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REPORT

IR study of degradation of acetaminophen by iron nano-structured catalyst

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Abstract: Full degradation of acetaminophen (paracetamol) in aqueous solution was investigated at room temperature through heterogeneous iron nano-structured as catalyst in this article. Iron Nano-structured was prepared through simple hydrothermal processes using Iron oxide (Fe_2O_3) as precursor. The catalytic activity of as prepared Nano-catalyst (NC) was investigated in the degradation of the acetaminophen as an environmental pollutant, commonly called paracetamol, under different operating parameters like pH, dosages of acetaminophen and dose of NC. Remarkable differences in IR spectra were observed after reaction which showed complete degradation of 15 ppm of Acetaminophen using 0.1 g of nano-structured with the recovery of NC followed by its activity four times with full catalytic performance.

Keywords: N-acetyl-p-aminophenol, iron nano-structured, degradation, drug released.

INTRODUCTION

Paracetamol (acetaminophen, N-acetyl-p-aminophenol) is a potent drug that can be obtained without any prescription and commonly used worldwide as an analgesic and anti-pyretic. It is a para substituted benzene ring by a hydroxyl radical on one side and the nitrogen of the amide group on the other (Bales *et al*., 1985). Its half-life in the plasma is 1.5 to 2.5h (Wu *et al*., 2012). It is among the top three and top 200 prescribed medicine in England and USA respectively (Sebastine and Wakeman, 2003). It is used for the treatment of headache, tooth pain, aching throat, osteoarthritis pain, fever (Young *et al*., 2015) etc. Beside its advantages as a drug it is very toxic if overdose, to the liver specially, then others over the counter drugs. Cases reported where Acetaminophen used for suicide attempts and even the change of mind happened but the suspect died due to severe irreparable damage to the lung and liver (Yoon *et al*., 2016). Acetaminophen reaches to the environment through waste water. In fact, human body excretes up to 9% of Acetaminophen intake (without changing) to the wastewater through urine and a total of 58-68% is excreted during therapeutic dosage (Muir *et al*., 1997). It also reaches to the main water streams when it is improperly discarded upon expiration. Pharmaceutical manufacturer is also the main source of reaching this to the environment and the medical waste is also a source of it (Thomas and Langford, 2007). It can be easily accumulated in the water due to its high solubility and hydrophilicity. In the wastewater it may interfere with the development of embryo, survival, growth phenomenon, reproduction characteristics and endocrine system of fishes (Andreozzi *et al*., 2003). Authorities of USA, UK, Canada etc., found acetaminophen contents in drinking water, waste water and in treated waste water as well (Hirsch *et al*., 1999; Kolpin *et al*., 2002), but in Pakistan no such comprehensive study conducted in this regards to the best of Author's knowledge. In drinking water, it will be more toxic for the human being. This medicine is available under different brand names while in Pakistan, Panadol tablet is the brand leader of the active ingredient of Paracetamol or Acetaminophen. One of the suspected ways to remove Paracetamol in waste water is through chlorination which is the most commonly used disinfectant process and analysis of the degraded material was done through HPLC (Bedner and MacCrehan, 2006). In another research, degradation of Acetaminophen was studies through use of halides (Li *et al*., 2015).

The aims and objective of current research is the degradation of Acetaminophen (Paracetamol) using Fe_2O_3 NPs. The degradation study conducted on advanced technology like FTIR analysis which reflects complete degradation of the tablets through active sites of functional groups before and after application of NPs.

MATERIALS AND METHODS

Reagents/material

Sodium Hydroxide (NaOH), Sulfuric Acid (H_2SO_4) and Potassium Bromide (KBr) were purchased from Merck (Darmstadt, Germany). Paracetamol tablet was purchased from GlaxoSmithKline (Karachi, Pakistan). Iron nano structured were prepared through simple solvent hydrothermal method using bulk precursor of Iron oxide (Fe_2O_3) with ethanol solvent (both from Merck, Darmstadt, Germany). FTIR studies conducted using Shimadzu (IR Prestige-21 Fourier Transform Infrared Spectrophotometer) (Tokyo, Japan) and UV

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spectrophotometer from Shimadzu (UV-1800A) (Tokyo, Japan).

Preparation of paracetamol solution

Three tablets of paracetamol 500 mg were crushed and finely grounded using a clean pestle and mortar. 50 mg of powder was weighed and transferred into 100mL volumetric flask. 50mL of 0.1 M NaOH was added to the volumetric flask and sonicated for 10 minutes to dissolve the drug molecule. After that the volume was made up to the mark with distilled water. The solution was filtered through filter paper. From the filtrate, 10mL solution was transferred into another 100mL volumetric flask and the volume was made up to the mark with distilled water. From the resultant solution, 30mL solution was transferred into 100mL volumetric flask. 10mL of 0.1M NaOH was added to this flask and then the volume was made up to the mark with distilled water. The resultant solution was 15 ppm paracetamol solution (Kumar *et al*., 2014).

Removal studies of paracetamol

25mL of 15 ppm acetaminophen solution was transferred into 100mL beaker. pH of the solution was adjusted to 2.7 with 0.1M sulfuric acid (H_2SO_4) and 0.1M sodium hydroxide (NaOH). 0.1g as prepared Fe NPs was accurately weighed and transferred into the solution. Solution was left for stirring on magnetic stirrer. After 20 minutes 5mL of the solution was pipette out and filtered through filter paper. The filtrate was centrifuged for 10 min at 3000 rpm. The clear transparent solution was analyzed on Shimadzu spectrophotometer (UV-1800A) by taking the absorption spectrum between 200 to 400 nm using NaOH as blank. Control solution was also carried out in the same manner except the Fe NPs that was replaced by Fe_2O_3 commercial grade compound. Initial spectra of 15 ppm acetaminophen solution was also taken with the same operational parameters of spectrophotometer.

FTIR of paracetamol tablet

FTIR spectra of acetaminophen tablet was carried out by IR Prestige-21 spectrophotometer for the analysis of functional groups present in it. IR grade Potassium Bromide (KBr) and small amount of acetaminophen tablet was grinded into powder like fine particles and mixed using mortar and pastel and then converted into disc by high pressure hand pump. The KBr disc was then placed inside FTIR probe. The samples were scanned from 450 to 4000 cm^{-1} and resulting absorptions spectra were recorded.

FTIR of Acetaminophen Tablet Solution

For the analysis of functional groups in acetaminophen in solution form, FTIR spectrum was taken using IR Prestige-21 Fourier Transform Infrared Spectrophotometer (Shimadzu). IR grade Potassium Bromide (KBr) was grinded into powdered like fine particles using mortar and pastel followed by conversion into disc through high pressure hand pump. Acetaminophen after reaction and complete degradation solution dropped onto the KBr disc and the disc was then place inside FTIR probe. The samples were scanned from 450 to 4000 cm^{-1} and resulting absorptions were recorded.

RESULTS

Removal of acetaminophen from waste water through Fe_2O_3 NPs

The synthesized Fe_2O_3 NPs used for degradation of acetaminophen as it is a widely used over the counter drug and sometime discarded into open atmosphere. Paracetamol, more commonly acetaminophen, has the chemical name as *N*-acetyl-*p*-aminophenol. It has the chemical structure as shown in fig. 1. It consists of various functional groups like hydroxyl radical, carbonyl group, methyl group, amine group and an aromatic ring. The solution of acetaminophen was prepared in which Fe_2O_3 NPs were introduced 100µM Paracetamol (acetaminophen) solution, removal of acetaminophen was confirmed by UV and FTIR spectroscopy. Due to the presence of various functional groups and additionally the presence of excipients (substances that are used along with the active compounds to increase the stability, form a hard tablet and to deliver the compound) like sorbitol, sodium lauryl sulfate, lactose, magnesium stearate etc. made the study of acetaminophen more interesting.

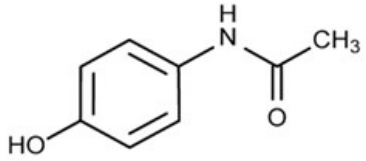

Fig. 1: Chemical Structure of Acetaminophen

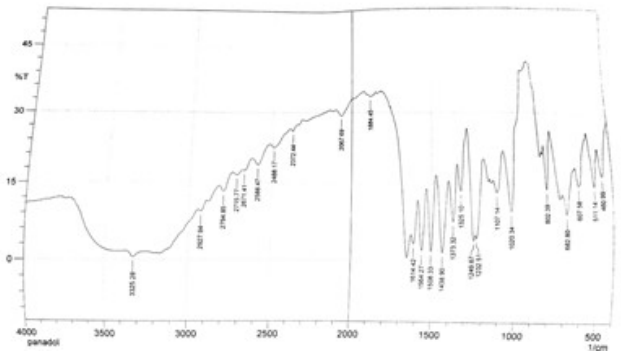

Fig. 2: Fourier Transform Infrared Spectroscopy image of Acetaminophen Tablet.

Optimization of Fe NPs Dosage

The optimization of the parameters required for any reaction to avoid extra amount of NC with full active surface area to make processes cost effective and ecofriendly. Removal of paracetamol directly related to

the dosages of NPs as higher amount on NPs provide larger surface area for effective degradation. Therefore, different amount of NPs like 0.05-1.0 g were added by keeping constant concentration of the paracetamol as 15 ppm, volume as 25mL, reaction time 20 min. Experiment reveals that 0.1 g was optimum NPs dosage for complete degradation of the Acetaminophen.

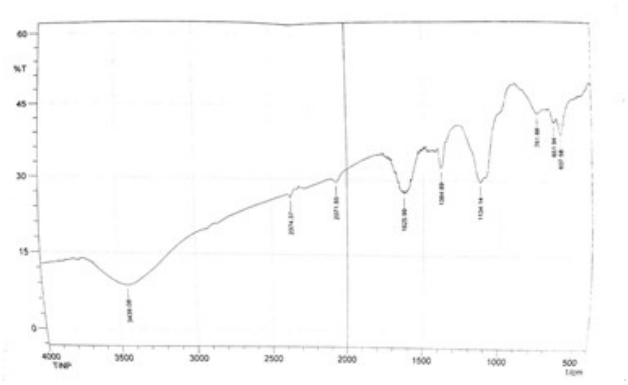

Fig. 3: Fourier Transform Infrared Spectroscopy image of acetaminophen solution with Fe nano particles

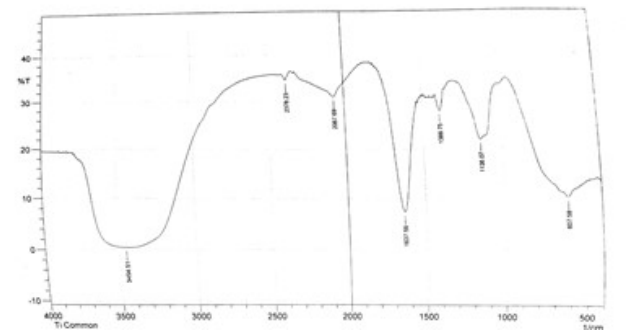

Fig. 4: Fourier Transform Infrared Spectroscopy image Acetaminophen solution with commercial bulk Fe_2O_3

Optimum pH of the Reaction

The role of pH was investigated in degradation of the acetaminophen solution with Fe_2O_3 NC as the acetaminophen solution was prepared in basic medium, the pH of the solution was found to be 9.5. When the reaction was conducted without altering the pH, the reaction was found to be very slow and the removal of acetaminophen was not observed. Furthermore, initially HCl was used to maintain the low pH but no degradation was observed (Naveed *et al*., 2016) therefore H_2SO_4 was used to maintain the pH to 2.7 before start of the reaction, where reaction found to be completed in 4 h with removal of acetaminophen. Therefore, 2.7 pH is found to be the optimum pH for the degradation of acetaminophen through Fe_2O_3 NPs reaction.

FTIR Study of Removal of Acetaminophen through Fe_2O_3 NPs

The FTIR spectroscopy is used as the fingerprint identity of the specific compound therefore more dominant and specific peaks were used for the analysis of acetaminophen. Fig. 2 showed the FTIR spectra of the acetaminophen tablet. Medium intensity peaks between 1475 and 1600 cm^{-1} were due the C=C stretch of the aromatic ring present in acetaminophen structure. Peak at 682 cm^{-1} represents the para substitution on the aromatic ring. Broad band at about 3200–3600 cm^{-1} is due to the hydroxyl radical of the acetaminophen. On this broad band, peak at 3325 cm^{-1} may be assigned to the N-H stretch. Peak at 1614 cm^{-1} is assigned to the stretching of the carbonyl group of the amide structure. Actually, the C=O partially overlaps the N-H bending band which usually appears in the range 1640-1620 cm^{-1} making the C=O band appears as a doublet. C-N absorption of secondary amine results in peaks 1232 and 1249 cm^{-1}. Peak at 1373 cm^{-1} is the characteristic bending absorption of the methyl group. Rest of weak peaks may be assigned to the excipients of the Acetaminophen tablet and it depends on the excipients used.

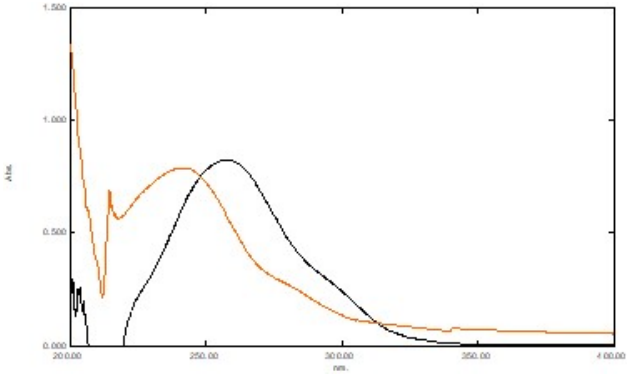

Fig. 5: UV spectrum for Acetaminophen degradation. (a) Acetaminophen (b) Degraded product

When Fe NPs were used for treating the solution containing acetaminophen tablet contents as a result of which removal of acetaminophen occurred successfully which was confirmed by the FTIR spectra as shown in fig. 3. Peak at 682 cm^{-1} that represents the para substitution on the aromatic ring in the standard spectra was disappeared now. Broad band at 3439cm^{-1} is attributed to the hydroxyl radical which was due to the water present in the aqueous solution. N-H stretch of acetaminophen on the O-H band and the peaks of carbonyl group of amide at 1614 cm^{-1} as present on acetaminophen spectra (fig. 2) absent now after interaction with the iron NPs (fig. 3). Weak peak at 1625 cm^{-1} may be due to presence of N-H or due to the formation of some other product or the some of the excipients. While the complex spectra of acetaminophen tablet were now converted into very simple IR spectra having very less peaks showing clearly that the acetaminophen structure is no more persist in the solution.

Control experiment was also conducted with the commercial grade Fe_2O_3 and the FTIR spectra is shown in fig. 4. This spectrum indicates that sharp peak present at

1637 cm^{-1} assigned to the N-H bending showing some acetaminophen structure continued to persist in the solution.

UV-Photometric Study of Removal of Acetaminophen through Fe_2O_3 NPs

Acetaminophen analysis performed by dissolving tablet in basic medium and analyze at 257 nm (Kumar *et al*., 2014) through UV/Visible spectrophotometry. The Hydrothermal Phase Transformed (HPT) Fe_2O_3 NPs introduced into the acetaminophen solution and filtered followed by centrifugation and UV/Visible analysis. The standard spectra of tablet shown in fig. 5 with dominant peak at λ_{max} 257 nm. The filtered and centrifuged clear solution after addition and stirring with Fe NPs showed shift in λ_{max} that showed the conversion of acetaminophen into another intermediate which is not as complex as acetaminophen shown in FTIR scan of Acetaminophen solution with Fe NPs (fig. 5).

DISCUSSION

Acetaminophen (Paracetamol) being the mostly used over the counter drug reached to the environment through various means and found in wastewater, rivers, canals etc. Fe_2O_3 NPs synthesized by HPT method found effective in removing Acetaminophen from aqueous solution. Disappearance of characteristic functional groups detected by FTIR extensively through taking spectra of Acetaminophen tablet, control solution containing only Acetaminophen and the test solution containing Fe_2O_3 NPs along with the Acetaminophen solution. UV-spectrophotometry also aids in determining the analysis.

The degradation of acetaminophen using Fe NPs found to be effective in comparison of earlier reports where chlorination is commonly employed as disinfectant and Acetaminophen removal process of wastewater producing more hazardous compounds (Bedner and MacCrehan, 2006). The current investigation is simple, cost effective and renewable source of material used for managing wastewater in comparison of the work (Zhang *et al*., 2008) who carried out photo degradation of acetaminophen by reacting solution of acetaminophen with TiO_2 NPs to achieve 95% degradation in 100 $\mu molL^{-1}$ in 100 min in special reaction vessel through metal halide lamp (250 W). While in the current research, Fe NPs were used for 100 $\mu molL^{-1}$ (15 ppm) solution of acetaminophen in simple reaction vessel without reactions conditions such as irradiation through halide lamp, constant bubbling of oxygen and maintaining specific temperature. Special critical and complicated requirements of the reactions made it difficult for processing wastewater on industrial scale, also increased in the cost of treatment. Present study proved to be successful, ecofriendly as well as cost effective as HPT method is feasible for the production of Fe NC on industrial scale to used against the Acetaminophen degradation.

Present study found comparatively more successful in ecofriendly approach because no peroxide reagent is used and the reaction was conducted at room temperature while in related study (Velichkova *et al*., 2013) against acetaminophen, hydrogen peroxide is used for the oxidation purpose whereas the temperature up to 60 °C was used which itself create environmental issues. The current study more suitable, simple and cost effective and economical in comparison of the work of Andreozzi *et al*. (2003), who investigated the removal of acetaminophen by H_2O_2 and ozonation in the presence of UV light to achieved up to 80% removal in initial 20 minutes. Contrast to current study that involves HPT method synthesized Fe NC to remove Acetaminophen in aqueous solution conducted at room temperature, atmospheric pressure without using any hazardous oxidizing agents. The current investigation proved to dominant as for managing medicinal waste in comparison to the reported work of (Bedner and MacCrehan, 2006) who established the processing of Acetaminophen containing water, where they found that during chlorination of acetaminophen two more toxic compounds formed along with other products. These two compounds are N-acetyl-p-benzoquinone imine and 1,4-benzoquinone produce further complexity as well as toxicity. In current study NPs synthesized from HPT method is proved to be nontoxic and is renewable for further use.

Limitation of studies

As FTIR is mainly used for qualitative analysis and UV-spectrophotometric analysis in current study involve masking of acetaminophen absorbance with interfering species. Therefore, the current results of degradation may possibly be analyzed quantitatively using, HPLC. Furthermore, this method should be tested for degradation of para aminophenol (major degradation of Paracetamol) because it is toxic for kidney (renal failure is proven in rats).

CONCLUSION

Acetaminophen found in environment and toxic even at low concentrations. Synthesized Fe_2O_3 NPs through HPT method used for the degradation of acetaminophen from wastewater. It is established that the synthesized NPs remove it efficiently without involving complex procedure with recovery of NC. Removal was confirmed by FTIR and UV-spectroscopy showing disappearance of characteristics peaks. Current study directed to use NPs for the removal of drugs from eco-system for a healthy environment.

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