SUMMARY

There is a growing concern about the presence of pharmaceuticals, personal care products and illicit drugs in the aquatic environment (Kasprzyk – Hordern *et al.* 2009). Following use, pharmaceuticals / drugs are excreted as the parent compound, water soluble conjugate or as metabolites and thus enter sewage treatment works (STWs). Disposal of unused pharmaceuticals can also be a route to the aquatic environment either through dumping to sewer via the toilets or drain, or to land – fills in domestic refuse or as special water by licensed waste contractors (Kanda *et al.* 2003). Despite their likely continuous discharge, little is known about the ultimate fate and transport of many drug substances after their intended application. Fewer studies have documented the effect of drugs like salicylate, acetaminophen, and ibuprofen on fish. These are endocrine disruptors in fish and have the potential to impair the adaptive cortisol response to stressors (Gravel and Vijayan 2006). Such reports have led to pharmaceuticals attracting increasing attention as environmental pollutants due to their possible environmental effects (Jones et al. 2003). The type / group of pharmaceuticals detected in aquatic system are fairly broad e.g. contraceptive hormones, lipid regulators, pain – killers, antibiotics, anti – cancer drugs, anti – epileptic drugs and those regulating blood pressure. Where pharmaceuticals have been detected in sewage effluents or surface water, the levels are generally at the ng L^{-1} or at most, low mg L^{-1} level (Kanda *et al.* 2003).

Analyses of such trace level organic pollutants in environmental samples is usually carried out by Gas Chromatography – Mass Spectrometry (GC – MS) or Liquid chromatography – Mass Spectrometry (LC – MS) techniques (Jones *et al.* 2003; Batt and Aga 2005). However, these techniques are relatively expensive and not easily available at several places. Need of the hour; therefore, is to use simpler techniques which however, require higher concentration of target drug molecules. Therefore, prior to the instrumental analysis, attention has to be paid to the sample preparation and enrichment procedure.

Solid Phase Extraction (SPE) is the method of choice for sample enrichment / pre – concentration in environmental analytical chemistry. There are several solid phases on which the sample can be concentrated (Batt and Aga 2005; Psillakis *et al.* 2003).

Drugs have been shown to pass intact through conventional STPs, into water ways, lake and aquifers and discharged pharmaceuticals may end up at landfill sites posing a threat to underlying ground water (Jones *et al.* 2003). Presently, STPs are not designed to completely remove most pharmaceuticals and these compounds are consequently released into surface water, (Zuccato *et al.* 2008; Carballa *et al.* 2004; Stackelberg *et al.* 2007) making it important to develop new methods to treat water containing such pollutants. For removal of such organic compounds charcoal (activated charcoal) is often used as an adsorbent. This sorbent is highly inert, thermally stable, has porous structure and large internal surface area. Literature reports several studies on use of activated charcoal for removal of a variety of pollutants from water (Garcia – Araya *et al.* 2003; Safarik *et al.* 1997).

Aim of our work was to develop simple, accurate and cost effective techniques to determine such low concentration drugs present in aquatic environment. Such studies have not been done in India till now. For our pre – concentration studies we have selected five drugs of different categories: aspirin, paracetamol, esomeprazole magnesium, fenofibrate, and venlafaxine HCl.

Adsorption by activated charcoal is frequently the most efficient and most economical method for removing pollutants from water, particularly when these are present in low concentrations, whether it is a batch process or continuous flow treatment method. The removal efficiency of activated charcoal may be increased by presence of some metal complexes on the surface of activated charcoal. Concept was to use the activated charcoal which has previously been used for removal of metals in effluents. Since disposal of such carbon is a problem. So before disposing, whether we can use the metal loaded carbon once more for removing pharmaceuticals or organic compounds. Aspirin and paracetamol were considered as target drugs for the study of removal efficiency of commercially available activated charcoal (granular) and effect of metal complexes on it. Effect of oxygen on the efficiency of activated charcoal loaded with metal complex to remove these compounds was also studied. It was expected that in presence of metal complexes and oxygen the non – polar part of organic pollutants would be oxidized and become more polar, increasing its affinity for carbon. Hence its removal should be more complete from water. This is because

several transition metal ions and metal complexes are known to act as catalyst for oxidation of organic compounds in presence of oxygen (Jana *et al.* 2007; Silva *et al.* 2004; Silva *et al.* 2002).

The overall work is organized in five chapters. Chapter one describes the literature survey in the area. Chapter two contains pre – concentration method developed for aspirin and paracetamol. The drugs were analysed by UV – Visible spectrometer. Chapter three discusses pre – concentration method developed for esomeprazole magnesium, fenofibrate, and venlafaxine HCl. The drugs were analysed by HPLC. Chapter four describes validation of gradient HPLC method developed for simultaneous determination of esomeprazole magnesium, fenofibrate and venlafaxine HCl. Chapter five is concerned with treatment studies of drugs from water using activated charcoal loaded with metal and metal complex.

Aspirin and paracetamol are components of multidrug pharmaceuticals preparations for the therapy of pain and are widely used as analgesic and antipyretic drugs. There are various methods for the determination of aspirin and paracetamol in various pharmaceutical products, including derivative spectrophotometry (Nogowska *et al.* 1999). Presence of aspirin and paracetamol in water is also reported (Gravel and Vijayan 2006; Jones *et al.* 2003; Kasprzyk – Horden *et al.* 2008, 2009). For our work, Polystyrene divinylbenzene (PSDVB) beads were used as adsorbent for solid phase extraction. aspirin as target drug was pre – concentrated from aqueous solutions on PSDVB beads of gel type and macro – porous type with different cross – linkings and on anion – exchanger. Later it was recovered by different solvents and analysed by UV – Visible spectrometer. Pre – concentration using SPE was carried out using a glass column packed with adsorbent material. Flow rate was maintained using stop – cock attached with the column. Studies were conducted to work out the experimental conditions for the optimum adsorption and recovery.

A typical experiment was performed using synthetic sample of aspirin. A sample of 100mg L^{-1} aspirin aqueous solution of 100mL volume was prepared by diluting an appropriate aliquote of stock solution. The column packed with 1g of the adsorbent material (PSDVB polymer beads) was activated by passing 5mL acetonitrile through it followed by 5mL of acetonitrile: water (80:20) (v/v) and then

by 5mL of water. The aqueous drug sample was passed through the activated column at the rate of 0.66mL min^{-1}. The adsorbed drug was eluted with 10mL of methanol. Amounts of drug adsorbed and recovered in methanol were determined by recording absorbance at 225nm. Optimization was carried out by varying the following parameters one at a time while maintaining all others constant: initial volume of aqueous drug solution, amount of adsorbent, concentration of aqueous drug solution, volume of solvent for recovery and flow rate.

After optimizing the conditions the drug samples of aspirin and paracetamol individually; these conditions were used for analysis of mixture of aqueous solution of aspirin and paracetamol together. For recovery of adsorbed drugs different solvents were used. Later the method was applied for environmental samples collected from the outlet of secondary clarifier of the Sewage Treatment Plant operating with Up – Flow Anaerobic Sludge Blanket (UASB) principle.

Samples of aspirin and paracetamol were analysed by UV spectrometer and HPLC. For UV – Visible spectrometery, the two drugs were analysed together by using Beer – Lambert's law. A chromatographic method was also developed for the analysis of two drugs in mixture by HPLC using UV detector at 280nm and using a C – 18 column. Analytical performance characteristics studies were also performed for two methods.

It was concluded that method developed for pre – concentration of aqueous samples containing aspirin and paracetamol using UV – Visible spectrometer for quantification enabled the determination of the target pharmaceuticals in synthetic water samples at 0.025mg L^{-1}. By using commercially available macro – porous polymer of PSDVB with varying cross – linking and anion – exchanger (Amberlite IRA – 93), in simple laboratory conditions water samples containing aspirin and paracetamol can be pre – concentrated. Quantitative analysis of aspirin and paracetamol individually and in mixture can be done by UV – spectrometer even at low levels though in mixture, pre – concentration of paracetamol is not achieved. The treated water samples collected from STP (Vadodara – India) did not show presence of aspirin and paracetamol up to the detection level of 0.03mg L^{-1} using the developed method when the samples were analysed by HPLC method.

These optimized conditions were used as starting set of conditions for three other drugs: Esomeprazole magnesium, fenofibrate and venlafaxine HCl and further improved for each of the three drugs individually. Quantification of the pre – concentrated drugs from synthetic samples was carried out using HPLC method reported in literature and modified wherever necessary for out conditions. The methods were validated.

Esomeprazole magnesium is a proton pump inhibitor (PPI) developed as an optical isomer (*S* – Esomeprazole) for the treatment of acid – related diseases (Lind *et al.* 2000). Esomeprazole does not undergo chiral inversion in vivo (Andersson *et al.* 2001) and therefore can be determined using the same methodology as for its racemate, omeprazole. The literature survey reveals that omeprazole has been analysed in different products by various methods (Hernando *et al.* 2007). Fenofibrate is fibric acid derivative, used for regulating plasma lipids and treatment of hyperlipoproteinaemias (Sweetman 2002). Fenofibrate has been analysed in pharmaceutical products by different methods (Reddersen and Heberer 2003, Sacher *et al.* 2001; British Pharmacopeia 2007; Romanyshyn and Tiller 2001; Streel *et al.* 2000; Masnatta *et al.* 1996; Ramusino and Carozzi 1986; Rao and Nagaraju 2003; Lacroix *et al.* 1998). Vanlafaxine HCl is a non – tricyclic antidepressant. There are various methods reported in literature for determination of venlafaxine HCl for different purposes (Hicks *et al.* 1994; Vu *et al.* 1997; Schultz and Furlong 2008).

Omeprazole is excreted in an unaltered form in the low proportion and its presence in aquatic environment has been reported (Hernando *et al.* 2007). Presence of fenofibrate in aquatic environment has been reported recently (Redderson and Heberer 2003; Hernando *et al.* 2006). Venlafaxine HCl is soluble in water, which suggests that significant amount of active unused venlafaxine HCl may reach municipal sewage treatment plants through toilets and drains. Number of reports on the occurrence of a wide variety of antidepressants in the aquatic environment have been increasing steadily in recent times, (Weigel 2004) predominantly venlafaxine (Schultz and Furlong 2008).

Optimized conditions obtained in the pre – concentration study of aspirin and paracetamol viz. 1g adsorbent, 100mL aqueous solution of drug and 5mL solvent for

recovery were used as starting set of conditions for the drug esomeprazole magnesium. Aqueous solutions of the pure drug with known concentration were prepared and the pre – concentration conditions optimized by varying experimental parameters one – by – one. Synthetic aqueous samples for esomeprazole magnesium were analysed by HPLC using mobile phase which was prepared by mixing phosphate buffer and acetonitrile in a ratio 70: 30(v/v). Flow rate was 1.0mL min^{-1}. Detection was carried out at 302nm. Sample injection volume was 20μL. All determinations were performed at room temperature. Under these conditions the retention time of esomeprazole prepared in methanol and water was in the range of 15.0 to 15.3min.

Influence of changing the following parameters on pre – concentration of drug was studied in the sequence: i) flow rate of aqueous solution of drug, ii) volume of aqueous solution of drug, iii) amount of adsorbent, iv) different concentrations of aqueous drug solution, and v) different volumes of solvent for recovery. Initially effect of flow rate of aqueous esomeprazole solution on adsorption was studied. With increase in flow rate, adsorption of drug on adsorbent decreases. For subsequent experiments the 0.66mL min^{-1} flow rate was maintained, which resulted into maximum drug absorption of up to 70%. Effect of changing volume of aqueous solution containing the drug, effect of changing amount of adsorbent while keeping volume and concentration of drug solution constant have been studied and optimized in the present work for esomeprazole. Results show that when 100mL esomeprazole aqueous solution is passed through column containing 1g of polymer beads, 70% esomeprazole gets adsorbed on the polymer. While with 50mL of initial drug solution the percentage of drug adsorption increases to 87.95. With this percentage of adsorption, methanol was used for recovery. The percentage of recovery was studied with four different volumes of methanol (3, 5, 7 and 10mL). Maximum drug recovery of up to 102.91% was observed with 10mL of methanol resulting in pre – concentration factor of 6.05. With the decrease in volume of methanol for recovery the percentage of drug recovered decreases but the pre – concentration factor increases. Considering this trend, the condition for recovery of drug adsorbed on 1g of adsorbent was optimized to 5mL of methanol. With these optimized conditions for recovery, pre – concentration experiments were performed taking higher volumes of aqueous drug solutions keeping the amount of drug same. These experiments show

that with increase in volume of initial aqueous drug solution, the percentage of amount of drug adsorbed remains almost same but after its recovery with 5mL methanol, pre – concentration factor for respective experiments increases. However this trend changes with higher volume of initial drug solution. To study effect of initial volume different sets of experiments were carried out with 50, 100, 150, 250 and 500mL of initial aqueous drug solutions respectively. With 250mL initial drug solution, maximum of 96.51% drug was found to get adsorbed. Results also show that volume of 5mL methanol can recover 100% drug at lower amount up to 1.47mg.

The optimized conditions for maximum adsorption of drug and its recovery with better per – concentration factor for esomeprazole are: 250mL of initial aqueous drug solution passed through 1g PSDVB beads with flow rate 0.66mL min^{-1}, followed by 5mL methanol used for recovery of drug adsorbed.

For fenofibrate similar studies were carried out and conditions were optimized. Samples of fenofibrate were analysed by HPLC method using mobile phase which was prepared by mixing acetonitrile and milli – Q water in a ratio of 80:20(v/v) and adjusted to pH 4.0 using phosphoric acid. The flow rate was 1.5mL min^{-1}. Detection was carried out at 287nm. The injection volume was 20µL. All determinations were performed at room temperature. Under these conditions the retention time of fenofibrate prepared in methanol, water and acetonitrile was in the range of 6.0 to 6.3min.

Initially methanol was used for recovery of fenofibrate adsorbed on polymer beads. Due to poor recovery, methanol was replaced by acetonitrile. The optimized conditions for maximum adsorption of drug and its recovery with better pre – concentration factor for fenofibrate are: 50mL of initial aqueous drug solution passed through 1g PSDVB beads with flow rate 0.66mL min^{-1}, followed by 5mL acetonitrile used for recovery of drugs adsorbed.

Similar experiments were performed for venlafaxine HCl and the optimized conditions are: 50mL of initial aqueous drug solution passed through 1g PSDVB beads with flow rate 0.66mL min^{-1}, followed by 5mL methanol used for recovery of drugs adsorbed. Samples of venlafaxine HCl were analysed by HPLC using mobile

phase consisting of acetonitrile: phosphate buffer, 75:25(v/v) at a flow rate of 1.5mL min^{-1}. Detection was carried out at 224nm. All determinations were performed at room temperature. Under these conditions the retention time of venlafaxine HCl prepared in methanol and water was in the range of 2.7 to 2.9min.

The validity of these chromatographic procedures was established through studies of linearity, sensitivity, repeatability. Linearity was established with a series of working standard solutions prepared by diluting the stock solution with respective solvents individually to the final concentrations. Each concentration was injected in triplicate and the mean value of peak area was taken for the calibration curve. The calibration graphs involved at least five experiment points for each drug and they are described by the following equations: for esomeprazole in water: $y = 43243x + 3294.5$ ($r^2 = 1.0000$); for esomeprazole in methanol: $y = 43257 x + 2539.5$ ($r^2 = 1.0000$). Limit of detection (LOD) and quantification (LOQ) were calculated from visual determination method of % RSD of area. LOD for esomeprazole in water and methanol was 0.09mg L^{-1} respectively and LOQ in water and methanol was 0.19mg L^{-1} respectively. Equations for standard curve: for fenofibrate in acetonitrile: $y = 39353x - 1379.7$ ($r^2 = 0.9997$); for fenofibrate in water: acetonitrile (60:40)(v/v): $y = 39385 x + 19766$ ($r^2 = 0.9991$). LOD for fenofibrate in water: acetonitrile (60:40)(v/v) and acetonitrile is 0.06mg L^{-1} respectively and LOQ in water: acetonitrile (60:40)(v/v) and acetonitrile is 0.48 mg L^{-1} respectively. Standard curve equations: for venlafaxine HCl in water: $y = 22423x + 157.57$ ($r^2 = 1.0000$); for venlafaxine HCl in methanol: $y = 23924 x + 167.52$ ($r^2 = 1.0000$). LOD for venlafaxine HCl in water and methanol is 0.03mg L^{-1} respectively and LOQ in water and methanol is 0.24mg L^{-1} respectively.

Developed optimized methods for pre – concentration of esomeprazole, fenofibrate and venlafaxine HCl were applied to environmental water sample which was also analysed by HPLC after pre – concentration. In this case, no peaks were observed in the chromatogram for all three drugs. The samples were spiked with a known amount of drugs (1mg L^{-1}) and analysed but the signal enhancement for 1mg L^{-1} added drug was not seen. Results indicate no presence of esomeprazole,

fenofibrate and venlafaxine HCl in the sample collected from the STP which was confirmed by a LC – MS method.

Accuracy of the pre – concentration methods for esomeprazole magnesium, fenofibrate and venlafaxine HCl was studied individually by fortifying the synthetic aqueous and live samples with a known amount of all three drugs respectively. The methods developed for pre – concentration of aqueous solutions containing esomeprazole, fenofibrate and venlafaxine HCl using HPLC method for quantification, are accurate, sensitive and reliable and enable the determination of the target drug in water sample at concentration levels of 0.006mg L^{-1} for esomeprazole, 0.046mg L^{-1} for fenofibrate and 0.024mg L^{-1} for venlafaxine HCl respectively. Thus, in simple laboratory conditions aqueous solution of esomeprazole, fenofibrate and venlafaxine HCl can be pre – concentrated by a factor of 30, 20 and 10 respectively by using, commercially available macro – porous polymer of PSDVB with 8% cross – linking.

The water sample collected from STP (Vadodara – India) after treatment does not show presence of esomeprazole, fenofibrate and venlafaxine HCl up to the detection level of 0.003mg L^{-1} considering the pre – concentration factor in optimized conditions. This means concentration of these drugs in the treated sewage water is below this level possibly due to dilution or STP is efficient in removing the drug effectively.

According to the information collected from literature there is no reported method for simultaneous determination of esomeprazole, fenofibrate and venlafaxine HCl using HPLC which can be applied for detection of these drugs present in water at low concentrations. In this chapter we report development and validation of a new HPLC method for simultaneous determination of esomeprazole, venlafaxine HCl and fenofibrate in a synthetic mixture. For recovery studies, treated sewage water collected from a STP, Vadodara, India was used.

The new HPLC method is simple and sensitive, with total run time less than twenty minutes for the simultaneous determination of esomeprazole, venlafaxine HCl and fenofibrate. Separation was carried out on a C18 column. Mobile phase A

contained a mixture of buffer and acetonitrile in the ratio 75:25(v/v). Mobile phase B consisted of buffer and acetonitrile in the ratio of 30:70(v/v). The buffer consists of 0.3% formic acid. The mobile phase was premixed, filtered through a 0.45µm nylon filter and degassed. The flow rate was kept at 1.1mL min^{-1} throughout. The LC gradient was time (min.) / mobile phase: 0.00 / A, 6.01 / B and 15.01 / A. The detection was monitored at 230nm. The injection volume was 10µL.

At the beginning of method development a chromatographic condition was set for the separation of esomeprazole, venlafaxine HCl and fenofibrate individually by BDS Hypersil C8 column (250 x 4.6mm, 5µ particle size) using a mixture of acetonitrile: buffer (0.13% formic acid, 15.50% 0.1mol L^{-1} ammonium acetate) in the ratio 25:75(v/v) (pH 3.8) as mobile phase A and acetonitrile as mobile phase B at a wavelength of 302nm with flow rate 1.0mL min^{-1} with run time 45 minutes. To reduce the run time chromatographic conditions were changed. This was achieved on a C18 (150cm x 4.6mm, 3.5µm particle size) column and mixture of acetonitrile: buffer (0.3% formic acid) in the ratio 25:75(v/v) as mobile phase A and in the ratio 30:70(v/v) as mobile phase B. At the wavelength of 230nm all the three drugs gave a good response. Under these conditions, sharp peaks that belong to esomeprazole, venlafaxine HCl and fenofibrate were obtained at retention time 3.25, 4.77 and 13.12 minutes respectively. The tailing factor for esomeprazole, venlafaxine HCl and fenofibrate was 1.288, 1.478 and 1.290 respectively.

The gradient RP – LC method developed for determination of esomeprazole, venlafaxine HCl and fenofibrate is precise, accurate and specific. The developed, validated method could separate esomeprazole, venlafaxine HCl and fenofibrate with good resolution.

The limit of detection of esomeprazole, venlafaxine HCl and fenofibrate was 1.02mg L^{-1}, 1.02mg L^{-1} and 1.05mg L^{-1} (for test concentration) respectively; the limit of quantification was 5.18mg L^{-1}, 5.09mg L^{-1} and 5.22mg L^{-1} (of test concentration) respectively. The method can be used for routine analysis.

For removal study from water, aspirin and paracetamol were considered as pollutant target drugs. The drug solutions containing a known concentration of aspirin and paracetamol were treated with activated charcoal loaded with metal complexes

(MACs) or metal ions (MCs). Effect of oxygen on removal efficiency of impregnated activated carbon was also studied. The amount of unadsorbed drug in filtrate was measured by UV – Visible spectrometer and the adsorbed percent was calculated. Metal complexes, copper bisacetylacetonate, manganese salen and copper salen were synthesized using reported methods, characterized by FTIR and CHN micro analysis and loaded on activated charcoal. The copper bisacetylacetonate complex was dissolved in chloroform (500mg L^{-1}). 5g of activated charcoal (AC) was placed in the copper bisacetylacetonate chloroform solution for 3 hours at room temperature with occasional swirling. The resulting material (MAC_1) was filtered off, washed, dried (100°C) and stored in bottle. Similarly manganese salen was loaded on activated charcoal by dissolving in acetonitrile to get manganese salen loaded activated charcoal (MAC_2) and copper salen by dissolving in chloroform to get copper salen loaded activated charcoal (MAC_3) respectively. The metal salts, copper sulphate, nickel sulphate, cobalt chloride and nickel chloride were loaded individually on activated charcoal to get MC_1, MC_2, MC_3 and MC_4 respectively. For determining percentage loading of metal ion or metal complex the amount of the metal complex or metal salt remaining in the filtrate was determined by recording absorbance of the solution at the λ_{max} of the respective metal complex and metal solution, and the concentration computed from corresponding calibration curves of respective metal complex or metal salt. The amount of metal complex or metal salt adsorbed on charcoal was computed using absorbance value for solution before passing it through charcoal. Analytical characteristics and linearity of calibration for each metal complex and metal solution were studied. These materials were used for removal of drugs from aqueous solution. The following two sets of experiments were applied to the three aqueous solutions of aspirin, paracetamol and mixture of aspirin and paracetamol.

Set 1: 10mL (50mg L^{-1}) aspirin solution was added into two different stoppered tubes containing AC and MAC respectively for 30 minutes with constant stirring. Resultant solution was filtered and absorbance was measured using UV – Visible Spectrometer.

Set 2: 10mL (50mg L^{-1})) aspirin solution was added into two different stoppered tubes containing AC and MAC respectively for 30 minutes with constant supply of oxygen.

Resultant solution was filtered and absorbance was measured using UV – Visible Spectrometer.

These set of conditions were applied individually to all activated charcoal samples loaded with three metal complexes and metal salts respectively. Results show that AC removes 14.29% aspirin and 47% paracetamol from water when the individual aqueous drug solutions where treated with it, but the percentage of removal increases for both drugs in presence of oxygen. The trend remains almost similar when the individual aqueous drug solutions were treated with metal complex loaded activated charcoal MAC_1, MAC_2 and MAC_3, except MAC_1 which separates 70% aspirin from water in presence of oxygen. When the mixture of aqueous drug solution was treated with AC the percentage removal of individual drug increases compared to the individual treatment with AC In case of paracetamol, however, adsorption from mixture decrease in absence of oxygen.

In case of individual drug solutions, MAC_1 separates maximum amount of aspirin from water when compared with other three adsorbents in absence of oxygen. In presence of oxygen the trend remains same but removal efficiency of MAC_1 for aspirin increases to 38% compared to that with absence of oxygen. Whereas MAC_3 separates maximum amount of paracetamol from water when compared with other three adsorbent in absence of oxygen. In presence of oxygen the removal efficiency of all four adsorbents increases.

In case of treatment of drugs in presence of each other, MAC_2 separates maximum amount of aspirin from water when compared with other three adsorbent in absence of oxygen, whereas in presence of oxygen MAC_1 separates maximum amount of paracetamol. When paracetamol is considered, MAC_3 adsorbs maximum amount of paracetamol in absence of oxygen and almost 100% in presence of oxygen.

The adsorption of drugs on impregnated AC increases in presence of oxygen compared to that in absence of oxygen. In case of MAC_1 a distinct difference on the adsorption behavior of aspirin and paracetamol is observed: aspirin and paracetamol in presence of each other get less adsorbed compared to individual treatment in absence of oxygen, but in presence of oxygen adsorption of aspirin increases and

paracetamol decreases in presence of each other. Similarly in case of MAC3 amount of aspirin adsorbs in less amount when treated with paracetamol in absence of oxygen compared to its individual treatment but in presence of oxygen adsorption efficiency of MAC_3 increases both for aspirin and paracetamol in presence of each other as compared to their individual treatment. At this juncture we are unable to provide suitable explanation for the observed trend.

All most in all cases of metal salts loaded activated charcoal, the adsorption of drugs increases in absence of oxygen with respect to activated charcoal which is not loaded with metal salts. The effect of oxygen was not observed on the absorption of adsorbents except AC. MC_2 removes maximum about of drugs in absence of oxygen and presence of oxygen increases removal efficiency of MC_2. In case of MC_1 and MC_3 a distinct difference on the adsorption behavior of aspirin and paracetamol is observed: When treated individual aspirin adsorbed more compared to paracetamol and where as paracetamol adsorbed more compared to aspirin when treated in presence of each other. In case of MC_4, the percentage removal of both aspirin and paracetamol in presence of each other decreases compared to its individual treatment.

From the removal study it can be concluded that metal complex and metal ion loaded activated charcoal can remove drugs present in water. Its removal efficiency increases in presence of oxygen. Metal loaded charcoal can be used for removal of drugs present in water as tertiary treatment in water treatment plants. However, no specific trend could be observed in terms of use of metal salt or metal complex.