

Separation, Analysis, And Conductivity Measurements Of Active Pharmaceutical Ingredient (API) Of Ibuprofen

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Abstract:

This study was conducted to achieve the following objectives: Determination of an appropriate separation method for the active pharmaceutical universe from tablets of ibuprofen, Preserving the environment by separating the active substance from the expired drug and using it for other purposes. Discover the effect of sunlight on the active substance by exposing it to ultraviolet rays. Determine the pH of the active ingredient, draw the curve, measure the conductivity and the percentage of salts

The drug used to conduct this study was Ibuprofen is derived from propionic acid and is a non-steroidal anti-inflammatory drug used to treat pain, fever, and inflammation. This includes menstrual pain, migraines, and rheumatoid arthritis. It can be used to block an open ductus arteriosus in premature babies. It is taken orally or intravenously, and it will take effect within an hour. A mortar and pestle was used to crush (10) tablet of ibuprofen then used 50ml of ether and 50ml of distilled water (1:1) as solvent, stirrer to enhance solubility and separatory funnel for extraction process then dried at room temperature 25°C for five couple of days. melting point apparatus used to confirm identification of the pure sample of ibuprofen and acid base titration to determine the acidity concentration of it .The EC,PPM and pH measured by(Adwa PH meter , AD31 Waterproof Conductivity-TDS-TEMP Pocket Testers) measurement started after taken 100mg of ibuprofen powder crystal dissolved in 50ml ethanol and 50ml of distilled water followed by addition of known volume of NaOH 4.8ml (to know the exact volume needed see page no.) repeated eight times with addition of 4.8ml of NaOH and 100mg of ibuprofen powder each time of measurement, the next measurement done after exposure under UV lamp by using 100mg of ibuprofen powder dissolved in 50ml ethanol and 50ml of distilled water and addition of 4ml of NaOH .The results presented showed a formed crystal of pure ibuprofen after five days , for purity identification melting point apparatus was used , sample start to melt at 77°C as listed, noticeable increase in EC,PPM and pH values ,proportionally related with the weight because of interaction between acidic group in ibuprofen (COOH) with NaOH, law and curve was

used to determine the relationship between weight and Concentration ,pH was marked and curve plotted through acid base titration. Chang in drug Solution values EC, PPM and pH after UV exposure for six hours due breaking of drug salt particles. This method proposed here was simple, cheap and acceptable which fulfil the aims needed.

Keywords: Ibuprofen , Active Pharmaceutical Ingredient, Conductivity measurements, Separation, Analysis.

I. INTRODUCTION

1.1 Ibuprofen Definition and history:

Ibuprofen is (2RS)-1[4-(2-methyl propyl) phenyl] propionic acid (BP. 2004). Ibuprofen was the first member of propionic acid derivatives to be introduced in 1969 as a better alternative to Aspirin. Gastric discomfort, nausea and vomiting, though less than aspirin or indomethacin, are still the most common side effects.¹Ibuprofen is the most commonly used and most frequently prescribed NSAID.^{2,3} It is a nonselective inhibitor of cyclo-oxygenase-1 (COX-1) and Cyclooxygenase-2 (COX-2).⁴ Although its anti-inflammatory properties may be weaker than those of some other NSAIDs, it has a prominent analgesic and antipyretic role. Its effects are due to the inhibitory actions on cyclo-oxygenase, which are involved in the synthesis of prostaglandins. Prostaglandins have an important role in the production of pain, inflammation and fever.⁵

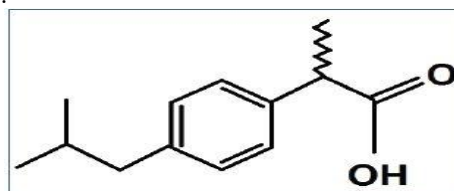


Figure (1): Structural formula of ibuprofen.

1.2. Properties:

Table (1): Physical properties of ibuprofen.

S.N	Property title	Value
1	Melting point	77-78 °C
2	Boiling point	157 °C
3	Density	1.0364 (rough estimate)
4	Flash point	9°C
5	Solubility	Practically insoluble in water, freely soluble in acetone, in methanol and in methylene chloride. It dissolves in dilute solutions of alkali hydroxides and carbonates.
6	Color	white to off-white
7	Water Solubility	Insoluble
8	Stability	Stable. Combustible. Incompatible with strong oxidizing agents.
9	Structure Activity Relationship	<ul style="list-style-type: none"> • Anti-inflammatory activity of the drug can be increased and related side effects can be reduced by substitution of n α-methyl group on the alkanolic acid portion of acetic acid derivatives. • Ibuprofen is less hepatotoxicant more potent than ibufenac. • (+)-enantiomer possess greater activity than (-)-enantiomer. • Endemic (S/R) ration for the inhibition of bovine prostaglandin synthesis is 160.
10	Molecular weight	206.28 g/mol.
11	Form	Crystalline Powder.

1.3. Physical and Chemical Proprieties of Ibuprofen:

Ibuprofen, 2-(4-isobutylphenyl) _ propionic acid, is a non-steroidal drug that is widely used as an anti-inflammatory analgesic and has been a nonprescription drug since 1984. It is slightly soluble in water and has poor flow and compaction

characteristics owing to its needle –like (acicular) crystalline structure and viscoelastic properties respectively ¹.

Ibuprofen is prescribed in high doses (200-600 mg), which precludes its direct-compression manufacture into suitable – sized tables. A crystal change of ibuprofen's fine cohesive crystals into more spherical particles that possess better compressibility general improves its processing into tablet and capsule forms. Drug particles with optimized properties suitable for processing in solid dosage forms are generally prepared by developing suitable individual crystals or by spherical crystal agglomeration.

1.4. Pharmacology of Ibuprofen:

1.4.1. Mechanism of action:

Non-steroidal anti-inflammatory drugs such as ibuprofen work by inhibiting the cyclooxygenase (COX), which converts arachidonic Acid to prostaglandin (PGH₂). PGH₂ in turn, is converted by other enzymes to several other. Prostaglandins (which are mediators of pain, inflammation, and fever) and to thromboxane A₂ (Which stimulates platelet aggregation, leading to the formation of blood clots).

1.4.2. Pharmacokinetics:

After oral administration, peak serum concentration is reached after 1–2 hours and up to 99% of the drug is bound to plasma proteins. The majority of ibuprofen is metabolized and eliminated within 24 hours in the urine; however, 1% of the unchanged drug is removed through biliary excretion.

1.4.3. Pharmacodynamics:

Ibuprofen exerts its anti-inflammatory and analgesic effects through inhibition of both COX isoforms. In addition, ibuprofen scavenges HO. radical, NO and ONOO and can potentiate or inhibit nitric oxide formation through its effects on nitric oxide synthase (NOS) isoforms.

1.4.4. Contraindication:

- Ibuprofen tablets are contraindicated in patients with known hypersensitivity to Ibuprofen.
- Asthma.
- Hypertensive patients.
- Heart Attack.
- Stomach or Intestinal Ulcer.
- Liver problems and blood clotting disorder.
- Bleeding of the stomach or intestines.
- Kidney disease.
- Pregnant in 3rd trimester.

1.4.5. Drug Interaction:

- **ACE-inhibitors:** NSAIDs may diminish the antihypertensive effect of ACE inhibitors.

- **Aspirin:** Administration of ibuprofen and aspirin is not generally recommended because of the potential for increased adverse effects.
- **Diuretics:** Ibuprofen can reduce the natriuretic effect of furosemide and thiazides in patients. The patient should be observed closely for signs of renal failure as well as to assure diuretic efficacy.
- **Warfarin-type anticoagulants:** Users of both drugs together have a risk of serious bleeding higher than users of either drug alone.

1.4.6. Side Effects:

Ibuprofen appears to have the lowest incidence of digestive adverse effect reaction of all the nonselective NSAIDs, Nausea, Dyspepsia gastrointestinal ulceration, bleeding, Diarrhea, constipation and Hypertension.

1.5. Methods for separating materials:

- **Hand Sorting:** In separating some types of mixtures by hand, such as separating beads, separating kernels and parts from each other, separating pieces from various varieties of fruit, separating pieces from various types of fruit, by hand, by hand, as appropriate.
- **Sieving:** When the amount of mixture is large, it can be separated using a sieve; So that the small-sized particles fall through the holes in the sieve and the large particles remain inside the sieve. An example of the screening separation process is the separation of stones or gravel from the sand; The sand particles fall off the sieve, and the large grains like stones and pebbles remain inside the sieve. ¹
- **Centrifuge:** It is difficult to separate small solid pellets from solution at times; Therefore, a centrifuge is used, which is a mechanical device that rotates at a very high speed that helps to separate solid particles from the solution, as large solution particles are directed outwards away from the axis of rotation, while small solid particles settle at the bottom, an example is the sand separation process From water, where it takes a lot of time to separate them by regular methods, while using a centrifuge the separation process takes place within seconds, and centrifugation is used to separate blood samples into plasma and red blood cells, separate milk pellets from water, and separate uranium isotopes in nuclear power plants, and from It is worth noting that sometimes the centrifuge speed may reach 30,000 times per minute, depending on the nature of the materials to be separated.²
- **Filtration:** The mixtures are separated through filtration if the size of the particles to be separated is small, or the particles differ in them sizes, or if the two materials to be separated from each other are different in the physical state, by using a filter or a filter paper paper), ¹⁻³ and

there are many examples of the filtration process in daily life. The coffee maker contains a filter paper through which the coffee powder passes and the larger coffee beans remain stuck at the top, ⁴ and tea leaves can also be separated in a solution. Tea and water are also filtered. ⁵

- **Distillation:** Is known as an effective way to separate a mixture consisting of two or more liquid substances, by evaporating the liquid and then re-condensing it based on the difference in the vapor pressure of the materials. Less, then the vapor travels through the condenser, which is cold, condenses on it and returns to the liquid state, and the resulting liquid in this case is called the distillate liquid. ⁶The distillation method can be used to separate a solution of liquid alcohol and water or a solution of vinegar and water, ⁵ and a mixture of water, ink, and vinegar can also be separated by means of distillation. This is due to the difference in boiling points of the three materials. ⁷
- **Magnetic separation:** The magnetic separation is used to separate a metallic ore consisting of two materials, one magnetic and the other non-magnetic, so that the two materials pass over a rotating belt at the end of which there is a magnetic wheel, so the magnetic particles stick to the belt and the other pellets fall, and when the belt begins to move away from the magnetic wheel, the magnetic beads fall into a container Another. ¹
- **Evaporation:** Evaporation is defined as a method of separating homogeneous mixtures containing a soluble solid. Where the liquid substance is separated from the solid by evaporating the liquid substance completely until the solid substance remains only, and this method is only valid if there is one type of liquid material or if it is not important to separate the liquid materials from each other, and in many countries of the world Table salt is obtained through the process of evaporating sea water using the heat energy of the sun. ⁶
- **Chromatography:** Can be defined as a method for separating chemicals according to their ability to adhere to a solid rod, ⁸ and it is one of the most important methods of separation. Because it is used to separate a mixture of solids and liquid, or a mixture of solids, or a mixture of liquid substances, or a mixture of gaseous substances, and the chromatography process takes place in two phases; The stationary phase in which silica, aluminum oxide, or a sheet of cellulose is used, and the mobile phase whose components differ according to the materials to be separated, where the mixture to be separated passes through the materials of the stationary phase. The materials to be separated with the components of this phase will move a shorter distance, but if they are more attractive to the materials of the mobile phase, they move a longer distance to be attracted to them. ⁹ There are three types of chromatography: Column chromatography and gas chromatography and thin layer

chromatography. In the solubility between the two phases, as for gaseous chromatography, the liquid to be separated is evaporated into a gas that travels through a tube consisting of a solid absorbent material representing the static phase, and using a laxative gas with the carrier gas, which represents the mobile phase, it helps to transport the mixture to be separated through the tube, so the materials are separated based on the difference in attraction between the static and the mobile phase.¹⁰

- **Extraction:** It is considered one of the important practical methods used in separating and purifying organic compounds a wide range of organic compounds found in plant leaves and seeds are extracted living bodies.
- **Extraction:** can be defined as the process of separating a compound from a mixture with a suitable solvent. **Extraction:** is used to separate an organic compound from an aqueous solution, or to separate a suspended substance in a liquid in practice some solution. Extraction, for example, is done by shaking the aqueous solution with an organic solvent that does not mix with it. Water and then allow the two liquid layers to separate from each other.
- During this process the dissolved substance (to be extracted) is distributed between the aqueous and organic layers with a degree of concentration.
- Depending on the degree of substitution capacity of two solvents (water and organic solvent) called the organic solvent. Generally speaking, the solvent is extracted and its choice depends on two main factors:

The first: its good ability to dissolve the material to be extracted.

The second: Ease of separation from solute. It is the method that was used in this study and the substance used was ether.

1.6. An acid base titration:

- **Titration:** is a laboratory process in analytical chemistry for quantitative analysis in which the concentration of an unknown acidic solution is known by adding a base solution of known concentration, or vice versa.
- **Titration method:** We place a precisely measured amount of the solution to be titrated into a vial and a few drops of chromatography reagent. Place the vial under the burette containing the titrant. And we start by adding small amounts of burette to the vial until the color of the reagent changes, indicating the completion of the titration and reaching the equivalence point.
- **Equivalence point:** It is the point at which the number of moles of an acid is equal to the moles of a base, and the equivalence point is the equivalence point in the reactions of strong acids with strong bases only when a strong acid such as hydrochloric acid is titrated with a strong base

such as sodium hydroxide. The ions in the salt solution do not hydrate

- **Color reagent:** In the titration process, the chemist needs a color reagent to indicate the end of the reaction, provided that he does not enter the reaction. Often a visual indicator is used that changes color when the reaction is complete. Among the reagents used in simple titrations is phenolphthalein, which has the chemical formula $C_{20}H_{14}O_4$, which turns from colorless to pink when a certain pH "value" (about 8.3) is reached or exceeded.
- **Titration curve:** In the graph of the titration curve, the horizontal axis represents the volume of titrant that has been added from the burette to the vial solution since the titration process began. The vertical axis represents the concentration of the solution whose concentration is to be known by tracing the change in the pH value in the vial solution. In the case of acid-alkali titration, the titration curve shows the strength of the acid and alkali. For a strong acid and a strong alkali, the curve runs quietly until the point of neutralization, at which it changes rapidly. In view of this, we find that a small change of the solution added at the neutralization point causes a significant change in the pH, and a chromatic reagent such as phenolphthalein, litmus or bromothymol blue may be used. In the case of titration of a weak acid with a strong alkali or a strong acid with a weak alkali, we find that the titration curve is irregular and at the neutralization point there is no significant change in pH when adding a little burette solution. For example, the curve in the figure gives the titration curve of oxalic acid (a weak acid) with sodium hydroxide (a strong alkali). We find that the neutralization point lies between pH 8-10, which indicates the alkalinity of the solution.

1.7. Introduction to Conductivity:

Solutions electrical conductivity measures the electrical conductivity of solutions over the extent of current flowing Electrophoresis through the solution, where the electrical conductivity expresses the ability of the solutions to conduct electricity, depending on the presence of ions in the solution; Where the ions are derived from ionic compounds that dissolve in water such as sodium chloride, and the electrical conductivity of solutions depends on the concentration of the solution, so the more concentrated the solution, the higher the conductivity, which in most cases is a proportional relationship, so the higher the concentration of ions, the greater the conductivity, but there are some solutions Which is considered an exception to this rule, as it has a limit to the extent of electrical conductivity. Once this limit is reached, increasing the concentration of the solution will actually reduce the conductivity, and this was

observed in sulfuric acid solutions², and good conductors allow easy and continuous flow of electric current, as Ions carry a negative or positive electrical charge, and a good conductor possesses charged and free-moving particles, and in the case of dissolved salts in water ions represent charged particles with relatively high mobility, and in natural water bodies produce ions that contribute to the high conductivity of dissolved salts and minerals, and the type of ions Effect on the conduction of the solution, as the highly dissolved electrolyte materials are the best conductors.

1.8. Acid-Base drugs:

Medicines of an acidic nature: preferably given with food or immediately after it, and the explanation for that is the following:

- Medicines of an acidic nature are absorbed optimally in the stomach with an acidic environment because they transform in this medium into a non-ionic form that can be absorbed optimally as we mentioned, and the question remains: What is the role of food in that?
- The food stays in the stomach for about two hours until it is digested in it before moving to the intestine and following the digestion process, and when the drug is taken with food, this makes it remain in the stomach.

With an acidic environment for the same period and thus the drug becomes in its non-ionized form that can be absorbed optimally, so it is preferred Take these medications with or immediately after food. Among these acidic drugs are the following:

- 1- Clavulanic acid.
- 2- Ibuprofen, diclofenac, and all NSAIDs.
- 3- Some antihypertensive drugs such as captopril.
- 4- Lots of penicillin and cephalosporin, such as amoxicillin and cefadroxil.

Medicines of alkaline nature (alkaline): It is preferable to give them on an empty stomach half an hour before food or two hours after food.

These drugs are optimally absorbed in the intestine with an alkaline medium because they are transformed in the alkaline medium into a more absorbable non-ionized form, and since the food remains in the stomach for about two hours the presence of the drug with food will delay its arrival To the intestine with an alkaline medium and converting it to the non-ionized form that is optimally absorbable, and therefore it is preferable to take these drugs on an empty stomach, that is, at least half an hour before food or at least two hours after it, in order to reach the intestine more quickly

Examples of these drugs are alkaline in nature:

- 1- Many groups of antibiotics, such as fluoroquinolones, macrolides, and tetracycline.
- 2- Antispasmodics: such as Buscopan, Duspatline.

- 3- Muscle relaxants.
- 4- Paracetamol.
- 5- Proton pump inhibitors: such as omeprazole and lansoprazole.
- 6- Antihistamines and decongestants.
- 7- Some antihypertensive drugs: such as propranol and atenolol.

1.9. Aim of the study:

To determine the appropriate separation method for the active ingredient of ibuprofen and preserve the environment by separating the active ingredient from the expired medicine and using it for other purposes that the extent to which the active substance is affected by sunlight when exposed to it and determine of the PH curve of the active substance.

2.2. Methods of measure A.P.I. percent:

- **A qualitative or descriptive analysis:** It is the set of processes in which the composition of materials, compounds, or elements included in the composition of a particular
- substance or a mixture of substances, whether in a solid state or a solution in a specific solvent, is detected, and this analysis is not subject to the quantities of these components at all. He is concerned with the exterior appearance of the compound, such as color, smell and taste.
- **Quantitative analysis:** It examines the estimation of the quantities of the components or elements included in the composition of the chemical compound or mixture, and it becomes clear from this that the qualitative analysis of a substance of unknown composition usually precedes its quantitative analysis. Because it is not permissible to quantify a specific material unless it is confirmed that it is descriptive.
- **Gravimetric analysis:** The quantitative analysis by weight is carried out by precipitating the substance and quantifying it in the form of a single element or a specific derivative of known composition, separated from the solution by sedimentation or centrifugation, and then washing, drying and weighing it, so the weight of the material to be estimated is calculated from our knowledge of the weight and composition of the precipitate accurately. For example, the percentage of chlorine in table salt can be determined, for example, by dissolving a certain weight of salt in water, then adding a solution of silver nitrate to it, and it precipitates in the form of silver chloride, then the sediment is filtered, washed and dried, and then weighed to find out the amount and percentage of chlorine in the salt, and the gravimetric analysis includes the methods in which the estimation is made. Weights of materials or some of their components in two ways:

- **Direct method:** In it, the weight measurements of the products of the analytical process of known composition is determined.
- **Indirect method:** As it determines the measurements of lost or underweight weights as a result of the volatility property of the sample.
- **Volumetric analysis methods:** In this case, direct and indirect methods are used to determine the weights of materials or some of their components. These methods include the following:
- **Volumetric titration method:** It includes the use of solutions of known concentrations and the measurement of the volumes of such solutions that react quantitatively with the solution of the substance to be assessed up to a specific point called the equivalence point or the end point of the reaction that can be detected by evidence that includes a sharp change in the properties of the solution such as color or turbidity that you notice with the naked eye or It is measured by chemical-physical methods, such as potential difference or electrical conductivity. The solution with a known concentration is called a standard solution, and it is a solution that contains a certain volume of it containing a known weight of the solute. The process of adding the standard solution from a burette to a specific volume of the solution of the unknown substance in the conical flask or vice versa until the reaction takes place is called the titration process. From the laws of chemical equivalence and determining the volume of the standard solution used in titration, we can determine the weight of the unknown substance or the weight ratios for its components, whether directly or indirectly.
- **Automated analysis methods:** A material is estimated by measuring some of its physical or chemical properties such as density, color, refractive index, electrical conductivity, thermal and electrical changes...etc. These methods depend mainly on the following measurements:
- **Light energy emission:** This measurement includes excitation of the material to high levels of energy by light or electric energy, and then returning it to a low energy level, which emits it from the absorbed energy and is a measure of the amount of the substance by the following methods:
- **Emission spectrograph recording methods:** in which a material is excited using an electric arc.
- **Flame photometry:** in which a material is excited using different types of flame, and after the material is returned to a lower energy edge, the amount of light emitted is measured.
- **X-ray fluorescence (x-ray fluorescence):** where the material is excited by x-rays of a certain wavelength, and after returning to a low-energy state, the emitted rays are measured that distinguish the element.
- **Absorption of light energy:** It includes measuring the amount of light energy at a certain wavelength that is absorbed by the material to be analyzed. For this reason, the following can be used:
 - ✓ color spectral methods.
 - ✓ Spectral methods in the ultraviolet region.
 - ✓ Spectral roads in the infrared region.
 - ✓ X-ray method.
- **Nuclear Magnetic Resonance:** This method includes the interaction between radio waves and the nuclei of atoms that are in a magnetic field.
- **Electric methods:**
 - ✓ Analysis by the method of electrical conduction, where the change in the electrical conductivity coefficient of the model solution is measured.
 - ✓ Analysis by measuring the potential difference, where the electrical potential is measured during the reaction when the electrode is placed in the solution.
 - ✓ Analysis by measuring the electrical quantity, where the electrical quantity in coulombs necessary to complete the electrochemical reaction is measured.
 - ✓ Paleography, where the value of the electric current is measured in proportion to the concentration of the substance that is reduced or oxidized in an electrochemical reaction.

II. MATERIALS AND METHODS

2.1 Material and equipment.

- **Equipment: -**
 - ✓ Mortar and pestle.
 - ✓ beaker 250ml.
 - ✓ Graduated cylinder 10ml.
 - ✓ Erlenmeyer flask 250ml.
 - ✓ automatic Burette.
 - ✓ Separatory funnel 125ml with stand.
 - ✓ capillary melting point tubes.
 - ✓ Spatula.
 - ✓ Stand.



Fig (2): Mortar and pestle.

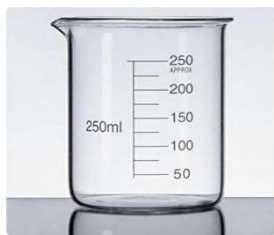


Fig (3): beaker 250ml.



Fig (7): Separatory funnel 125ml with stand.



Fig (4): Graduated cylinder 10ML.



Fig (5): Erlenmeyer flask 250ml.



Fig (6): automatic Burette.

• Devices.

- ✓ Electronic scale (Henan Lanphan Industry china).



Figure (8): Electrical balance.

- ✓ Stuart Bibby Hotplate Stirrer CB162 UK.



Figure (9): Stuart Bibby Hotplate Stirrer.

Adwa PH meter & Temperature gauge AD-11 (waterproof) Romania.



Figure (10): pH meter.

- ✓ AD31 Waterproof Conductivity-TDS-TEMP Pocket Testers with replaceable electrode Romania.



Figure (11):EC and TDS meter.

Ultraviolet lamp mode UVGL -58 /wave length for short wave 254nm, longwave 365nm USA.



Figure (12): Ultraviolet lamp mode UVGL -58.

Melting Point Apparatus, Stuart Scientific, Model SMP3, 240v Uk.



Figure (13): Melting Point Apparatus.

2.2. Chemicals:

1. Ibuprofen drug.



Figure (14): Ibuprofen drug.

2. NaOH solution 0.1M.



Figure (15): NaOH.

3. Ethanol conc. 96%.



Figure (16): Ethanol.

4. Di ethyl ether.

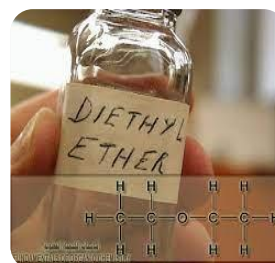


Figure (17): Ether.

5. Distilled water.

2.3. Methods:

✓ Purification (separation of active ingredient of ibuprofen by ether):

- The 10 tablets of ibuprofen drug was taken, then weighted to determine an average tablet weight (7g).
- A mortar and pestle were used to crush the tablets of ibuprofen and produced approximately 2g of tablet powder (was grinded precisely).



Fig (18): Crush the tablets of ibuprofen.

- The tablet powder was transformed into labeled 250 ml Erlenmeyer flask, followed by adding 50 ml of distilled water and 30 ml ether after that was putted on the stirrer for couple of minutes until the tablet powder was dissolved.



Fig (19): Ibuprofen dissolved by ether.

- The separator funnel was placed in the stand, then the mixture of drug to be extracted was added into it (make sure the stopcock closed).
- The separator funnel was taken out of the stand landholder tightly at the stopper and the stopcock then inverted slowly and vent (open the stopcock) towards the back of the hood. A sound of whistle was heard when the pressure is released.

- The separatory funnel was placed back in the stand, waited a couple of minutes which allow the layers to separate, (the mixture was separated into 3 layers).



Figure (20): The mixture of solution separates into 3 layers.

- The stopcock was opened and drained the middle and the bottom layer into a clean beaker (excipient and water), then separated the desired upper layer alone in clean beaker (ether and active ingredient) looked like clear liquid.
- The procedure was repeated by add the excipient and water mixture and add 10 ml of ether into Erlenmeyer flask then putted into the stirrer to dissolve, the mixture was transformed again into the separator funnel and repeated again the separation process.
- Previous step was repeated again.
- The mixture of active ingredient and ether was putted to dry for 5 days at room temperature.
- Melting point apparatus was used to confirm the identification of a sample of ibuprofen or to establish it is purity.
- First capillary tube was taken and sealed at one end by inserting the tip into a flame near the base of the flame and turning the tube around the fingers.
- The tube was packed by pressing the open end into a small amount of the sample of the crystalline powder of ibuprofen on filter paper.
- The crystals were transformed from the open end to the bottom of the tube by tapped the bottom gently on the bench top.
- A densely packed column of crystals about 3 mm high in the tube is all that is required.
- The packed capillary tube was inserted into melting point apparatus then started (the device is cooled before use).
- The sample was observed through the lens on the front of the apparatus, started to melt at 77 °C (melting point of ibuprofen 77-78°C).

- 2nd acid base titration (to determine the acidity concentration of pure ibuprofen).



Fig (21): Determine the melting point.

- A 300mg of pure ibuprofen crystal was weighted, then added 50ml water and 50ml of ethanol into labeled 250 ml beaker and putted the beaker on stirrer for 45 min until pure ibuprofen drug was dissolved.
- The pH meter was standardized with bottled water (Known pH).
- The pH of mixture was measured by Immerse the electrode in it without adding 0.1M NaOH (pH 5).
- M of NaOH was prepared by taken 500ml of distilled water into a cleaned and dried 1000 ml volumetric flask.
- gm of Sodium hydroxide was added to the volumetric flask of distilled water with continues stirring and allowed to cool to room temperature.
- The electrode was cleaned thoroughly with distilled water.
- Then the titration process was started: The pH was recorded each time 1mL of 0.1M NaOH was added.
- Started to notice for the region where the pH begins to change rapidly with each time 1ml of 0.1M NaOH added.
- After passed the equivalence point by several mL of 0.1M NaOH added the titration process was stopped.
- The values were recorded and the curve drew.
- 3rd measuring EC, ppm and PH of ibuprofen solution after adding NaOH:
- 50ml of water and 50ml of ethanol was added into labeled 250 ml beaker.
- The pH, EC and ppm of mixture was measure by Immerse the electrode in it without adding pure ibuprofen crystal and 0.1M NaOH.
- 100mg of pure ibuprofen powder was weighted and added to the previous mixture then putted the on stirrer for 15 min until pure ibuprofen drug was dissolved.
- The followed equation was used to know the amount need it from 0.1M from NaOH:

$$V \times M = Wt. / M.W.$$

$$V \times 0.1 \text{ mol/L} = 0.1 \text{ g} / 206.28 \text{ g/mol.}$$

$$V \times 0.1 \text{ mol/L} = 0.000484 \text{ mol.}$$

$$V = 4.8 \text{ ml.}$$

- The beaker was removed from the stirrer after 15min and added the known volume needed of 0.1M NaOH (4.8ml).
- The pH, EC and ppm of mixture was measured by Immerse the electrode in it and recorded.
- ml of 0.1M NaOH and 100mg of ibuprofen crystal was added to the mixture then putted on the stirrer for 15 minutes to dissolve, after that the pH, EC and ppm of mixture was measured.
- The previous step was repeated until reach eight times.
- The values were recorded each time in measurement and putted in curve.
- 4th Measuring PH, EC and ppm of after exposure it under the UV Lamp.
- 100mg of pure ibuprofen powder was weighted, 50ml water and 50ml of ethanol all was added into labeled 250 ml beaker then putted on stirrer for 45 min until pure naproxen crystal dissolve.
- The PH, EC and ppm of mixture was measured before exposure it under the UV Lamp.
- Make sure to not expose eye and skin to shortwave ultraviolet light as rays may be harmful to unprotected eyes and skin.
- ibuprofen solution was exposed to ultraviolet lamp for one hour and the PH, EC and PPM was measured.
- The previous step was repeated every hour until reach six hours, which was done quickly and precisely each time when measure PH, EC and PPM.

III. RESULTS AND DISCUSSIONS

After the separation process with ether, which was the best solvent in the separation process because of its ability to dissolve the API and not mix with water, therefore it was the upper layer with the active substance and we obtained a pure sample of ibuprofen, and the melting point of ibuprofen was set and it was at 77 °C and this indicates the purity of the sample and the success of the separation process.

When adding a solution of sodium hydroxide (a strong base) to the solution of ibuprofen (a weak acid), we observed a gradual increase in the pH with each addition of sodium hydroxide as shown in the titration curve and the equivalence point was at (8.8.) and then we noticed a sudden increase in the pH value (10.5) at 18 ml of NaOH which is The end point of the titration and the resulting salt is composed of a strong alkaline cleft and a weak acid cleft. Therefore, it is hydrated and its solution is alkaline and has a pH greater than 7, we showed that in figure (22) & table (2).

Table (2): Acid base titration values of ibuprofen solution measuring pH, EC and ppm after adding NaOH.

NaOH (ml)	pH	EC ($\mu\text{S/cm}$)	PPM
0	5	19	9
1	5.1	31	15
2	5.2	49	25
3	5.3	68	34
4	5.4	86	43
5	5.5	106	53
6	5.6	122	61
7	5.7	139	70
8	5.8	155	77
9	5.9	170	85
10	6.0	186	93
11	6.1	200	100
12	6.2	217	108
13	6.3	234	117
14	6.4	252	126
15	6.5	269	134
16	6.7	287	143
17	7.0	306	153
18	7.4	320	160
19	10.5	349	175
20	11.7	401	201
21	12.1	462	231
22	12.2	513	257
23	12.3	567	284
24	12.4	622	311
25	12.5	669	334
26	12.6	722	361

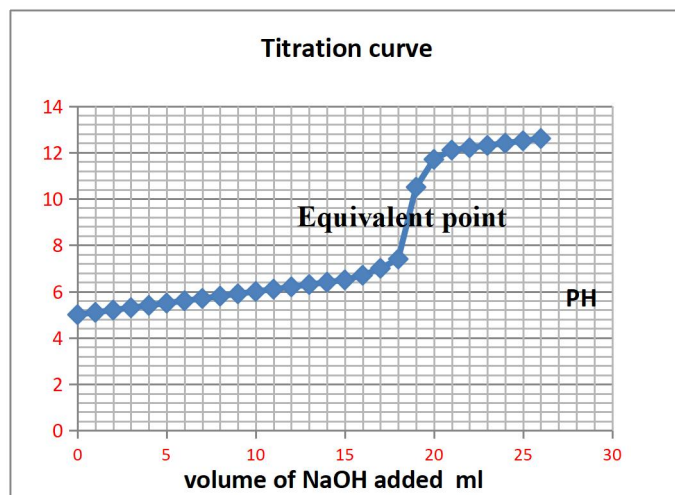


Figure (22): Titration curve of ibuprofen with NaOH.

In Table No. (3), we note that every time 100 mg of ibuprofen and 8.4 ml of sodium hydroxide are added, the EC and PPM increases, and this indicates that the relationship between weight, EC, PPM has a direct relationship resulting from the reaction that it occurs between the carboxyl group of ibuprofen and sodium hydroxide, which lead to the formation of salt ions, and the more of these ions, the higher the EC and PPM. This can be clearly seen on the curve graph 3,4. We note that the PH value does not change because the increase was from the same substance, and we notice this clearly through the graph of figure (23)

Table (3): Values of measuring EC, ppm and PH of ibuprofen solution.

n	pH	EC ($\mu\text{S/cm}$)	PPM	Wt.(mg)
1	6.5	2	1	0
2	6.5	116	58	100
3	6.6	199	99	200
4	6.6	276	138	300
5	6.6	352	176	400
6	6.6	430	215	500
7	6.6	500	250	600
8	6.6	572	286	700
9	6.6	640	320	800

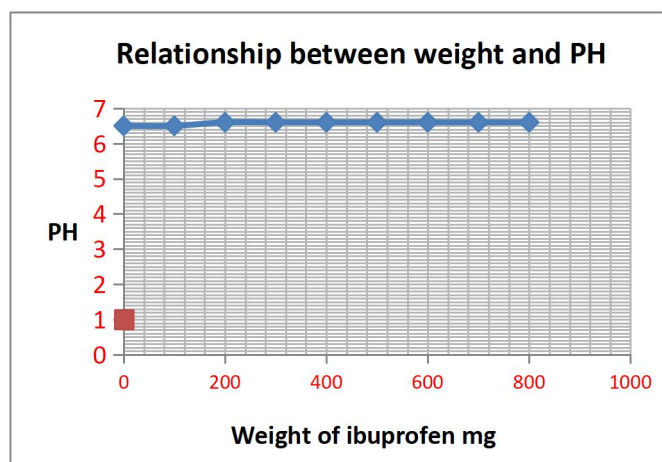


Figure (23): The relationship between weight and pH after adding NaOH

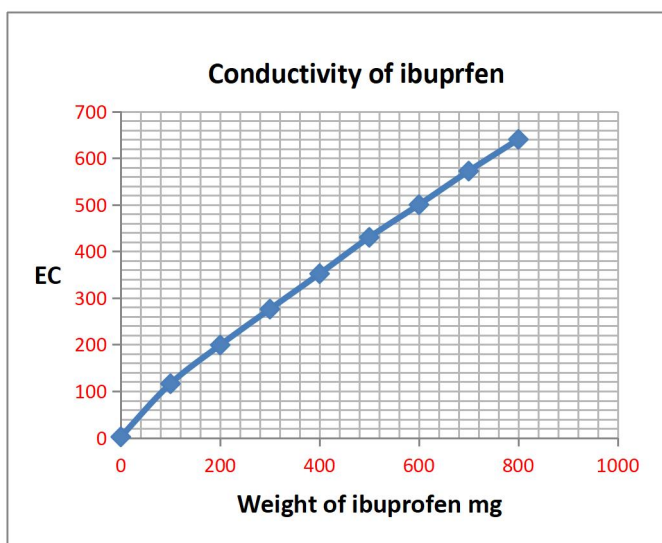


Figure (24): Electrical conductivity of ibuprofen

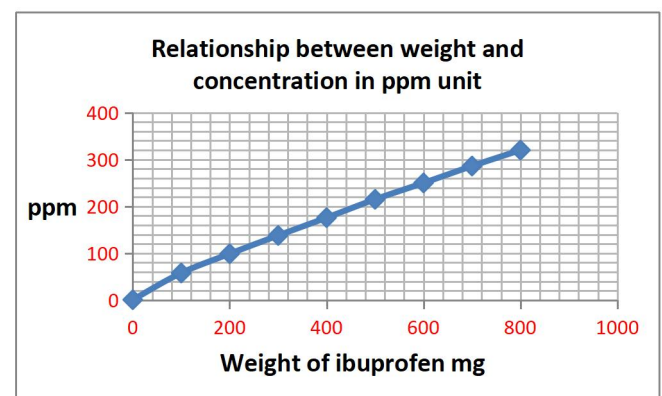


Figure (25): The relationship between weight and conc in ppm unit

The following law determine the relationship between weight and Concentration:

$$M = \frac{n}{V(L)}, n = \frac{Wt}{M.W} = M = \frac{Wt(g)}{M.W \times V(L)}$$

In the following table through the graph, we notice that the greater the concentration of ions, the higher the conductivity.

Table (4): Relationship between EC and concentration of dissolved salt at variant weight of ibuprofen.

n	pH	EC (μS/cm)	PPM	Wt.(mg)	Concentration
0	6.5	2	1	0	0
1	6.5	116	58	100	4.8×10^{-3}
2	6.6	199	99	200	9.7×10^{-3}
3	6.6	276	138	300	1.5×10^{-2}
4	6.6	352	176	400	1.9×10^{-2}
5	6.6	430	215	500	2.4×10^{-2}
6	6.6	500	250	600	2.9×10^{-2}
7	6.6	572	286	700	3.4×10^{-2}
8	6.6	640	320	800	3.9×10^{-2}

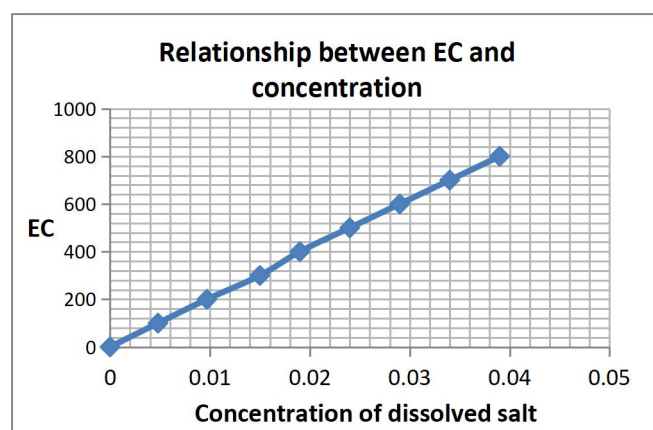


Figure (26): Relationship between EC and concentration.

Table data number (5) were recorded after exposure to ibuprofen solution to UV rays for 6 hours, and the reading was recorded hourly. We observe through the table and graph data of the curves a gradual decrease in pH (inverse relationship) corresponding to an increase in EC and PPM (direct relationship). This marked change in values is due to the breakdown of the ibuprofen particles.

Table (5): Values of PH, EC and ppm of ibuprofen solution after UV exposure.

HOURS	pH	EC ($\mu\text{S}/\text{cm}$)	PPM	Wt.(mg)
0	6.2	107	53	100
1	5.8	108	54	100
2	5.1	110	55	100
3	4.5	112	56	100
4	4.2	115	57	100
5	3.8	116	58	100
6	3	120	60	100

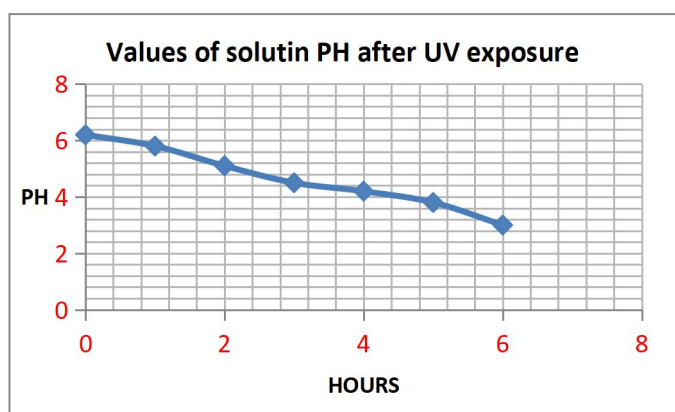


Figure (27): PH of ibuprofen solution after UV exposure.

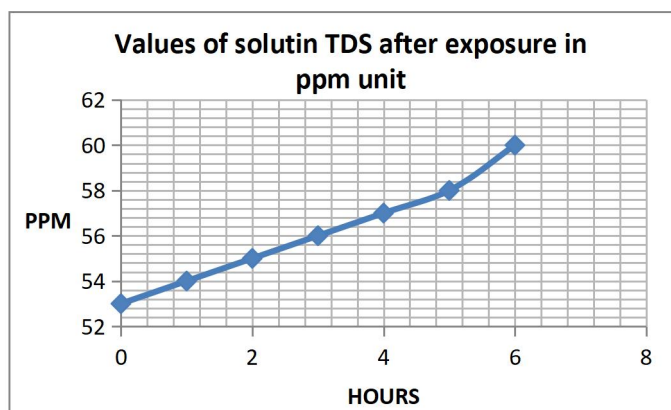


Figure (28): EC Values of ibuprofen solution after UV exposure.

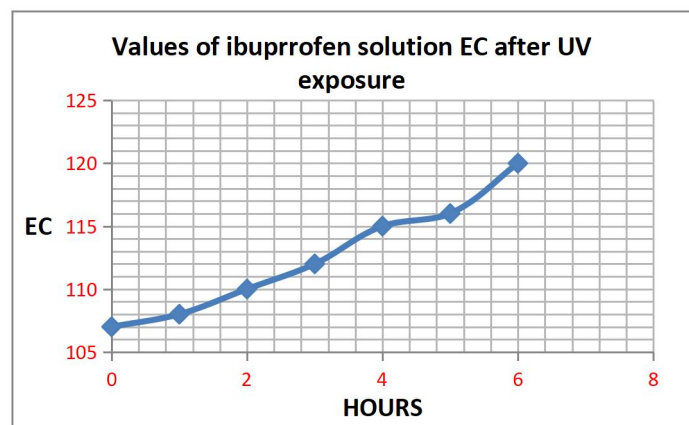


Figure (29): Values of TDS in ppm unit after UV exposure.

CONCLUSION

In this study we conducted the following four experiments:

The first experiment: - In it, the active ingredient (ibuprofen) was separated from the tablets and using a separation funnel and ether, which was the best solvent for ibuprofen.

The second experiment: - in which the EC, the ppm, and the pH of different concentrations of pure ibuprofen were measured in the solution, and we concluded that the pH, conductivity and salts ratio increased with the increase in the ibuprofen concentration.

The third experiment: - in which the acidity and alkalinity were titrated, where a weak acid (ibuprofen solution) was titrated with sodium hydroxide (a strong base) and a titration curve was drawn and the ibuprofen concentration was determined.

The fourth experiment: - In which the ibuprofen solution was exposed to UV and its effect on ibuprofen was studied, and we noticed that the EC values of ppm and the pH change as the drug solution was exposed to UV, and this is due to the breakdown of the ibuprofen salts.

ACKNOWLEDGMENTS

We thank International Qurina University- Benghazi – Libya, where we conducted the experiments of this study inside the laboratories of the Faculty of Pharmacy there.

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