Removal of pharmaceuticals and cosmetic ingredients under the presence of natural organic matters in coagulation-flocculation process

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フミン酸共存下における凝集沈殿処理による医薬品類・
香料・紫外線吸収剤の除去性についての検討

中陳　郁美

近年，医薬品とパーソナルケア製品を起源とする化学物質(PPCPs)が数多く水環境中から検出され，注目を集めている．さらに，2007年に日本にの水道水から多種の医薬品が検出されたことから，浄水処理場でのPPCPs除去に関心が集まっている．本研究では，原水中の共存物質として有機系溶存物質であるフミン酸を用い，凝集沈殿処理におけるPPCPsの挙動について明らかにすることを目的とした．また，ポリ塩化アルミニウムに代わる凝集剤としてポリシリカ鉄を用いた場合，及びポリアクリルアミドを凝集補助剤として用いた場合の除去性についても検討した．その結果，PPCPsの除去性は，試験原水中の有機炭素量に依存することが明らかになった. また，香料はポリシリカ鉄を用いた場合に比較的高い除去を得られることが示唆された.

Key Words : *Pharmaceuticals; Fragrances; Sun-screen Agents; Coagulation-flocculation; Humic acid*

1. Introduction

Increasing interest has been addressed to pharmaceuticals and personal care products (PPCPs) since 1990s. PPCPs comprise all pharmaceuticals and other consumer chemicals, such as polycyclic musk compounds frequently used as fragrances in perfumes and other household products. They have been detected in water environment where they can have adverse effects on aquatic ecosystem and have been recognized as popular contaminants in America and European countries (Ternes, 1998; Halling et al., 1998).

In 2007, a news paper article on the pharmaceutical residue in drinking water, raised the concern about the removal performances of PPCPs in drinking water treatment plants in Japan. Though the reported concentration of pharmaceuticals are in a very low range between 6 and 30ppt, many of them exceeded the European baseline (10ppt) that is used to determine whether further studies on long-term effects to human and ecosystem are needed or not. Though many studies on the removal of PPCPs have been conducted on the wastewater treatment and on advanced drinking water treatment, there are few studies on conventional drinking water treatment processes. These reports on advanced drinking water treatment processes indicated that PPCPs are almost fully removed in ozonation or granular-carbon filtration. Considering that, the most widely used process in Japan is still coagulation- flocculation in drinking water treatment, it is important to investigate the removal of PPCPs in coagulation- flocculation process.

The aim of this study is to improve the removal efficiencies of three groups of PPCPs (pharmaceuticals, fragrances and UV filters) with different chemical properties in coagulation-flocculation process. In addition, alternative coagulants(polysilicato-iron and polyacrylamide) which have been developed in these years after the generation of polyaluminum chloride, were also used in the experiments.

1.1 Pharmaceuticals

Pharmaceuticals were firstly found in the environment as pollutants around 30 years ago (Garrison et al., 1976; Hibnite and Azarnoff, 1977). By the mid 1990s, the improvements in the detection methods and the toxicity testing methods led to the increased interests of researchers into the field (Herberer et al., 1997; Ternes, 1998; Jones et al., 2001). Many studies have been conducted to investigate the discharge of human and veterinary medicines into the environment. The presence of a wide variety of

pharmaceuticals in wastewater effluents and receiving waters in countries across Europe and North America has been proven (Halling-Sorensen et al., 1998; Daughton and Ternes, 1999), and the evidences on their adverse effects in the environment are partially recognized. Now, the pharmaceuticals are widely recognized as hazardous substances in environments.

1.2 UV filters and fragrance

Synthetic polycyclic musks (HHCB, AHTN) are widely used as fragrance ingredients in washing and cleaning agents, personal care products and in other consumables (Kupper et al., 2004). Due to their high consumption volumes and their low degradation property, they have been detected in treated wastewater, surface water, fish and sediments (Bester, 2004, 2005; Heim et al, 2004; Schmid et al., 2004). Recently, antiestrogenic effects of HHCB and AHTN have been observed in an *in-vivo* fish assay (Schreurs et al., 2004).

The consumption of sunscreen agents is increasing due to the growing awareness of hazards posed by UV radiation and recommendations for the prevention of skin cancer. The sunscreen agents have been detected in fish, lake water, wastewater (Poiger et al., 2004; Balmer et al., 2005) and in sewage sludge (Plagellat et al., 2006). Some compounds such as benzophenone are considered as endocrine disrupting chemicals (Schlumpf et al., 2004).

The probrem is that, though many studies on pharmaceuticals which are recognized as hazardous substances in the environment have recentry been conducted, there are few studies on synthetic fragrance materials and organic UV filters in the environment.

1.3 Physical properties of PPCPs

The sorption of micropollutants onto solids and, accordingly, their behavior during the physical and chemical treatment processes such as coagulation- flocculation process, depends basically on their physical and chemical properties, such as acidity or hydrophilicity. The octanol-water partition coefficient (K_{ow}) is usually used to determine the sorption effectiveness. K_{ow} is defined as the ratio between the equilibrium concentrations of a cetain compound in octanol phase and in water phase at a specific pH where each compound is not ionized. Many pharmaceuticals are weak acids which contain at least one site that can reversibly dissociate a proton (hydrogen ion) to form a negatively charged anion. The equilibrium between two states of protonated and unprotonated forms is assumed.

Table 1
LogK_{ow} and LogD_{ow} of selected PPCPs

Chemical Name	abbrev.	Log K_{ow}	pKa	Log D_{ow}
Propyphenazone	PPZ	1.94	ND	1.94
Carbamazepine	CBZ	2.45	7.00	2.44
Clofibric acid	CA	2.57	3.15	0.22
Ketoprofen	KEP	3.12	3.90	1.51
Benzophenone	BP	3.18	ND	3.18
Naproxen	NPX	3.18	4.90	2.48
Fenoprofen	FEP	3.90	ND	-
Ibuprofen	IBP	3.97	4.50	2.93
Indomethacin	IDM	4.27	4.50	3.23
Diclofenac	DCF	4.51	4.00	3.00
Gemfibrozil	GFZ	4.77	ND	-
Tonalide	AHTN	5.70	ND	5.70
Galaxolide	HHCB	5.90	ND	5.90

ND: No Data

$$HA \Leftrightarrow H^+ + A^- \qquad Ka = [H^+][A^-]/[HA]$$

The fraction of ionized molecules depends on the pH. The equation for the dissociation constant Ka can be written as:

$$pKa = pH + \log(\text{protonated/unprotonated}),$$

where pKa = -log[Ka] and pH = -log[H^+]. The equation above indicates that the subutance in ionized in the case of higher pH condition above pKa. The partition coefficient LogK_{ow} is a constant for the neutral molecular without ionization. While distribution coefficient LogD_{ow} takes into account all neutral and charged forms of the molecule. Because the ionized forms connot bo distributed in the octanol phase, D_{ow} is dependent on pH. In the case of solutes which have both ionized and neutral forms, LogD_{ow} is a function of LogK_{ow}, pH and pKa. The assumption that the ionaizes molecules are not distributed in the octanol phase at all, can simplify the relation as folloing equation.

$$\text{Log}D_{ow} = \text{Log}\ K_{ow} - \text{Log}(1+10^{(\text{pH-pKa})})$$

Table 1 shows the relation between LogK_{ow} and LogD_{ow} of selected pharmaceuticals in this sutudy. The pH used here is 5.5, set as a value after rapid and slow mixing in coagulation-filtration examination. In the case of PPZ, BP, AHTN and HHCB, though these value of Ka could not be known, each value of Log D_{ow} was assumed to be same as the value of Log K_{ow}. Because it was able to be judged that the hydrogen ion of these compounds doesn't dissociate easily in water according to the

molecular structures shown in **Table 2**.

1.4 Coagulation-flocculation assays

Coagulation-flocculation processes have been designed to promote the removal of fine suspended solids and colloids from water which do not settle down by gravity. The addition of metal salts or specific organic compounds promotes the aggregation of these fine particles and the removal of the aggregates in the filtration process (Li and Gregory, 1991). **Figure 1** shows the size of materials in row water and the appropriate removal process of each size of materials. Literature informed about the removal of PPCPs by coagulation-filtration process is scarce. In addition the data available normally combined with other techniques, such as activated carbon or filtration (Tsrnes et al., 2002; Stackelberg et al., 2004).

2. Materials and methods

2.1 Target PPCPs in this study

The PPCPs used in this work were Carbamazepine, Clofibric acid, Diclofenac, Fenoprofen, Gemfibrozil, Ibuprofen, Indomethacin, Ketoprofen, Naproxen, Propyphenazon, Tonalide (AHTN), Galaxolide (HHCB) and Benzophenone. Their molecular

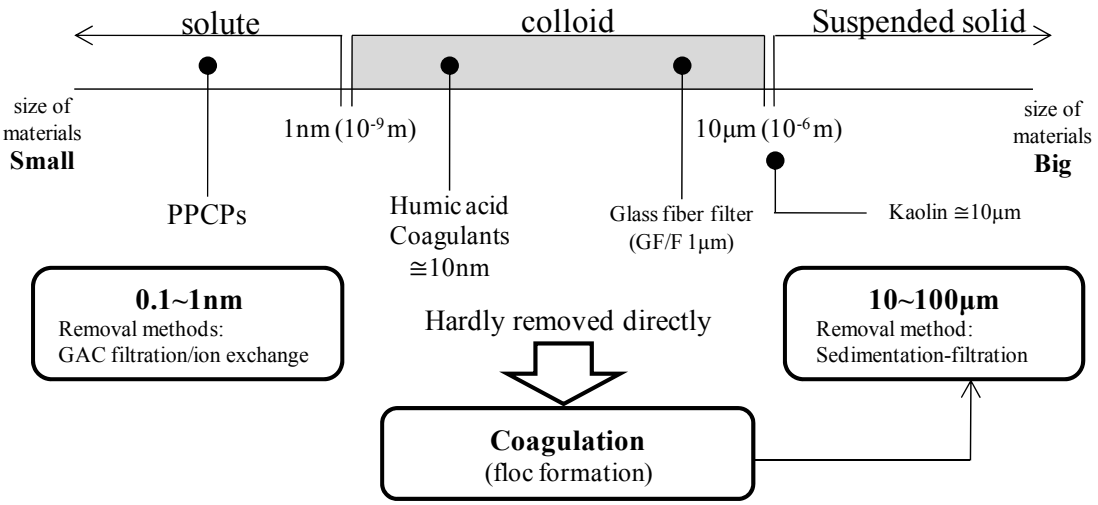
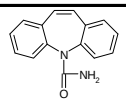
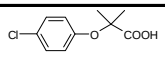
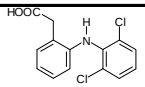
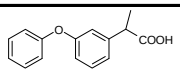
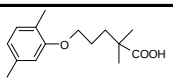
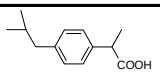
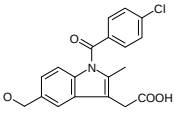
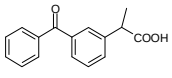
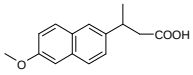
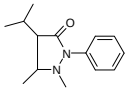
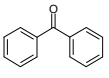
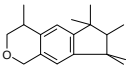
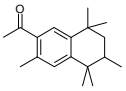


Figure 1 The size of materials in raw water and the appropriate removal process of materials with different sizes

Table 2
Physico-chemical properties of PPCPs selected in this work (Henry's L. C.; atm-m3/mole at 25 deg C)

Chem. Name	Carbamazepine	Clofibric acid	Diclofenac	Fenoprofen	Gemfibrozil	Ibuprofen
CAS No.	298-46-4	882-09-7	15307-86-5	31879-05-7	25812-30-0	15687-27-1
Structure						
log *Kow* [a]	2.45	2.57	4.51	3.90(estimated)	4.77(estimated)	3.97
pKa [b]	7.00	3.15	4.0	-	-	4.5
Henry's L. C.[a]	1.08×10^{-10}	2.19×10^{-8}	4.73×10^{-12}	1.28×10^{-9}	1.19×10^{-9}	1.52×10^{-7}

Chem. Name	Indomethacin	Ketoprofen	Naproxen	Propyphenazone	Benzophenone	Galaxolide	Tonalide
CAS No.	53-86-1	22071-15-4	22204-53-1	479-925	119-61-9	1222-05-5	21145-77-7
Structure							
log *Kow* [a]	4.27	3.12	3.18	1.94	3.18	5.9	5.7
pKa [b]	4.5	3.9	4.9	-	-	-	-
Henry's L. C.[a]	3.13×10^{-14}	2.12×10^{-11}	3.39×10^{-10}	1.84×10^{-9}	1.94×10^{-6}	1.32×10^{-4}	4.22×10^{-5}

[a]EPI Suite (including data base)

[b]Akira Tsuji et al.(2007)

structures and physic-chemical properties are shown in **Table 2**.

2.2 Examined samples

The raw water in this work was prepared by adding certain concentration of humic acid (10mg/L, 50mg/L, 100mg/L) or 10mg/L of kaolin, and CaCl2 (0.5mMol/L), Na2SO4 (0.2mMol/L), KHCO3 (0.6mMol/L) for adjusting the alkalinity to pure water (Milli-Q). Two types of pond water were also used which collected from *Senzoku-ike.* The total organic carbon concentration (TOC) of the pond water was 1.83 mg/L (senzoku- ike 1) and 11.9mg/L (senzoku-ike 2), respectively and that of humic acid was 13.5mg/L (50 mg/L humic acid). pH of the all samples were adjusted with H2SO4 to give pH at 5.5 when the flocculation was finished.

2.3 Coagulation-flocculation experiment

Coagulation-flocculation experiments were carried out in a Jar-test mixer with 1L of the liquid volume. Three additives were examined for coagulants: polyaluminum chloride (PAC, 11.9% as Al), polysilicato-iron (PSI-025, 10g/L as Fe), polyacrylamide (PAA, ACCOFLOC A-110PWG-S: MT Aquapolymer, Inc.). PAC is the most common coagulant and PSI-025 is an inorganic polymer coagulant which has been developed recently. PAA is an organic polymer coagulant, which has been banned for the use in drinking water treatment although it have used widely in waste water treatment.

The examination included an initial 5 min rapid stirring (120rpm), after the addition of coagulant and H_2SO_4 for the pH adjustment, followed by 25 min of slow mixing (50rpm) for floc formulation, and finally 30 min sedimentation by gtavity without mixing. The examinations were carried out with different concentration of humic acid or target compounds. And the effect of the type and dose of the coagulant was also studied. After the sedimentation, the samples filtrated by glass fiber filter (GF/F) were used for monitoring ultraviolet absorbance (E260) and for analyzing PPCPs.

Table 3 Retention times and m/z ratios of the derivertized pharmaceuticals

Chemical Name	Abbrev.	Retention Time [time]	SIM ions [m/z] target ion	qualifier ion
Benzophenone	BP	9.52	105	77
Phenanthrene D_{10}	Phe-D10	12.84	188	160
galaxolid	HHCB 1	14.78	243	213
galaxolid	HHCB 2	14.81	243	213
tonalide	AHTN	15.13	243	159
Clofibric acid	CA	17.49	128	181
Propyphrnazone	PPZ	17.69	215	230
2,4-DBA	24-DBA	17.76	181	173
Carbamazepine	CBZ 1	17.94	193	236
Ibuprofen	IBP	18.71	161	181
2,3-DPAA	23-DPAA	23.18	181	175
Gemfibrozil	GFZ	25.23	181	309
Carbamazepine	CBZ 2	26.23	193	236
Fenoprofen	FEP	26.46	197	181
Naproxen	NPX	27.4	185	410
Ketoprofen	KEP	29.15	209	181
Diclofenac	DCF	30.54	214	475
Perylene D_{12}	Phery-D12	33.57	264	132
Indomethacin	IDM	50.04	139	537

2.4 Analytical Methods

Solid-phase extraction

The pH of the water samples were adjusted below 2 with HCl, and the samples were spiked with 50μL of internal standard mix (50mg/L) and 50μL 2.3-DPAA (100mg/L). These compounds were used as internal surrogate through the analytical process. The preconditioned samples were applied to the C18 SPE cartridge absorber (at 10ml/min) that have been sequentially preconditioned with acetone, methanol and Milli-Q water with pH below 2. The cartridge was then dried by air and eluted with 5mL of dichloromethane.

Derivatization

Samples spiked with 50μL of 2.4-DBAA (100mg/L) as surrogate were dried up with a stream of nitrogen. The dried samples were mixed with 40μL of PFBBr (20%) and 20μL of triethylamine. The vials were then sealed and kept at 110 deg C for 1h. In this process, acidic pharmaceuticals (Clofibric acid, Diclofenac, Fenoprofen, Gemfi-brozil, Ibprofen, Indomethacin, Ketoprofen, Naproxen) were derivatized with PFBBr. After that, they were dried up in the nitrogen stream and diluted with 1mL of Tluene.

Equipment

The derivatized pharmaceuticals were determined by GC/MS. The system consisted of the HP6890series Gas Chromatograph (Agilent) equipped with a split-splitless injector and equipped with HP5973series Mass Selective Detector (Agilent).The GC oven was programmed as follows: 1 min at 100℃, first ramp at 30℃/min to 150℃ (held for 1 min), second ramp at 3℃/min to 205℃, third ramp at 10 ℃ /min to 260 ℃ . The injections were performed in the splitless mode and the injection volume was 2μL. Retention times and ratio m/z used for quantitative purposes were those given in **Table 2**.

Quantification

The concentration of eight acidic pharmaceuticals were corrected by 2,3-DPAA, and those of other compounds were corrected by the internal standard (phe-D_{10}).

3. Results and discussion

A preliminary experiment with PAC, PSI-025 and PAA was performed in order to adjust the dose range for each coagulant. Several steps of the concentrations of PAC (1.5-4.5mg/L), PSI-025 (2.0-6.0mg/L), PAA (0.5mg/L) were tested under the presence of 10mg/L humic acid, and after the sedimentation-filtration, the ultraviolet absorbance (E260) were monitored. PAA was added one minute after the addition of PAC. Although the differences in the removal of PPCPs were not significant in the range considered, it was observed that over 90% removal efficiencies for humic acid were achieved in the following dose conditions: 3.8mg/L for PAC, 4.0mg/L for PSI-025. When PAC was used with PAA, the smaller amount of PAC (3.0mg/L) achieved the same efficiency of the coagulation than that required with the case that only PAC was used for the coagulant.

3.1 Relation between the amount of organic compound and PPCPs removal

In this study, the removal of 100μg/L target compounds was examined in various conditions. The coagulant used in this examination was PAC, which is the most popular coagulant in drinking water treatment plant in Japan. From the result of the preliminary experiment, all examinations were carried out with the condition of E260 in the finish water below 0.05 after the sedimentation-filtration. In this level of low E260 corresponded with more than 98% removal of humic acid when the initial concentration of humic acid was 50mg/L.

Fig. 2 shows the observed concentrations of PPCPs after the coagulation-flocculation test under the presence of kaolin or humic acid. There was no significant PPCPs removal under the presence of kaolin in the coagulation-filtration process. Though the low removal was expected for pharmaceuticals based on the previous publications, this study showed the low removal also of UV filters and fragrances. The average removal of the all target compounds were 1.4% under the presence of kaolin and

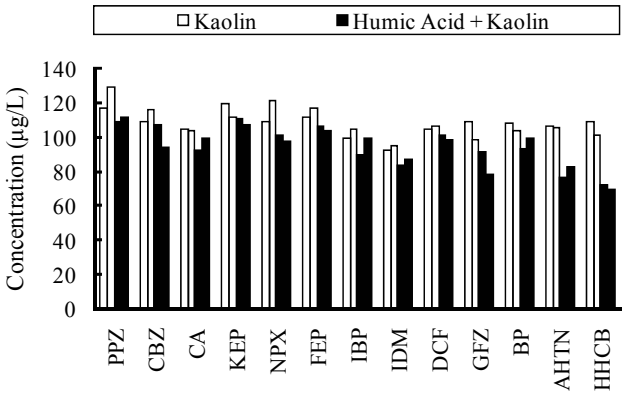


Fig.2 Observed concentration of PPCPs after the coagulation test under the presence of kaolin and humic acid

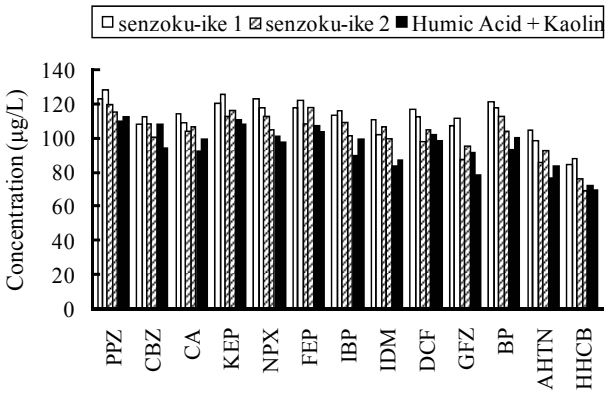


Fig.3 Observed concentrations of PPCPs after the coagulation test for the collected natural water and artificial water containing humic acid and kaolin

16.5% under the presence of both kaolin and humic acid. Comparing with water containing only kaolin, higher removals of PPCPs were observed in the presence of both kaolin and humic acid, especially in the case of fragrances.

Fig.3 shows the observed concentrations of PPCPs after the coagulation test for the collected natural water and artificial water containing 50mg/L of humic acid and 10mg/L of kaolin. The average removals of all target compounds were 1.09% (senzoku-ike 1), 9.62% (senzoku-ike 2) and 16.5% (huimic acid and kaolin). This result indicated that the removal of PPCPs increased with the increase in organic matters in the raw water.

Fig.4 shows the observed concentrations of PPCPs with different concentration of humic acid. This result indicated that the average removal of PPCPs increased with the increase in the concentration of humic acid, which is the main constituents of the dissolved organic matter in natural water. The average removal rate of all target compounds were 4.24% (10mg/L), 17.2%

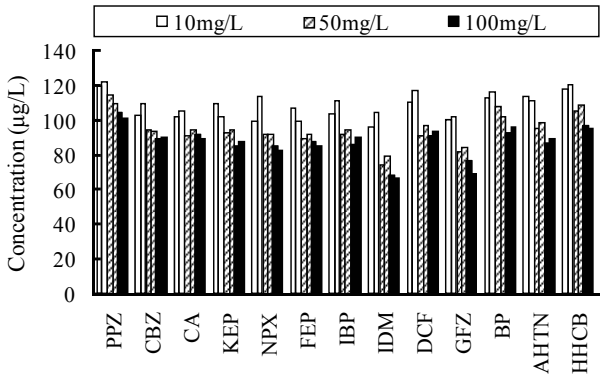


Fig. 4 Observed concentrations of PPCPs with different concentration of humic acid.

(50mg/L), 23.0% (100mg/L).

3.2 Relation between the initial concentration and the removal of PPCPs

Fig. 5 shows the measured concentrations of PPCPs in artificially prepared raw water containing 50mg/L of humic acid with target compounds whose initial concentrations were 500 μg/L, 100μg/L, 50μg/L respectively. And the blank examination without addition of coagulants was also carried out. When the initial concentration of PPCPs was 500μg/L, the removals of GFZ, AHTN and HHCB which have high hydrophobicity were observed. But from the other two cases, clear relations between PPCPs removal and its hydrophobicity as represented by the LogK_{ow} were not observed.

The influence of three types of coagulants was analyzed under the presence of 50ppm humic acid. The results were shown in **Figure 6**. The removal of target compounds except for IDM, AHTN, HHCB were about 10 to 20%. In the case of IDM, whose removal was comparatively high, the removal was 22.2% with PAC, 33.3% with PSI-025 and 25.0% with both PAC and PAA. In the case of AHTN and HHCB, as well as IDM, the removal was the highest when PSI-025 was used for the coagulant and the removal ratio was 28.0% for AHTN and 44.2% for HHCB. On the other hand, there was no significant dependence on the type of coagulant used in this study of the remorval of other PPCPs.

3.3 Relation between the removal rate of PPCPs and hydrophobicity considering the ionization

Considering the relation between hydrophobicity and the removal rate of PPCPs, **Figure 7** shows the dependency of the removal

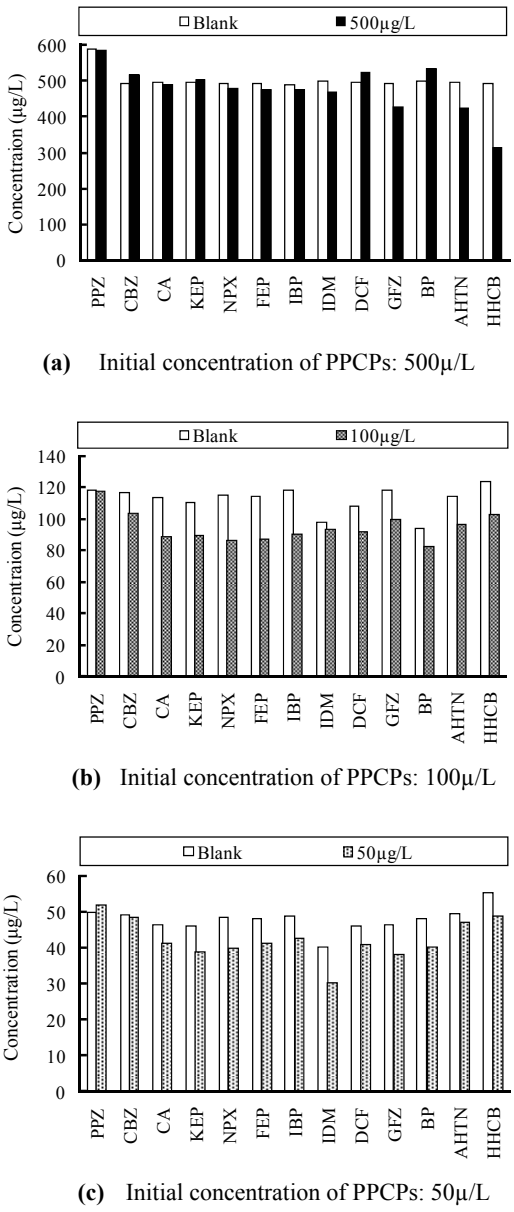


Fig. 5 Observed concentrations of PPCPs after coagulation in the case of artificial water containing 50mg/L of humic acid with several concentration of target compounds

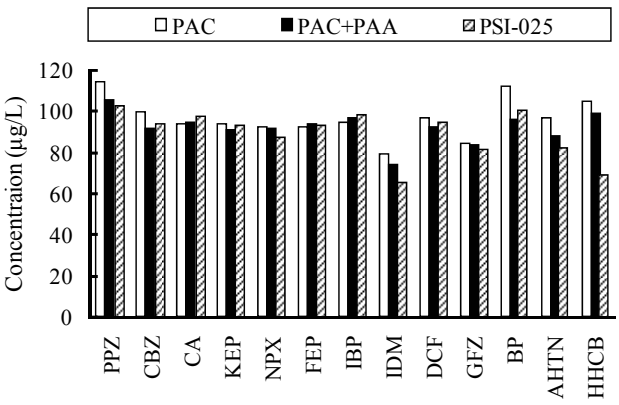
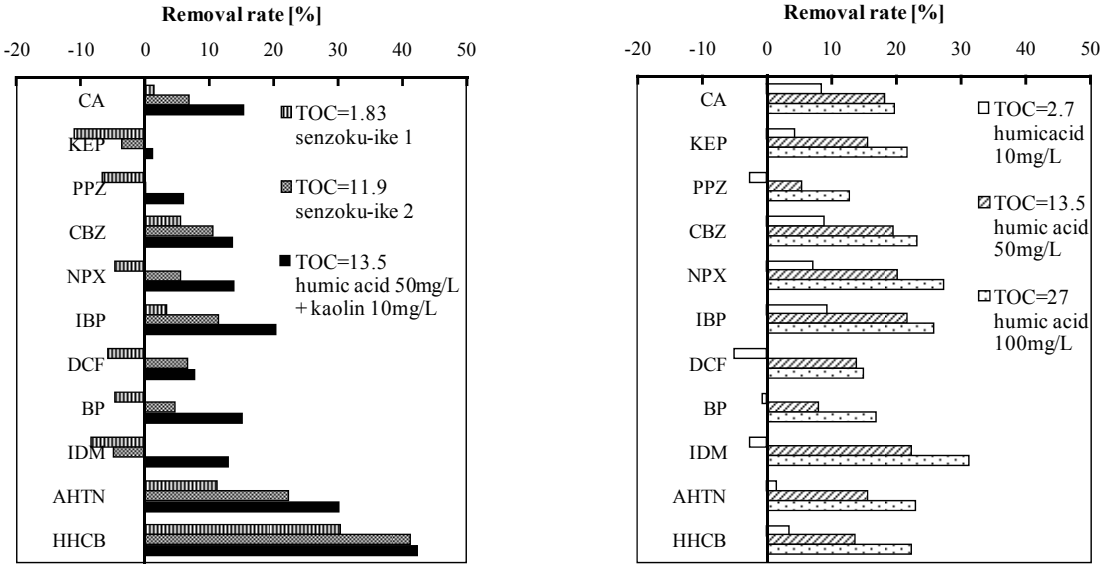


Fig. 6 The influence of three steps of coagulant dose under the presence of 50ppm humic acid.



(a) collected natural water and artificial water containing humic acid and kaolin

(b) Observed concentrations of PPCPs with different concentration of humic acid.

Figure 7 Relation between the removal rate of PPCPs and hydrophobicity considering the ionization

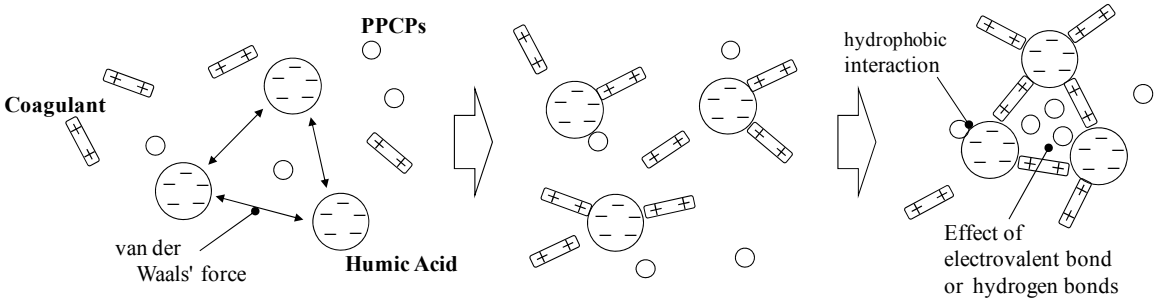


Figure 8 A possibility PPCPs were absorbed onto flocs of organic colloids due to electrovalent bond or the hydrogen bonds

of the target compounds on the order of Log D_{ow}. This result did not show the dependency of the removal of PPCPs on the hydrophobicity especially when organic suspended solids were not included in the raw water. Because a specific tendency was not seen between hydrophobicity and the elimination of the target compounds, the mechanism of PPCPs removal in the coagulation-flocculation was considered not fully associated with the hydrophobic interaction between the PPCPs and the dissolved organic matters. A possibility was suggested that PPCPs were adsorbed onto flocs of organic colloids due to the electrovalent bond or the hydrogen bonds (**Figure 8**).

4. Conclusions

In this study, the elimination efficiency of pharmaceuticals and cosmetic ingredients under the presence of natural organic matters in the coagulation-flocculation process was investigated. All substances were not removed under the presence of 10mg/L kaolin alone. The presence of 50mg/L humic acid, a kind of natural organic matters, increased the average removal ratio to 16.5%. From the result that the removal of PPCPs was increased with the increase in TOC in raw water or the concentration of humic acid, it was indicated that the removal efficiency of PPCPs depended on dissolved organic matter in raw water. On the other hand, because a specific tendency was not seen between the hydrophobicity and the removal of the target compounds, the removal of PPCPs in the coagulation-flocculation process was probably not a result of the hydrophobic interaction

between the target compounds and the organic suspended solid. A possibility was suggested that PPCPs were adsorbed onto flocs of organic colloids because of electrovalent bond or the hydrogen bonds.

Acknowledgements

The experiment of this study was supported mainly by National Institute of Public Health (NIPH). The author appreciate Prof Taro Urase of Tokyo University of Technology as well as Dai SHIMAZAKI of NIPH, for their kind advices.

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