EXPERIMENT: 19

AIM:

TO PERFORM ASSAY OF PARACETAMOL (REDOX TITRATION) BY CERIMETRY AND STANDARDIZATION OF TITRANT

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REQUIREMENTS

A. Glassware & Instruments

1. Pipette
2. Burette
3. Filter funnel
4. Conical flask
5. Graduated cylinders
6. Retort stand
7. Clamp

B. Chemicals & Reagents

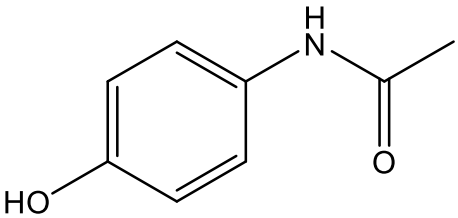
1. Methylene chloride
2. N-acetyl-p-aminophenol
3. Carboxylic acid
4. Ammonium cerium (IV) sulphate
5. Sulfuric acid
6. Ceric ammonium sulphate
7. HCl

THEORY

N-acetyl-p-aminophenol, also known as paracetamol (acetaminophen), is a widely used analgesic (pain reliever) and antipyretic (fever reduce). A mild analgesic is classified as paracetamol. It is frequently used for the relief of headaches and other minor aches and pains, and it is a key component in a number of cold and flu remedies.

In conjunction with opioid analgesics, paracetamol can be used to manage more severe pain, such as post-pot-surgery pains and to provide palliative care to patients with advanced cancer. Although paracetamol is used to treat inflammatory pain, it is not classified as a nonsteroidal anti-inflammatory drug (NSAID) because its anti-inflammatory activity is weak.

99.0 percent to 101.0% of its content (dried substance). It has a white crystal powder appearance and is sparingly soluble in water, freely soluble in alcohol, and slightly soluble in methylene chloride. Its melting point ranges from 168 to 172 degrees Celsius. A saturated aqueous solution has a pH of approximately 6 and is stable (half-life over 20 years), but its stability decreases in acidic or alkaline conditions, as the paracetamol is gradually converted into acetic acid..



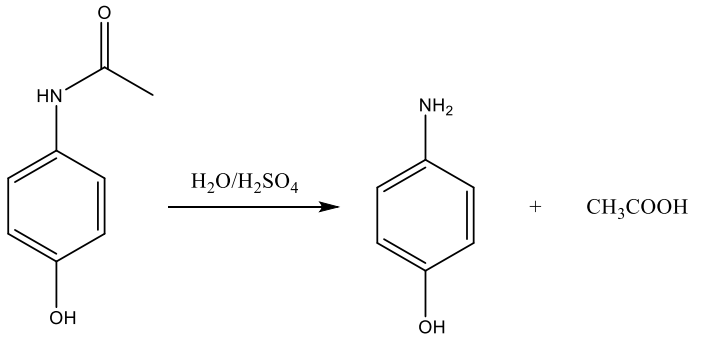
Paracetamol
M.Wt. = 151.2 g/mol

Paracetamol is 4-acetamidophenol and has the formula (C8H9NO2), molecular weight (151.2), and pKa values shown below (9.5).

Multiple publications describe the assay of Paracetamol and its combination in pharmaceuticals or biological fluids. Electrical method, Spectrophotometry high performance liquid chromatography, and titration method have all been reported for the determination of paracetamol.

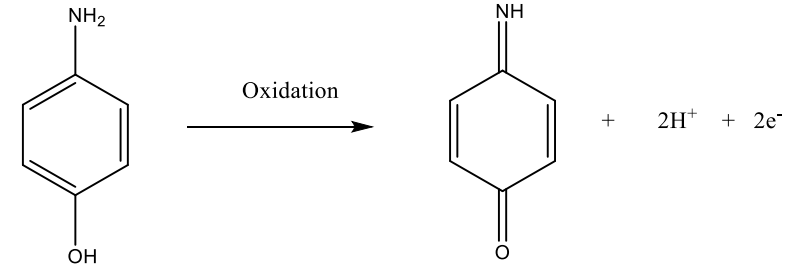
PRINCIPLE

The British Pharmacopoeia method for analysing paracetamol entails heating it with sulfuric acid in reflux. This is a simple, acid-catalyzed hydrolysis of an amide to produce an amine and a carboxylic acid. The formed 4-aminophenol is then titrated using ferroin as an indicator with an oxidising agent, ammonium cerium (IV) sulphate. The initial response is as follows:



Paracetamol 4-Aminophenol Acetic acid

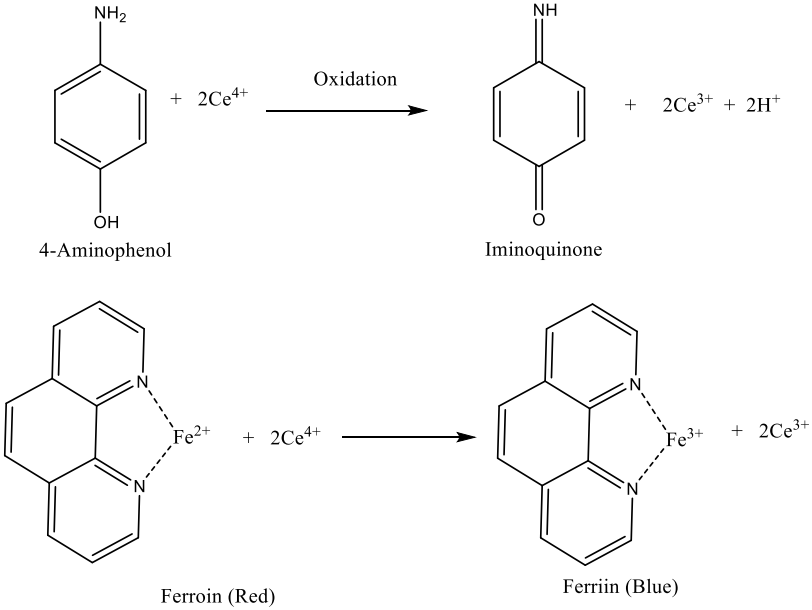
The titration step is considerably more interesting. 4-Aminophenol is easily oxidised in the following manner:



4-Aminophenol Iminoquinone

Ammonium cerium(IV) sulphate's function is to oxidise 4-aminophenol to iminoquinone. After the 4-aminophenol has been

completely oxidised, the cerium (IV) reagent will convert the ferroin indicator from Fe^{2+} to Fe^{3+} (ferroin).



The solution should be red during the titration, and the yellow endpoint is the transition from red to pale blue. Since 1 mole of Ce^{4+} is equivalent to 0.5 mole of paracetamol, it is simple to determine that the conversion factor provided in the method is accurate.

PROCEDURE

Preparation of 0.1N Mohr's salt

- Molecular weight of **Mohr's salt**= 392g/mol
- $N = \frac{weight * 1000}{molecular\ weight * volume\ taken}$

- Weight= $\frac{0.1N*\frac{392g}{mol}*250ml}{1000}$
- Weight= 0.98g
- Dissolve 0.98g of Isoniazid in sufficient quantity of water to produce 250ml.

Preparation of 0.1N Ceric sulphate solution

- Molecular weight of **Ceric sulphate**= 332g/mol
- N = $\frac{weight*1000}{molecular\ weight*volume\ taken}$
- Weight= $\frac{0.1N*\frac{332g}{mol}*250ml}{1000}$
- Weight= 8.3g
- Dissolve 8.3g of Ceric sulphate in sufficient quantity of water to produce 250ml.

Standardization of 0.1N Ceric sulphate solution with Mohr's salt

1. Pipette out 25ml of Ferrous ammonium sulphate solution into a conical flask.
2. Ferroin indicator is prepared by dissolving 0.695g of $FeSO_4.7H_2O$ in 100ml of DW and then dissolving 1.485g of o-pheno anthraline in it.
3. Add 25ml of H_2SO_4 and 2 drops of ferroin indicator.
4. Titrate against Ceric sulphate solution till orange red colour changes to colourless and finally to blue.

Assay of Paracetamol

1. Weigh an amount of powdered pills equal to 0.300 grammes of paracetamol.

2. Dissolve it in a mixture of 10ml of water and 30ml of 10 percent (w/v) diluted H2SO4.
3. Boil for one hour under a reflux condenser, then cool and dilute with 100 ml of water.
4. Add 40ml of ice, 15ml of diluted HCl (10 percent w/v), and 0.1ml of ferroin to 20ml of a solution.
5. Titrate with 0.1N ceric ammonium sulphate until a greenish yellow color is achieved.

CALCULATION

Observation table

With Mohr's salt

S No.	Volume of Ceric sulphate solution (ml)	Burette reading (ml)		Volume of Mohr's salt used (ml)
		Initial	Final	
1.				
2.				
3.				

With Ceric sulphate solution

S No.	Volume of Paracetamol solution (ml)	Burette reading (ml)		Volume of Ceric sulphate solution used (ml)
		Initial	Final	
1.				
2.				
3.				

Calculation of actual normality of Ceric sulphate solution

N1V1 (Mohr's salt) = N2V2 (Ceric sulphate solution)

Factor calculation of Paracetamol

Molecular weight of Paracetamol = 151 g/mol

1N 1000ml Paracetamol = 151g

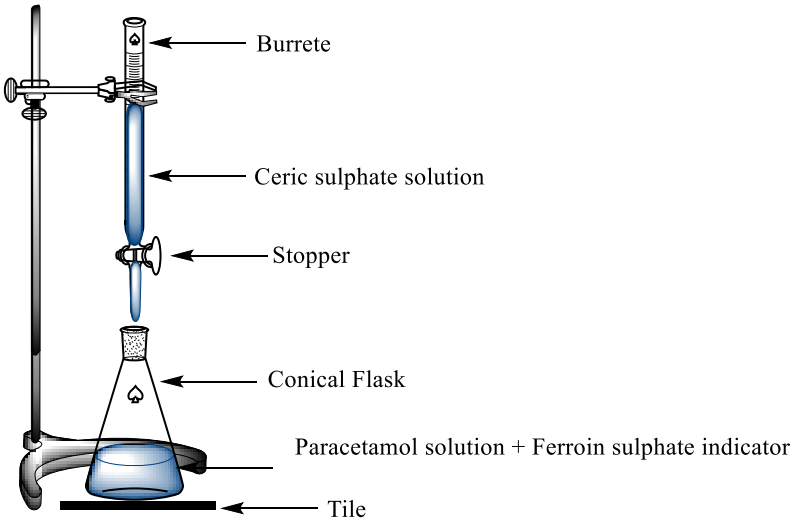
0.1 N 1ml Paracetamol = 151/10000= 0.0151g

Percentage purity calculation of Paracetamol

% Paracetamol (by weight) =

$$\frac{Observed\ normality * Volume\ of\ Ceric\ sulphate\ (burette\ reading) * Factor * 100}{Theoritical\ normality * Weight\ (\textbf{Paracetamol})}$$

DIAGRAM



APPLICATIONS

1. Paracetamol is a commonly used painkiller for the treatment of aches and pains.
2. Additionally, it can be utilised to lower a high temperature.
3. It is offered in combination with other analgesics and antiemetics.
4. It is also a component in numerous cold and flu cures.

RESULT

% Purity of Paracetamol is ……...