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# Titrimetric Analysis of Aceclofenac Sodium by Using Mixed Solvency

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**Abstract:-** Titration is a method of quantitative/chemical analysis which can be used to determine the concentration of a known reactant. Mixed solvency has been widely used to enhance the aqueous solubility of a large number of poorly water-soluble drugs. Various organic solvents like methanol, chloroform, dimethyl formamide and ethanol have been employed for solubilization of poorly water-soluble drugs. Organic solvents because of their higher cost, toxicities and pollution are not used as solvent. In the present investigation a sodium benzoate, sodium citrate, sodium salicylate solution (an economic agent) was employed as a hydrotropic solubilizing agent to solubilize the poorly water-soluble drug aceclofenac for its titrimetric analysis in bulk sample and tablets precluding the use of organic solvent. The proposed method is new, simple, precise and inexpensive. The results of the analysis have been validated statistically. The mean % recoveries were found to be close to 100, indicating the accuracy of the proposed method.

**Keywords**:- Solubilisation, Solvency, Solvent.

**Introduction:-** Titration is a method of quantitative/chemical analysis which can be used to determine the concentration of a known reactant. Because volume measurements play a key role in titration, the titrant, of known concentration (a standard solution) and volume is used to react with a measured quantity of reactant (analyte). By using a calibrated burette to add the titrant, it is possible to determine the exact amount that has been consumed when the endpoint is reached. The endpoint is the point in which the titration is stopped. This is a point at which the number of moles of titrant is equal to the number of moles of analyte, In the

 

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strong acid-strong base titration the endpoint of a titration is when the pH of the reactant is just about equal to 7, and often when the solution permanently changes color due to an indicator. Many methods can be used to indicate the endpoint of a reaction; titrations often use visual indicators (the reactant mixture changes colour). In simple acid-base titrations a pH indicator may be used, such as phenolphthalein, which turns (and stays) pink when a certain pH is reached or exceeded. Methyl orange can also be used, which is red in acids and yellow in alkalis.

Not every titration requires an indicator. In some cases, either the reactants or the products are strongly coloured and can serve as the "indicator". For example, an oxidation-reduction titration using potassium permanganate (pink/purple) as the titrant does not require an indicator. When the titrant is reduced, it turns colourless. After the equivalence point, there is excess titrant present. The equivalence point is identified from the first faint pink colour that persists in the solution being titrated.

Acid base titration:- An acid–base titration is method of quantitative analysis for determining the concentration of an acid or base by exactly neutralizing it with a standard solution of base or acid having known concentration. A pH indicator is used to monitor the progress of the acid–base reaction. If the acid dissociation constant (pKa) of the acid or base in the analyte solution is known, its solution concentration (molarity) can be determined. Alternately, the pKa can be determined if the analyte solution has a known solution concentration by constructing a titration curve.

Alkalimetry and acidimetry:- Alkalimetry and acidimetry are a kind of volumetric analysis in which the fundamental reaction is a neutralization reaction. Alkalimetry is the specialized analytic use of acid-base titration to determine the concentration of a basic (synonymous to alkaline) substance. Acidimetry, sometimes spelled acidometry, is the same concept of specialized analytic acid-base titration, but for an acidic substance.

**Hydrotrophy / mixed solvency**:- Hydrotropy refers to the ability of a concentrated solution of a chemical compound to increase the aqueous solubility of another compound [usually a

 

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sparingly soluble organic compound]. Compounds that have this property are called 'hydrotopes'. Sodium benzoate, sodium salicylate, sodium acetate, sodium ascorbate, niacinamide and sodium citrate are the most popular examples of hydrotropic agents which have been used to solubilize a large number of poorly water-soluble compounds: - Hydrotropic solution, sodium benzoate, sodiumacetate, sodium salicylate was employed as solubilizing agent to carry out the analysis of aceclofenac [a poorly water-soluble NSAID] by titrimetric estimation.

**Advantages of Mixed Solvancy method**

1. It reduces the large concentration of hydrotropic agents to produce modest increase in solubility.
2. It is used as a permeation enhancer.
3. It is used to develop injection dosage forms of poorly water-soluble drugs.
4. It used in nanotechnology (by controlled precipitation).
5. It is used in extraction of active constituents from crude drugs.

**Pharmaceutical applications of hydrotropic solubilization in pharmacy**

1. Quantitative determination of poorly water-soluble drugs by titrimetric analysis.

2. Quantitative determinations of poorly water-soluble drugs by UV-Visible spectrophotometric analysis.

3. The use of hydrotropy to give fast release of poorly water-soluble drugs from the suppositories.

4. Mixed hydrotropy is used to develop injection dosage forms of poorly water soluble drugs.

5. The use of hydrotropic solubilizers as permeation enhancers.

6. It is used to Preparation of injection of poorly water soluble drugs.

7. Hydrotropic solubilisation is used in extraction of active constituents from crude drugs.

 

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**Aceclofenac:-** Aceclofenac [[2-(2', 6'-dichlorophenyl) amino] phenyl acetoxy acetic acid] is a phenyl acetic acid derivative belongs to the group of non-steroidal anti-inflammatory drug (NSAID). It is a pro-drug of diclofenac, and decomposed under hydrolytic stress (neutral, acidic, and alkaline) and also on exposure to light (in solution form).It is used as anti-rheumatic, anti-inflammatory (both acute and chronic), analgesic (effective pain killer in lower backache, dental or gynecological pain) and antipyretic.Dysmenorrhea it is effective to treat dysmenorrheal pain. A single oral dose of aceclofenac 100 mg is sufficient to reduce primary dysmenorrhoea. In addition combination of aceclofenac and drotaverine is also functional and well tolerated treatment choice for primary dysmenorrhoea.

**Sodium benzoate:-** Sodium benzoate is a substance which has the chemical formula $NaC_7H_5O_2$. It is a widely used food preservative, with an E number of E211. It is the sodium salt of benzoic acid and exists in this form when dissolved in water. It can be produced by reacting sodium hydroxide with benzoic acid.Solubility in ethanol: 2.3 g/100 g (25 °C), Melting point: 410 °C (770 °F; 683 K)

**Sodium citrate**:- Tri-sodium citrate has the chemical formula of $Na_3\ C_6\ H_5\ O_7$ . It is sometimes referred to simply as "sodium citrate", though sodium citrate can refer to any of the three sodium salts of citric acid. It possesses a saline, mildly tart flavour. Formula: $Na_3C_6H_5O_7$,Melting point: 300 °C,Soluble in: Water

**Sodium salicylate**:- Sodium salicylate is a sodium salt of salicylic acid.It can be prepared from sodium phenolate and carbon dioxide under higher temperature and pressure. Historically, it has been synthesized by hydrolysis of methyl salicylate with an excess of sodium hydroxide and heating it under reflux. Formula: $C_7H_5NaO_3$,Melting point: 200 °C, Solubility: soluble in glycerol, 1, 4-Dioxane, alcohol.

 

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## Material & Method

**Materials**:- Acelofenec(150gm), Sodium Benzoate(18%), Sodium Citrate(12%), Sodium Salicylate(6%), Phenopthelin indicator(2-3 drops),Burette, Pipette, Conical flask, Electronic balance.

### Method

### Analysis of aceclofenac bulk drug sample by the proposed analytical

Method: -Accurately weighed [0.3 g] aceclofenac bulk drug sample was solubilized in 40 ml of 2.5 M sodium salicylate solution in a conical flask by shaking for about 5 minutes and titrated with 0.1 M sodium hydroxide solution using phenolphthalein solution as indicator. Blank determination was conducted to make the required corrections and the amount of aceclofenac was computed.

### Analysis of aceclofenac tablets by the analytical

**Method:-** Twenty tablets of aceclofenac were weighed and powdered finely. The powder, equivalent to 300 mg aceclofenac was accurately weighed and transferred to a conical flask. After adding, 40 ml of 2.5 M sodium salicylate solution, the flask was shaken for 10 minutes for solubilization of drug from the fine powder of tablets. The drug was titrated with 0.1 M sodium hydroxide solution using phenolphthalein solution as indicator. Blank determination was conducted to make the required corrections and the amount of aceclofenac was computed.

 

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## Results and Discussion

### 1. Titration of 0.1N NaOH with Aceclofenac Sodium

| S. No | Reading | | Average |
|---|---|---|---|
| | Initial | Final | |
| 1 | 1 | 5 | 10.02 |
| 2 | 6 | 10 | |
| 3 | 10 | 14 | |

### 2. Titration of 0.1 N NaOH with Oxalic acid

| S. No | Reading | | Average |
|---|---|---|---|
| | Initial | Final | |
| 1 | 1 | 5 | 6.01 |
| 2 | 6 | 9.5 | |
| 3 | 9.5 | 13 | |

Molecular weight of NaOH is 40gm

Molecular weight of Aceclofenac sodium is 353.0gm

Molecular weight of Aceclofenac sodium for 1 gm is 35.3gm

Molecular weight of Oxalic acid is 630gm

Molecular weight of Oxalic acid for 1gm is 63gm

**Calculation: -**Find out the normality: N1V1=N2V2……. (1)

N1=Normality of Standard NaOH

V1=Average of Aceclofenac & NaOH titration—Average of NaOH& Oxalic acid titration

10.02-6.01=4.01

N2=Normality of Aceclofenac So that put the value in equation (1)

$$0.0198\times 4.01=0.1\times V2$$

 

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$$V2=0.0198\times4.01\div0.1$$

$$V2=5.599$$

We know that 1ml of NaOH contain 35.3mg of Aceclofenac

So $5.59\times35.5=197.32$mg

It means total contain of drug 197.32mg

**Conclusion:-** Titrimetric analysis by using mixed solvency compared very well with the results of Pharmacopeia method. The Proposed method of analysis is new, simple, accurate, environmentally friendly and reproducible. In this concluded that the proposed method is simple, cost-effective, accurate, safe, precise, and can be successfully employed in routine analysis of aceclofenac bulk drug as well as aceclofenac tablets. There is good scope for other poorly water-soluble drugs which may be solubilized by hydrotropic agents to carry out titrimetric analysis, precluding the use of costlier and unsafe organic solvents.

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