentrations greater than 4.7 ng/L (Fick et al., 2010). The combined activity of two estrogenic hormones were reported to affect the endocrine system and particularly the thyroid cascade of aquatic biota (McGee et al., 2009; Elliott and VanderMeulen, 2017; Brown et al., 2004). Fluoroquinolones, which were mostly detected in African and Asian lake waters, are known to impact the feeding behavior of starlings and fish, and to be harmful to algae, because concentrations of 1×10^3 ng/L impose a risk to Microcystis aeruginosa (Hedgespeth et al., 2014; Bean et al., 2014; Painter et al., 2009; Li et al., 2012; Robinson et al., 2009). Diclofenac, with maximum lake water concentration of 4×10^3 ng/L and average concentration of 198.4 ng/L (see Fig. 7), can influence the biological functions of rainbow trouts after 21 days of exposure to concentrations of 1×10^3 ng/L (Brozinski et al., 2013). Sulfamethoxazole, erythromycin, sulfadiazine, tetracycline and oxytetracycline, were shown to be detrimental to algae (Li et al., 2012; Wang et al., 2017). A mixture of gemfibrozil, acetaminophen, venlafaxine, and carbamazepine can change the kidney morphology and reduce embryo production of the zebrafish, Danio rerio (Galus et al., 2013). Furthermore, a mixture of 16 pharmaceuticals was reported to weaken the immune system of the pond snail Limnaea stagnalis (Gust et al., 2013; Kovalakova et al., 2020; Gonzalez-Pleiter et al., 2013).

Fluoroquinolones at extreme concentrations were frequently detected in lakes within the 4 continents. Studies indicated the adverse effects of ciprofloxacin to water organisms, the toxic effects of enoxacin to Vibrio fischeri bacteria, the negative impact of norfloxacin to production processes of water organisms, and that enrofloxacin may be more toxic to algae than other fluoroquinolones, but it poses no risk to water organisms at typical environmental concentrations (Ebert et al., 2011; Backhaus et al., 2000; Bartoskova et al., 2014). Additionally, cetirizine, which is found in extreme concentrations within lakes, was reported to have adverse effects in mussels (Moore et al., 2008; Steger-Hartmann et al., 1999; Straub, 2009).

Several studies concluded that pharmaceuticals in natural aquatic environments, which are ultimately transmitted to drinking water and biota, pose no serious risk to human health. Nevertheless, some pharmaceuticals, such as enoxacin, after chlorination can reduce drinking-water safety (Praveena et al., 2019; Vulliet et al., 2011; Cunningham et al., 2009; Schwab et al., 2005; Zhang et al., 2019).

4. Summary and conclusions

This review provides a collection of PPCPs reported to be present in waters, sediments and biota in lakes throughout the world, over a 26-year time period (1996–2021). PPCPs were found to be present in 260 lakes distributed within 44 different countries. In Asia, PPCPs were found to be present in 115 lakes distributed within 13 different countries, most of these lakes are in China, India and Sri Lanka. In Europe, PPCPs were found to be present in 95 lakes distributed within 18 different countries, most of these lakes are in Germany, Sweden and Switzerland. In North America, PPCPs were found to be present in 51 lakes located in Canada and USA (Colorado, Minnesota). In Oceania, PPCPs were found to be present in three lakes in Australia. Finally, in South America, PPCPs were found to be present in 7 lakes distributed within 5 different countries.

Among the 289 pharmaceuticals which were found to be present in lakes throughout the world, most were detected in Asian, European and North American lakes. The pharmaceuticals most frequently detected in lake waters are: sulfamethoxazole, caffeine, carbamazepine, ibuprofen and naproxen; in lake sediments are: caffeine, ciprofloxacin, sulfadiazine, sulfamethoxazole and 17β-Estradiol; and in biota are: ofloxacin, sulfamethoxazole and 17β-Estradiol, whereas ofloxacin was most frequently detected to be simultaneously present in waters, sediments and biota of the same lake. In lake waters the maximum concentration of ofloxacin ranged from 5.7 to 3.1×10^3 ng/L, with an average concentration of 359 ng/L, in lake sediments ranged from 17.16 to 362 ng/g, with an average concentration of 63 ng/g and in lake biota ranged from 4.5 to 99.48 ng/g, with an average concentration of 33 ng/g (see Table S1).

Among the 76 PCPs which were found to be present in lakes throughout the world, 45 were present in Asian lakes, whereas no PCPs were present in Antarctican lakes. The most frequently detected PCPs present in lake waters are: DEET, TCS, OP, BZP and 4-Nonylphenol; in lake sediments are: OP, 4-Nonylphenol, D5, TCS and BZP; and in biota are: D5, AHTN, HHCB, AHMI and ATII (see Table S2).

The maximum concentration of the various pharmaceuticals ranged from 0.019 to 6.5×10^6 ng/L in waters, 0.0019 to 1.35×10^5 ng/g in sediments, and 0.105 to 6.31×10^3 ng/g in biota; whereas, the maximum concentration of the PCPs were reported from 0.029 to 7.31×10^5 ng/L in waters, 0.0075 to 5.76×10^3 ng/g in sediments, and <0.1 to 719 ng/g in biota (see Figs. 5, 6). Fluoroquinolones were reported as the group of antibiotics, with the highest pharmaceutical extreme concentrations in lake waters, whereas the maximum concentration ranged from 2.5×10^4 to 6.5×10^6 ng/L (see Table S1). The majority of pharmaceuticals with the highest extreme concentrations had a great detection frequency in lakes throughout the world. It should be noted that in many lake waters there is a clear trend of increasing average of PPCP concentrations with time. (see Fig. 2). It is worth to noting that the concentrations of 194 pharmaceuticals and 56 PCPs were detected in lake waters were over 5 ng/L. Consequently, PPCP pollution should be efficiently controlled especially in Asia in order to avoid possible serious health risks to humans and living organisms and to reduce the possibility of developing antibiotic-resistant microorganisms.

Rapid reduction of the extreme concentrations of pharmaceuticals in the lakes throughout the world can be achieved if pharmaceutical industries and hospitals use of on-site WWTPs. The findings from this review also suggest that many lakes, mainly in Africa, Antarctica, Oceania and South America, require much more attention, because they have not been systematically analysed for the presence of PPCPs.

Appendix A. Supplementary data

Supplementary data associated with this article can be found in the online version at:

CRediT authorship contribution statement

Antonios G. Katsikaros: Investigation, Data curation, Formal analysis, Writing – original draft. **Constantinos V. Chrysikopoulos:** Conceptualization, Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

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