JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

PREFORMULATION STUDIES: RECRYSTALLIZED CHARACTERIZATION OF ASPIRIN UNDER ELECTROMAGNETIC FIELD

[1]Abhishek Kumar Verma, [2]Tushar Verma

[1]Associate Professor, Department of Pharmacy, Pharmaceutics, RITEE College of Pharmacy, Raipur, Mandir Hasaud (C.G.)

[2]Assistant Professor, Department of Pharmacy, Pharmaceutics, RITEE College of Pharmacy, Raipur, Mandir Hasaud (C.G.)

Abstract:

Modification of crystal by recrystallization alters physicochemical properties of the drug development of standard preformulation studies. The present aim of the study was achieved recrystallization of the drug to investigate effect of time and strength of electromagnetic filed on crystallization to improve the preformulation studies of Aspirin drug. The general application of crystallization is purification of drug, ease of handling, better chemical stability, better physical stability and improved bioavailability, better processing characteristics and sustained /controlled release on the bases of performed following parameters of Aspirin: physical appearance, melting point, determination of pH & dissolution. Aspirin used as model drug belonging from salicylic acid analogous which is used as antipyretic, anti-inflammatory and analgesic in verities of conditions ranging from headache, discomfort, and fever associated with the common cold, and muscular pains and aches. The study Report as well experimentation indicate simple crystallization require few hours to start nucleation followed by the crystal growth, while crystallization under electromagnetic field take less time for nucleation and crystal growth start within 2-10 minute, decreasing the time lag. Moreover the amount of nuclei formed is enormously increased in the time system. Increased in time of electromagnetic field exhibited appreciable change not only crystal morphology but also in the thermodynamic and other chemical properties. Hence preparation of crystal under electromagnetic field would offer advantages over simple crystallization and would be able to prepare desired crystal with better therapeutics.

Index terms: Recrystallization, Electromagnetic filed, Lag time, Physical characterization, Therapeutics, Bioavailability.

1. INTRODUCTION:

On the bases of the crystal by recrystallization the fundamental of study is experimentation of determination of recrystallization on Aspirin drug under the electromagnetic field, comparative study on recrystallization of aspirin with-out electromagnetic field and with ethanol & isopropyl alcohol under different electromagnetic field.

The basic configuration of crystallization : Crystallization is the (natural or artificial) process of formation of solid crystals precipitating from a solution, melt or more rarely deposited directly from a gas. Crystallization is also a chemical solid–liquid separation technique, in which mass transfer of a solute from the liquid solution to a pure solid crystalline phase occurs. In chemical engineering crystallization occurs in a crystallizer. Crystallization is therefore an aspect of precipitation, obtained through a variation of the solubility conditions of the solute in the solvent, as compared to precipitation due to chemical reaction.[1-3] The crystallization process consists of two major events, nucleation and crystal growth. *Nucleation* is the step where the solute molecules dispersed in the solvent start to gather into clusters, on the nanometer scale (elevating solute concentration in a small region), that become stable under the current operating conditions. These stable clusters constitute the nuclei. However, when the clusters are not stable, they dissolve. Therefore, the clusters need to reach a critical size in order to become stable nuclei. Such critical size is dictated by the operating conditions (temperature, super saturation, etc.).[4,5] It is at the stage of nucleation that the atoms arrange in a defined and periodic manner that defines the crystal structure note that "crystal structure" is a special term that refers to the relative arrangement of the atoms, not the macroscopic properties of the crystal (size and shape), although those are a result of the internal crystal structure.[6,7] The *crystal growth* is the subsequent growth of the nuclei that succeed in achieving the critical cluster size. Nucleation and growth continue to occur simultaneously while the super saturation exists. Super saturation is the driving force of the crystallization hence the rate of nucleation and growth is driven by the existing super saturation in the solution. Depending upon the conditions, either nucleation or growth may be predominant over the other, and as a result, crystals with different sizes and shapes are obtained (control of crystal size and shape constitutes one of the main challenges in industrial manufacturing, such as for pharmaceuticals). Once the super saturation is exhausted, the solid–liquid system reaches equilibrium and the crystallization is complete, unless the operating conditions are modified from equilibrium so as to supersaturate the solution again.[8-12] Crystallization dynamics: As mentioned above, a crystal is formed following a well-defined pattern, or structure, dictated by forces acting at the molecular level. As a consequence, during its formation process the crystal is in an environment where the solute concentration reaches a certain critical value, before changing status. Solid formation, impossible below the solubility threshold at the given temperature and pressure conditions, may then take place at a concentration higher than the theoretical solubility level. The difference between the actual value of the solute concentration at the crystallization limit and the theoretical (static) solubility threshold is called super saturation and is a fundamental factor in crystallization dynamics. Super saturation is the driving force for both the initial nucleation step and the following crystal growth, both of which could not occur in saturated or under saturated conditions. Nucleation**:** Nucleation is the extremely localized budding of a distinct thermodynamic phase.[13] It is the process in which ions, atoms or molecules arrange themselves in a pattern characteristic of a crystalline solid forming a site where additional particles deposits as the crystal grows. Some examples of phases that may form by way of nucleation in liquids are gaseous bubbles, crystals or glassy regions.

Creation of liquid droplets in saturated vapour is also characterized Nucleation of crystalline, amorphous and even vacancy clusters solid materials is also important, for example to the semiconductor industry. Most nucleation processes are physical, rather than chemical, but a few exceptions do exist (e.g. electrochemical nucleation). Nucleation is the initiation of a phase change in a small region, such as the formation of a solid crystal from a liquid solution. It is a consequence of rapid local fluctuations on a molecular scale in a homogeneous phase that is in a state of metastable equilibrium.[14] Crystal growth: Crystalline solids are typically formed by cooling and solidification from the molten (or liquid) state .classification of first-order phase transitions, there is a discontinuous change in volume (and thus a discontinuity in the slope or first derivative with respect to temperature, dV/dT) at the melting point. Within this context, the crystal and melt are distinct phases with an interfacial discontinuity having a surface of tension with a positive surface energy. Thus, a metastable parent phase is always stable with respect to the nucleation of small embryos or droplets from a daughter phase, provided it has a positive surface of tension. Such first-order transitions must proceed by the advancement of an interfacial region whose structure and properties vary discontinuously from the parent phase. The process of nucleation and growth generally occurs in two different stages. In the first nucleation stage, a small nucleus containing the newly forming crystal is created. Nucleation occurs relatively slowly as the initial crystal components must impinge on each other in the correct orientation and placement for them to adhere and form the crystal. After crystal nucleation, the second stage of growth rapidly ensues. Crystal growth spreads outwards from the nucleating site. In this faster process, the elements which form the motif add to the growing crystal in a prearranged system, the crystal lattice, started in crystal nucleation. As first pointed out by Frank, perfect crystals would only grow exceedingly slowly. Real crystals grow comparatively rapidly because they contain dislocations (and other defects), which provide the necessary growth points, thus providing the necessary catalyst for structural transformation and long-range order formation.[15,16]

2. MATERIAL & METHODS:

2.1 Drug Profile: [17, 18]

Aspirin also known as acetylsalicylic acid is a salicylate drug, it is used as an anti-inflammatory and an analgesic in a variety of condition ranging from headache ,discomfort and fever associated with common cold ,muscular pain and aches. aspirin is regarded as the drug of choice in the reduction of fever because of its high degree of effectiveness and wide range of safty.as aspirin inhibit platelet function .it has been employed prophylactically to minimize the incidence of myocardial infraction and transient ischemic attacks.

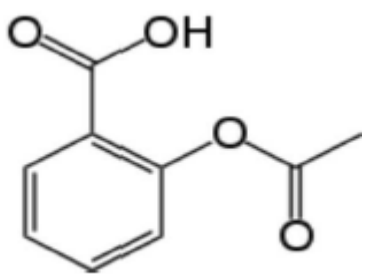


Fig.No.1: Structure of Aspirin

IUPAC Name:- 2 - acetoxybenzoic acid

Formula: $C_9H_80_4$

Mol.mass: 180.157g/mol

Melting point: 136 Ċ

Nature: White crystalline powder

Trade name: Disprin

Bioavailability: Rapidly and complete absorbed

Half –life: 300–650 mg dose: 3.1–3.2 h
1 g dose: 5 h ,2 g dose: 9 h

Metabolism: Hepatic

Excretion: Renal

Routes: Most commonly oral, also rectal, IV, IM

Aspirin (USAN), also known as acetylsalicylic acid (ASA), is a salicylate drug, often used as an analgesic to relieve minor aches and pains, as an antipyretic to reduce fever, and as an anti-inflammatory medication.

Aspirin also has an antiplatelet effect by inhibiting the production of thromboxane, which under normal circumstances binds platelet molecules together to create a patch over damaged walls of blood vessels. Because the platelet patch can become too large and also block blood flow, locally and downstream, aspirin is also used long-term, at low doses, to help prevent heart attacks, strokes, and blood clot formation in people at high risk of developing blood clots. It has also been established that low doses of aspirin may be given immediately after a heart attack to reduce the risk of another heart attack or of the death of cardiac tissue. Aspirin may be effective at preventing certain types of cancer, particularly colorectal cancer.

Aspirin is part of a group of medications called non steroidal anti-inflammatory drugs (NSAIDs), but differs from most other NSAIDs in the mechanism of action. Though it, and others with similar structure called the salicylates, have similar effects (antipyretic, anti-inflammatory, analgesic) to the other NSAIDs and inhibit the same enzyme cyclooxygenase, aspirin (but not the other salicylates) does so in an irreversible manner and, unlike others, affects more the COX-1 variant than the COX-2 variant of the enzyme.

USES:- Pain
Headache
Fever
Heart attacks and strokes
Post-surgery
Cancer prevention

Dosage

Adult aspirin tablets are produced in 300 mg in Britain and 325 mg in the United States. Smaller doses are based on these standards, *e.g.*, 75 mg and 81 mg tablets. The 81 mg tablets are called "babystrength", even though they are not intended to be administered to infants and children.

Contraindications

Aspirin should not be taken by people who are allergic to ibuprofen or naproxen, or who have salicylate intolerance or a more generalized drug intolerance to NSAIDs, and caution should be exercised in those with asthma or NSAID-precipitated bronchospasm. Owing to its effect on the stomach lining, manufacturers recommend people with peptic ulcers, mild diabetes, or gastritis seek medical advice before using aspirin. Even if none of these conditions is present, the risk of stomach bleeding is still increased when aspirin is taken with alcohol or warfarin.Patients with hemophilia or other bleeding tendencies should not take aspirin or other salicylates. Aspirin is known to cause hemolytic anemia in people who have the genetic disease glucose-6-phosphate dehydrogenase deficiency, particularly in large doses and depending on the severity of the disease. Use of aspirin during dengue fever is not recommended owing to increased bleeding tendency. People with kidney disease, hyperuricemia, or gout should not take aspirin because it inhibits the kidneys' ability to excrete uric acid, and thus may exacerbate these conditions. Aspirin should not be given to children or adolescents to control cold or influenza symptoms, as this has been linked with Reye's syndrome.

Gastrointestinal

Aspirin use has been shown to increase the risk of gastrointestinal bleeding. Although some enteric-coated formulations of aspirin are advertised as being "gentle to the stomach", in one study, enteric coating did not seem to reduce this risk. Combining aspirin with other NSAIDs has also been shown to further increase this risk. Using aspirin in combination with clopidogrel or warfarin also increases the risk of upper gastrointestinal bleeding.

Central effect:-

Large doses of salicylate, a metabolite of aspirin, have been proposed to cause tinnitus (ringing in the ears) based on experiments in rats, via the action on arachidonic acid and NMDA receptors cascade.

Aspirin can induce angioedema (swelling of skin tissues) in some people. In one study, angioedema appeared one to six hours after ingesting aspirin in some of the patients. However, when the aspirin was taken alone, it did not cause angioedema in these patients; the aspirin had been taken in combination with another NSAID-induced drug when angioedema appeared. Aspirin causes an increased risk of cerebral micro bleeds having the appearance on MRI scans of 5 to 10 mm or smaller, (dark holes) patches.[Such cerebral micro bleeds are important, since they often occur prior to ischemic stroke or intracerebral hemorrhage, Binswanger disease and Alzheimer's disease.

Aspirin and other NSAIDs can cause hyperkalemia by inducing a hyporenin hypoaldosteronic state via inhibition of prostaglandin synthesis; however, these agents do not typically cause hyperkalemia by themselves in the setting of normal renal function and euvolemic state.

Interactions

Aspirin is known to interact with other drugs. For example, acetazolamide and ammonium chloride are known to enhance the intoxicating effect of salicyclates, and alcohol also increases the gastrointestinal bleeding associated with these types of drugs. Aspirin is known to displace a number of drugs from protein-binding sites in the blood, including the antidiabetic drugs tolbutamide and chlorpropamide, the immunosuppressant methotrexate, phenytoin, probenecid, valproic acid (as well as interfering with beta oxidation, an important part of valproate metabolism) and any NSAID. Corticosteroids may also reduce the concentration of aspirin. Ibuprofen can negate the antiplatelet effect of aspirin used for cardioprotection and stroke prevention. The pharmacological activity of spironolactone may be reduced by taking aspirin, and aspirin is known to compete with penicillin G for renal tubular secretion. Aspirin may also inhibit the absorption of vitamin C.

Pharmacokinetics

Salicylic acid is a weak acid, and very little of it is ionized in the stomach after oral administration. Acetylsalicylic acid is poorly soluble in the acidic conditions of the stomach, which can delay absorption of high doses for eight to 24 hours. The increased pH and larger surface area of the small intestine causes aspirin to be absorbed rapidly there, which in turn allows more of the salicylate to dissolve. Owing to the issue of solubility, however, aspirin is absorbed much more slowly during overdose, and plasma concentrations can continue to rise for up to 24 hours after ingestion.

About 50–80% of salicylate in the blood is bound to albumin protein, while the rest remains in the active, ionized state; protein binding is concentration-dependent. Saturation of binding sites leads to more free salicylate and increased toxicity. The volume of distribution is 0.1–0.2 l/kg.

The volume of distribution is 0.1–0.2 l/kg As much as 80% of therapeutic doses of salicylic acid is metabolized in the liver Conjugation with glycine forms salicyluric acid, and with glucuronic acid it forms salicyl acyl and phenolic glucuronide.

Salicylates are excreted mainly by the kidneys as salicyluric acid (75%), free salicylic acid (10%), salicylic phenol (10%), and acyl glucuronides (5%), gentisic acid (< 1%), and 2,3-dihydroxybenzoic acid When small doses (less than 250 mg in an adult) are ingested, all pathways proceed by first-order kinetics, with an elimination half-life of about 2.0 to 4.5 hours. When higher doses of salicylate are ingested (more than 4 g), the half-life becomes much longer (15–30 hours),[137] because the biotransformation pathways concerned with the formation of salicyluric acid and salicyl phenolic glucuronide become saturated.[1Renal excretion of salicylic acid becomes increasingly important as the metabolic pathways become saturated, because it is extremely sensitive to changes in urinary pH. A 10- to 20-fold increase in renal clearance occurs when urine pH is increased from 5 to 8. The use of urinary alkalinization exploits this particular aspect of salicylate elimination.

Mode of action

COX-1 and COX-2 inhibition There are at least two different types of cyclooxygenase: COX-1 and COX-2. Aspirin irreversibly inhibits COX-1 and modifies the enzymatic activity of COX-2. COX-2 normally produces prostanoids, most of which are proinflammatory. Aspirin-modified PTGS2 produces lipoxins, most of which are anti-inflammatory. Newer NSAID drugs, COX-2 inhibitors (coxibs), have been developed to inhibit only PTGS2, with the intent to reduce the incidence of gastrointestinal side effects.

2.2 METHODOLOGY

2.2.1 Preparation of standard curve

Aspirin

Procedure: Accurately weighed 10 mg of drug was dissolved in 10 ml of 0.1N HCL, solutions in 10 ml of volumetric flask. The resulted solution (1000µg/ml) was used to prepare the concentration 10µg/ml. The spectrum of this solution was recorded in 200-400 nm range using U.V. spectrophotometer.

Preparation of calibration curve:

From stock solutions of 1 ml was taken and diluted up to 10 ml. from this solution 0.2, 0.4, 0.6, 0.8 and 1 ml solutions were transferred to 10ml volumetric flasks and make up the volume up to 10 ml with 0.1 N HCL, gives standard drug solution of 2, 4, 6, 8, 10µg/ ml concentration.

2.2.2 Evaluation of pure drug and crystal

General physicochemical parameter which are generally carried out in drug molecule are

a) pH
b) Melting point
c) Dissolution
d) Particle size

a)Determination of pH:

10 mg drug was dissolved in 3 ml of water checked using digital pH meter at constant temperature ,prior to this ,the pH meter was calibrated using buffer solution of pH 4 and pH 9.2 and then electrode was washed with demineralized water ,the electrode was then directly dipped into solution and constant reading noted.

b) Determination of melting point:

Melting point was determined by theile tube in this method one end of capillary tube was sealed. Small amount of drug was placed in than capillary which was tied with a thermometer and this thermometer was dipped in the liquid paraffin which was kept in the theile tube, and the heat source was given through the burner to the theile tube as the temperature increases drug particle begin to liquefy .the start time drug liquefaction to completely liquefaction was noted.

c) Dissolution study of drug and crystal: In vitro release profile drug and their crystal was performed by using usp type 2 dissolution apparatus .amount of was taken and placed in the beaker over a tissue paper which was dipped in the 900 ml 0.1N HCL and stirred at 50 rpm . 1 ml of was withdrawn at time interval of 15 minute the withdrawn volume was replaced with the same volume of dissolution medium in order to keep the total volume constant. The absorbance of the sample was measured at λmax.

d) Particle size determination

Particle size was determined by using optical microscopy method and the formula used to find particle size determination out of particle size is:

Magnification value

Zero division of stage micrometer (X_1) coincides with zero division of eyepiece (Y_1).

6 division of stage micrometer (X_2) coincide with 5 division of eyepiece (Y_2).

Magnification value = X_2-X_1/Y_2-Y_1×10

Mean size (um) = A +∑fd/∑fx magnification value

Standard deviation (SD) = $\sum fd_2/\sum f-(\sum fd/\sum f_2)^2$

Size range = (mean size +SD) to (mean-SD)

2.2.3. Preparation of electromagnetic crystal:

Electromagnetic crystal of given drug was prepared by slow cooling method in this method the saturated solution of the drug was prepared in suitable solvent ethanol and isopropyl alcohol .the Petridis kept on the different distant 1inch 2 inch 3inch from surfaces mobile on which Petridis was placed was allowed to receive phone at different time 10 minute 20 minute 30 minute.

Electromagnetic radiation was generated by received phone call. After thus allow the electromagnetic crystal to stay overnight or till electromagnetic crystal dried up the dried crystal were stored in cool and dry place in a container till further use.

2.2.4 Solubility:-

Solubility was determined by the dissolving of different Aspirin crystals prepared without emf and under emf in 0.1 N HCL. The result was observed after three day.

3. RESULTS AND DISCUSSION:

First the crystal were prepared without applying the electromagnetic field, the formed crystal were very less in number and also not so clear in the morphology as in figure. But when we applied the electromagnetic field, the obtained crystals were more clear, and when we increasing the time of electromagnetic radiation, crystal formation start within 2-10 minute and obtained crystal were thick having sharp edges and more number of crystal obtained as in figure

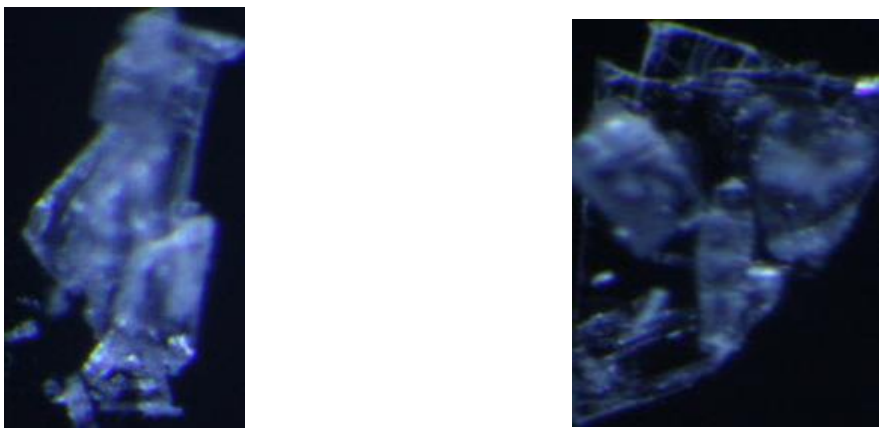
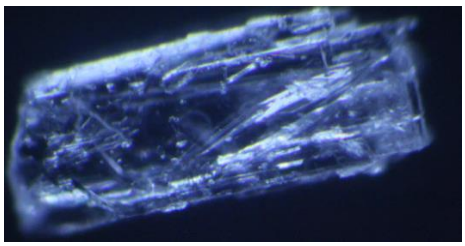
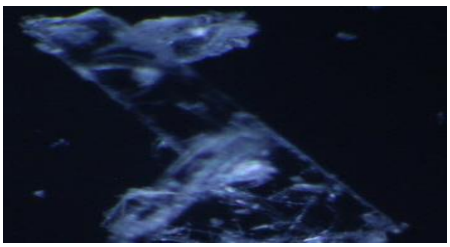


Fig.No.2: Shows the crystal of aspirin without electromagnetic field

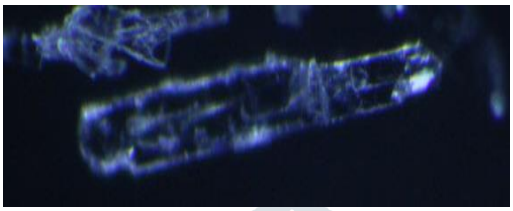
3.1 Electromagnetic crystal of aspirin in ethanol (Zero inch)



(a) 10min



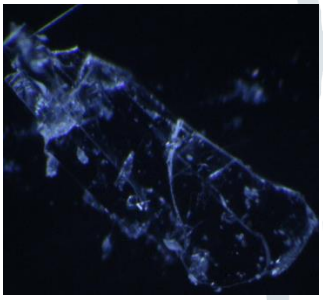
(b) 20 min



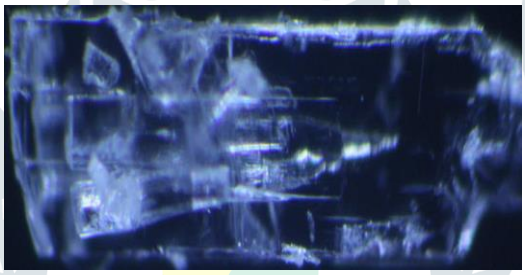
(c)30 min

Fig.No.3: Electromagnetic crystal of aspirin in ethanol (Zero inch) under Electromagnetic filed (emf), (a) 10min, (b) 20min (c) 30min

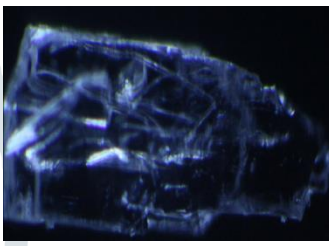
3.2 Electromagnetic crystal of aspirin in isopropyl alcohol (Zero inch)



(a) 10min



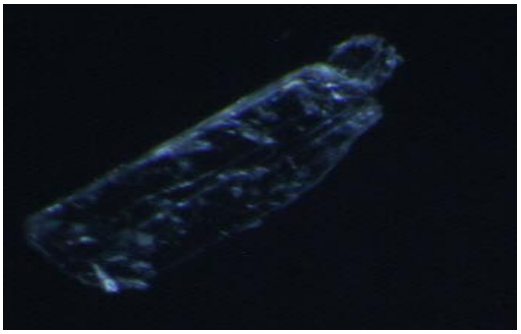
(b) 20min



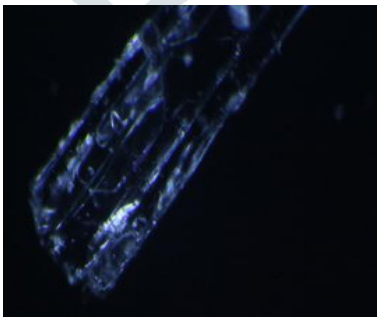
(c) 30min

Fig.No.4:Electromagnetic crystal of aspirin in isopropyl alcohol (Zero inch) under (emf), (a) 10min, (b) 20min (c) 30min

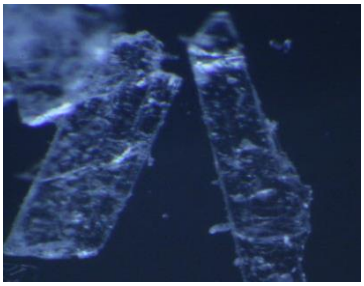
3.3 Electromagnetic crystal of aspirin in ethanol (One inch)



(a) 10min



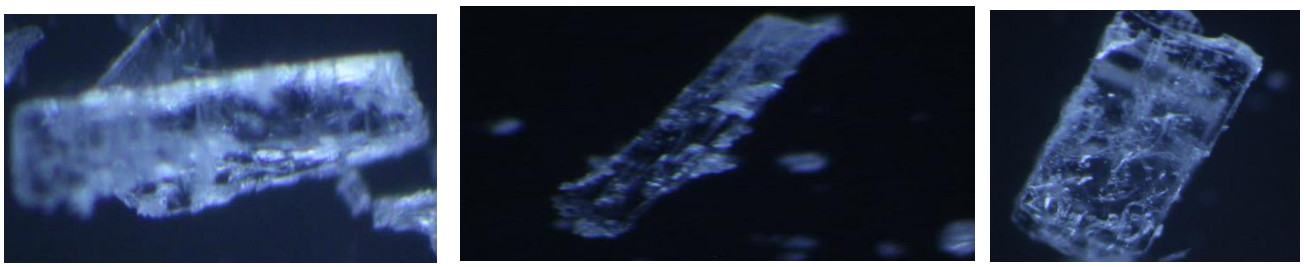
(b) 20min



(c) 30 min

Fig.No.5: Electromagnetic crystal of aspirin in ethanol (One inch) under (emf), (a) 10min, (b) 20min (c) 30min

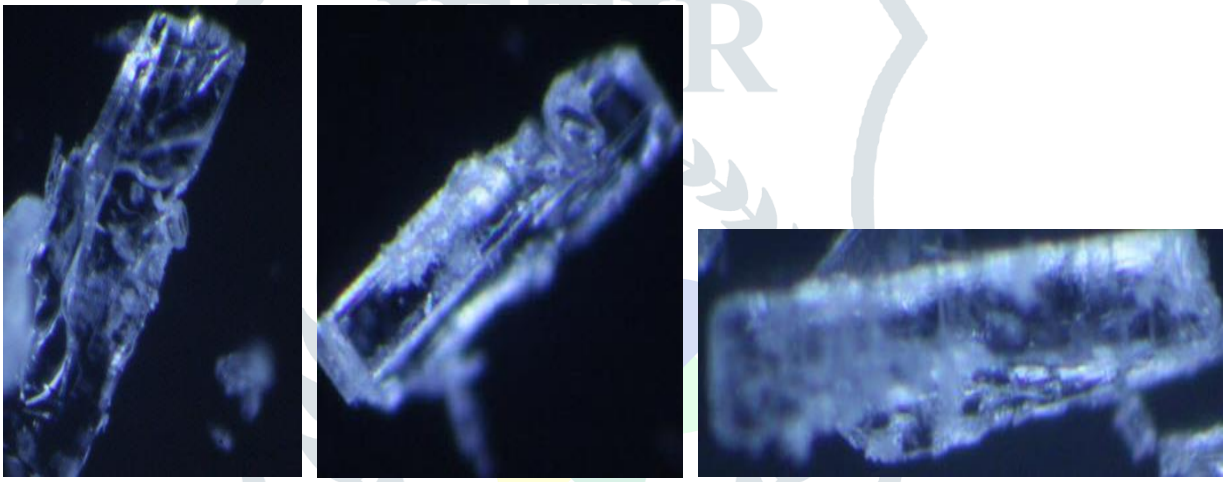
3.4 Electromagnetic crystal of aspirin in isopropyl alcohol (One inch)



(a) 10min (b) 20min (c) 30 min

Fig.No.6: Electromagnetic crystal of aspirin in isopropyl alcohol (One inch) under (emf), (a) 10min, (b) 20min (c) 30min

3.5 Electromagnetic crystal of aspirin in isopropyl alcohol (Two inch)



(a) 10min (b) 20min (c) 30 min

Fig.No.7: Electromagnetic crystal of aspirin in isopropyl alcohol (Two inch) under (emf), (a) 10min, (b) 20min (c) 30min

3.6 Calibration Curve

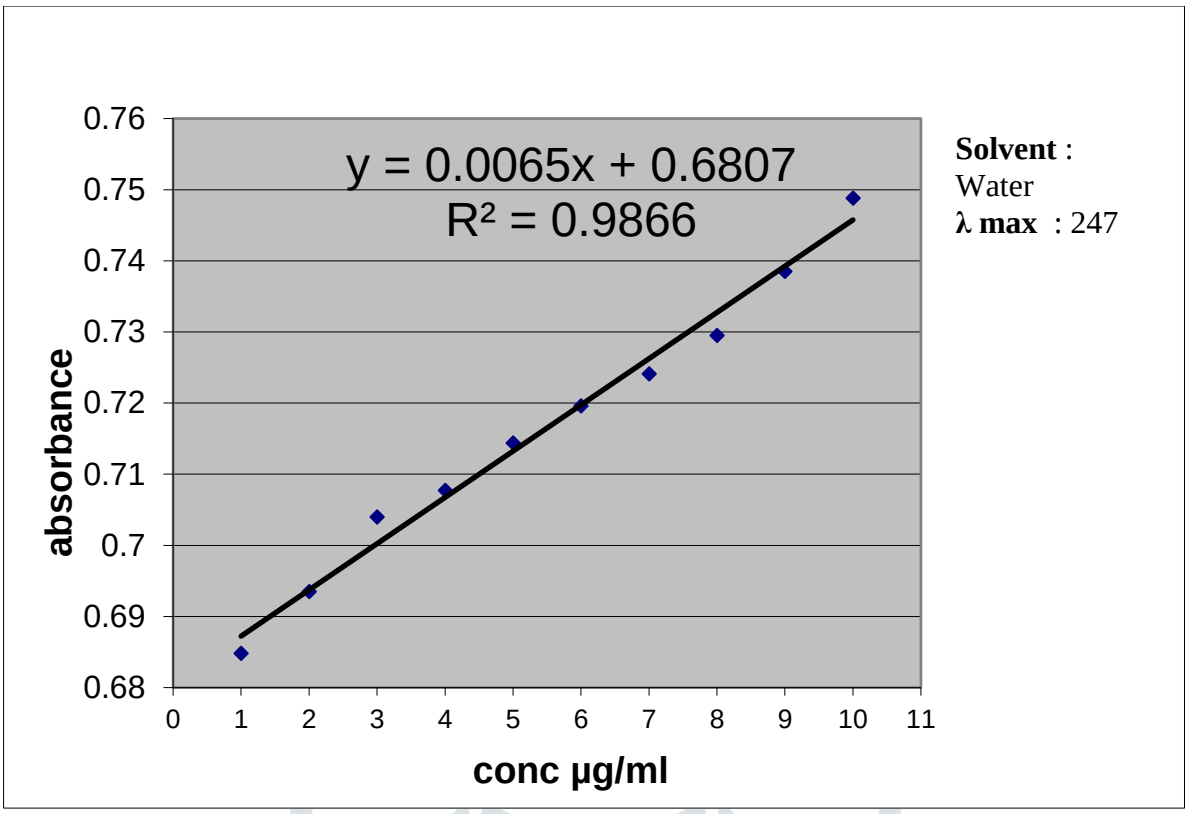


Fig.No.8: Calibration Curve of crystal Aspirin

Concentration varying from 1-10 µg/ml solution were prepared as described in 4a from which absorbance reading was taken 247 nm. The same is prepared in figure which gave R =0.9866 with equation y=0.0065x+0.6807.the graph was plotted between absorbance (x-axis)and concentration (µg/ml, y axis) shows absorbance were increased lineary with concentration .

3.7 pH PROFILE

3.7.1 pH of Aspirin in Ethanol

Tab.No.1: Comparative pH between Aspirin in Ethanol, Zero, One, Two inch under 10 min, 20 min, 30 min time interval

Drug	Control pH	pH of crystal in ethanol without electromagnetic field	Electromagnetic crystal of aspirin pH in ethanol (zero inch)	Electromagnetic crystal of aspirin pH in ethanol (one inch)	Electromagnetic crystal of aspirin pH in ethanol (two inch)
Aspirin	3.74	3.84	10 min.=3.25 20 min.=3.28 30 min.=3.20	10 min.=3.59 20 min.=3.72 30 min.=3.61	10 min.=3.88 20 min.=3.91 30 min.=3.82

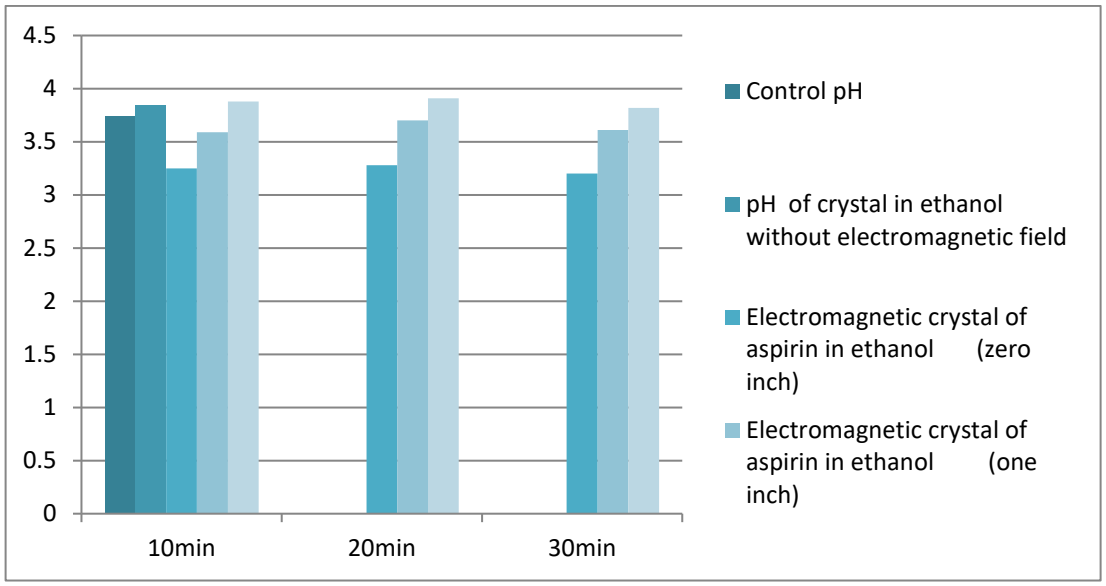


Fig.No.9: Comparative pH between Aspirin in Ethanol on Zero, One & Two inch under time 10min, 20min, 30min interval

Aspirin exhibit pH of 3.74 which on recrystallization from ethanol the pH was increased to 3.84.on other hand when crystal were prepared under electromagnetic field in zero inch(10,20,30.min)it show slightly decreased value by reaches to (3.25 ,3.26, 3.20) than control drug 3.74 .in one inch (10,20,30,)it shows lower value (3.59 ,3.72, 3.61) and it shows higher value in two inch crystal (10,20,30,)pH(3.88 ,3.91,3.82.).

3.7.2 pH of Aspirin in isopropyl alcohol

Tab.No.2: Comparative pH between Aspirin in Isopropyl alcohol, Zero, One, Two inch under 10 min, 20 min, 30min time interval

Drug	Control pH	pH of crystal in isopropyl alcohol without electromagnetic field	Electromagnetic crystal of aspirin pH in isopropyl alcohol (zero inch)	Electromagnetic crystal of aspirin pH in isopropyl alcohol (one inch)	Electromagnetic crystal of aspirin pH in isopropyl alcohol (two inch)
Aspirin	3.74	3.76	10 min.=3.93 20 min.=3.75 30 min.=3.75	10 min.=3.86 20 min.=3.90 30 min.=3.72	10 min.=3.72 20 min.=3.68 30 min.=3.32

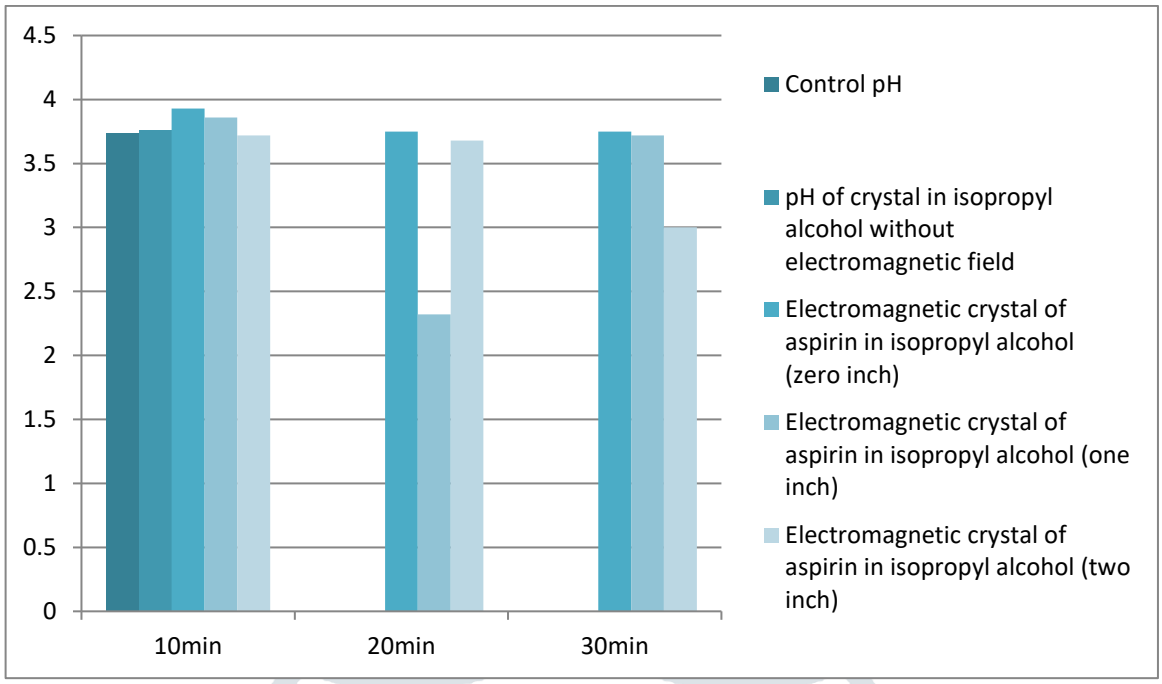


Fig.No.10: Comparative pH between Aspirin in Isopropyl alcohol on Zero, One & Two inch under time 10min, 20min, 30min interval

In the case of isopropylalcohol recrystallized aspirin crystal exhibited increased pH of 3.76.on other hand when crystal prepared under electromagnetic field in zero inch(10,20,30 min,)10 min. shows higher value (3.93,) but 20 and 30 min. shows lower value (3.75,3.75). in one inch electromagnetic crystal 10 and 20 min. shows higher value(3.86 and 3.90)and 30 min. shows lower value of pH (3.72) than control drug pH (3.74).in two inch crystal of 10 ,20 ,30 min. crystal shows lower value of pH(3.72 ,3.68,3.32) than control drug (pH 3.74).

3.8 Melting point Profile

3.8.1 Melting point of Aspirin Ethanol Crystals

Tab.No.3: Comparative Melting point of Aspirin in Ethanol, Zero, One, Two inch under 10 min, 20 min, 30min time interval

Drug	Control Melting point	Melting point of crystal in ethanol without electromagnetic field	Electromagnetic crystal of aspirin Melting point in ethanol (zero inch)	Electromagnetic crystal of aspirin Melting point in ethanol (one inch)	Electromagnetic crystal of aspirin Melting point in ethanol (two inch)
Aspirin	141	134	10min- 134 20min- 135 30min- 133	10min- 138 20min- 137 30min-137	10min- 137 20min- 137 30min- 135

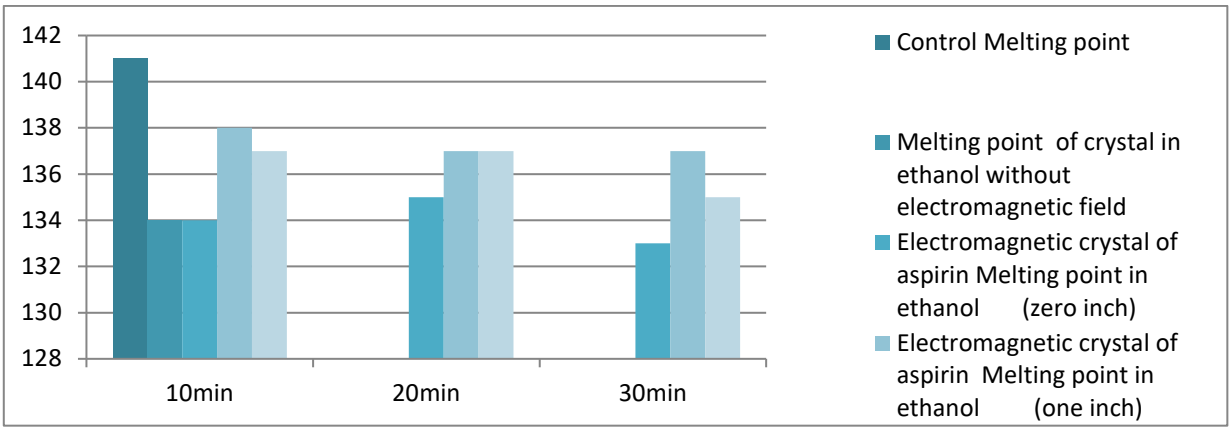


Fig.No.11: Comparative Melting point between Aspirin in Ethanol, Zero, One & Two inch under time 10min, 20min, 30min interval

When drug recrystallized in ethanol (control) melting point decreases to (134) and when drug recrystallized under electromagnetic field melting point of 30 min. crystal shows lower melting point(133) than 20 min(135) and 10 min.(137), when drug recrystallized in ethanol (control) melting point decreases to (134) and when drug recrystallized under electromagnetic field melting point of 30 min .and 20 min crystal shows lower melting point(137) than 10 min.(138) , when drug recrystallized in ethanol (control) melting point decreases to (134) and when drug recrystallized under electromagnetic field melting point of 30 min. crystal shows lower melting point(135) than 20 and 30 min.(137).

3.8.2 Melting point of Aspirin Isopropyl alcohol Crystal

Tab.No.4: Comparative pH between Aspirin in Isopropyl alcohol, Zero, One, Two inch under 10 min, 20 min, 30min

Drug	Control Melting point	Melting point of crystal in Isopropyl alcohol without electromagnetic field	Electromagnetic crystal of aspirin Melting point in Isopropyl alcohol (zero inch)	Electromagnetic crystal of aspirin Melting point in Isopropyl alcohol (one inch)	Electromagnetic crystal of aspirin Melting point in Isopropyl alcohol (two inch)
Aspirin	141	134	10min- 137 20min- 138 30min- 136	10min- 139 20min- 137 30min- 138	10min- 133 20min-135 30min- 137

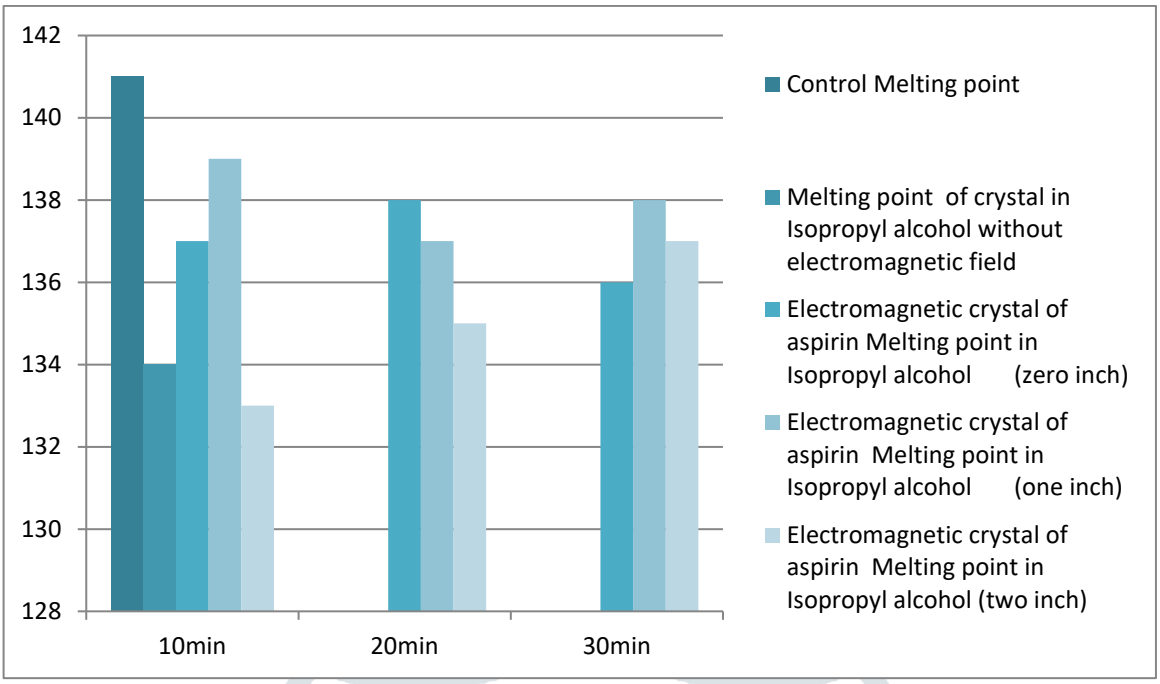


Fig.No.12: Comparative Melting point between Aspirin in Isopropyl alcohol on Zero, One & Two inch under time 10min, 20min, 30min interval

When drug recrystallized in isopropyl alcohol (control 2) melting point decreases to (138) and when drug recrystallized under electromagnetic field melting point of 30 min. crystal shows lower melting point(136) than 10 min(137) and 20 min.(138), when drug recrystallized in isopropyl alcohol (control 2) melting point decreases to (138) and when drug recrystallized under electromagnetic field melting point of 30 min. and 30 min. crystal shows lower melting point(138) than 10 min.(139), when drug recrystallized in isopropyl alcohol (control 2) melting point decreases to (138) and when drug recrystallized under electromagnetic field melting point of 30 min. and 10 min. crystal shows lower melting point(133) than 20 min(135) .

3.9 Dissolution profile

3.9.1 Dissolution of Aspirin Recrystallized Ethanol (Zero inch) under emf

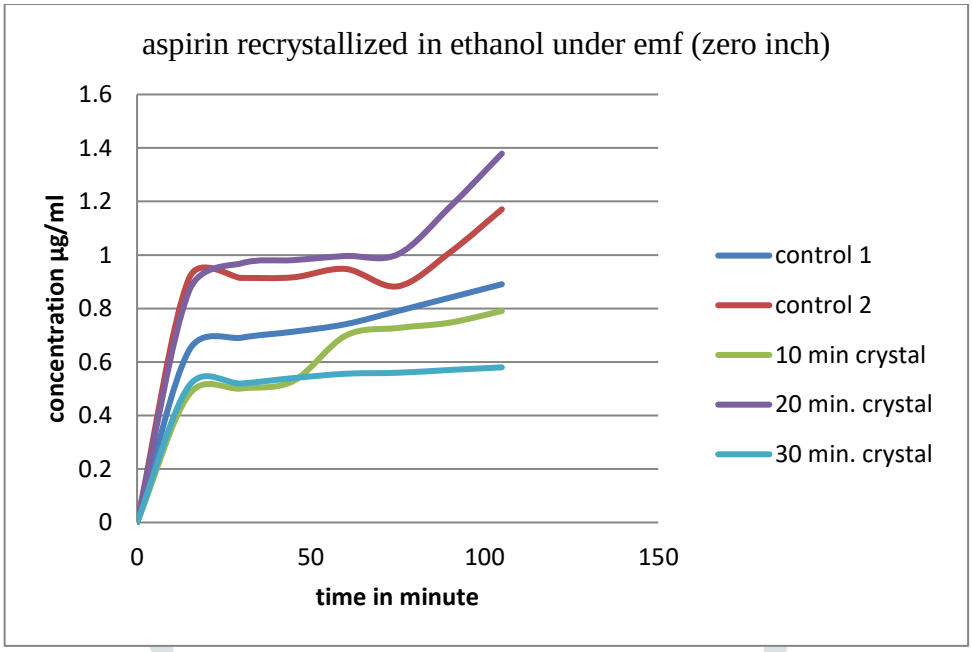


Fig.No.13: Dissolution of Aspirin Recrystallized Ethanol (Zero inch) under emf

The drug concentration was analyzed in every 15 minutes. It was observed that drug conc. of control 1 (without emf) crystals prepared (under emf) at t15-0.7998 µg/ml, t60-0.9971µg/ml, tios-1.2301µg/ml maximum than 10 min.crystals tis= 0.6981, t60-0.8374, tros- 1.174. 20 min crystals conc. at tis= 0.4179µg/ml, 160-0.8091µg/ml and tios= 0.1.071µg/ml. 30 minute crystals prepared (under emf) conc. at tis 0.6981µg/ml, t60= 0.7012µg/ml, and at tros-0.9010µg/ml. pure drug crystals prepared shows minimum drug conc. at tis= 0.6498µg/ml, too-0.7807µg/ml and tios-0.8977µg/ml.

3.9.2 Dissolution of Aspirin Recrystallized in Ethanol (One inch) under emf

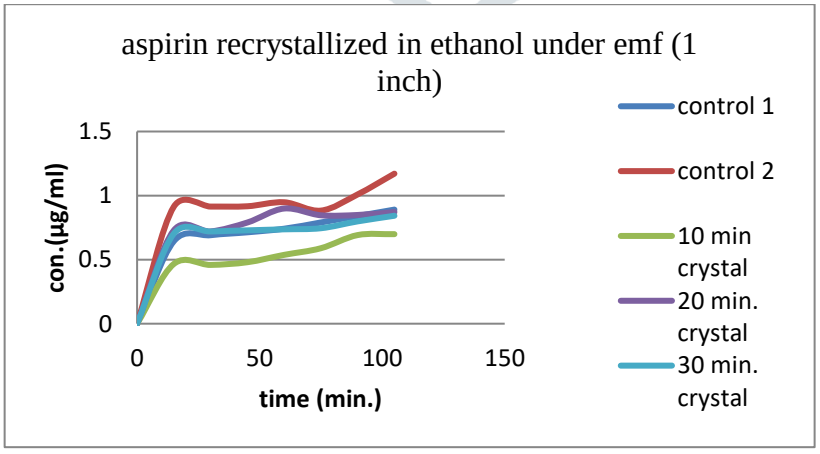


Fig.No.14: Dissolution of Aspirin Recrystallized in Ethanol (One inch) under emf

The drug concentration was analyzed in every 15 minutes. It was observed that drug conc. of control 1(without emf) at tis 0.7989µg/ml, t60 0.9006µg/ml, tios 1.2301µg/ml maximum then 30 min crystals at tis 0.7412µg/ml, 160= 0.8619µg/ml, tios= 0.9319µg/ml. 20 minute crystals prepared (under emf) tis 0.6397µg/ml, t60= 0.8371µg/ml, tios 0.9201µg/ml. pure drug con. at tis= 0.6498µg/ml, 160 0.7487µg/ml and tios= 0.8977µg/ml. 10 minute crystals prepared (under emf) shows minimum drug conc. at tis= 0.4371µg/ml, too= 0.6017µg/ml and at tios-0.7601µg/ml.

3.9.3 Dissolution of Aspirin Recrystallized Ethanol (Two inch) under emf

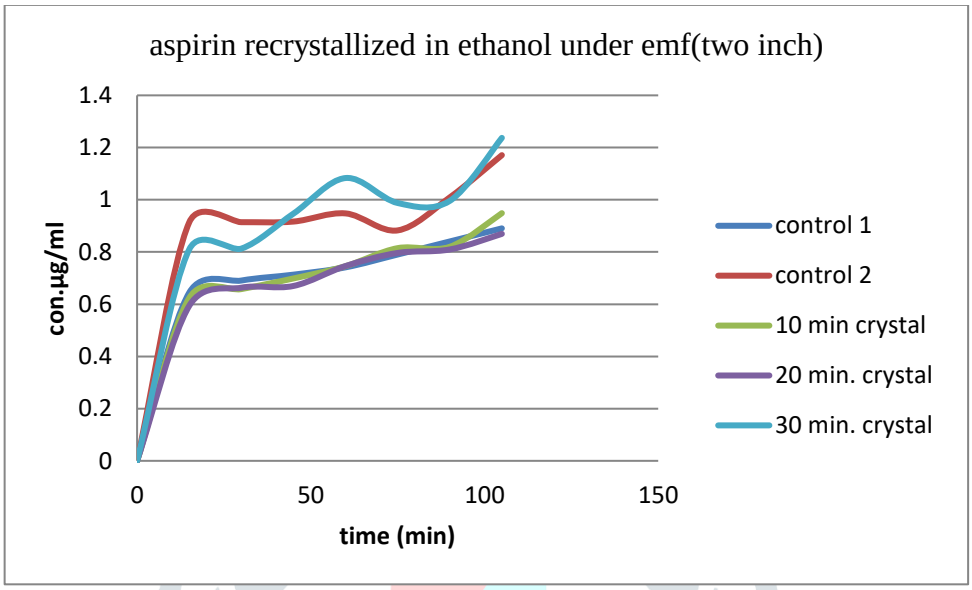


Fig.No.15: Dissolution of Aspirin Recrystallized Ethanol (Two inch) under emf

The drug concentration was analyzed in every 15 minutes. It was observed that drug conc. of 30 minute crystals prepared (under emf) at tis= 0.6418µg/ml, t60 0.9301µg/ml, tos-1.371µg/ml maximum then control ! (without emf) tis= 0.7998µg/ml, t60-0.9006µg/ml, tios 1.2301µg/ml. Drug conc. of 10 minute crystals prepared (under emf) at tis 0.5819µg/ml, t 60 0.7168µg/ml and 110s= 0.9107µg/ml. pure drug conc. at tis-0.6498µg/ml, too-0.7487µg/ml and at tros-0.8977µg/ml. 20 minute crystals prepared (under emf) shows minimum drug conc. at tis= 0.5171 µg/ml, too 0.7415µg/ml and tros-0.8497µg/ml.

3.9.4 Dissolution of Aspirin Recrystallized Isopropyl alcohol (Zero inch) under emf

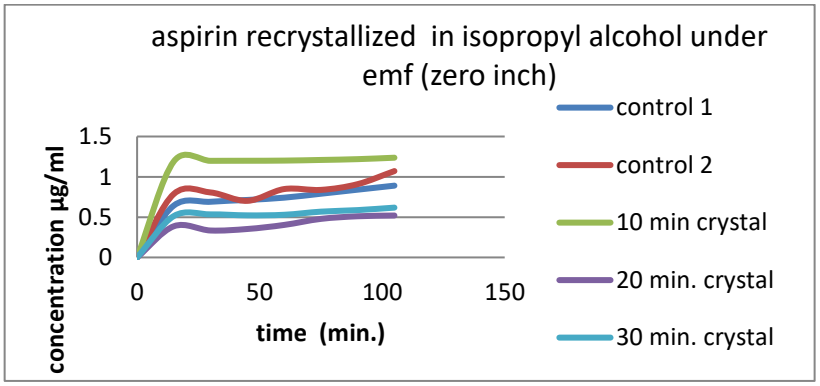


Fig.No.16: Dissolution of Aspirin Recrystallized Isopropyl alcohol (Zero inch) under emf

The drug concentration was monitored in every 15 minutes. It was observed that drug conc. of 20 minute crystals prepared (under emf) at tis= 7991µg/ml, t60= 0.9107µg/ml, tios 1.234µg/ml shows maximum drug conc. then control 2 (without emf) t15=0.7001µg/ml, t60-0.8616µg/ml, tios-0.9907µg/ml. Drug conc. 10 mn. Crystals at tis= 0.5891µg/ml, t60= 0.6413µg/ml and tros 0.9601µg/ml. 30 minute crystals prepared (under emf) conc. at tıs= 0.5912µg/ml, to= 0.7073µg/ml, and at 1105= 0.9413µg/ml. pure drug crystals shows minimum drug conc. at tıs = 0.6498µg/ml, t60 0.7487µg/ml and tios-0.8977µg/ml.

3.9.5 Dissolution of Aspirin Recrystallized Isopropyl alcohol (One inch) under emf

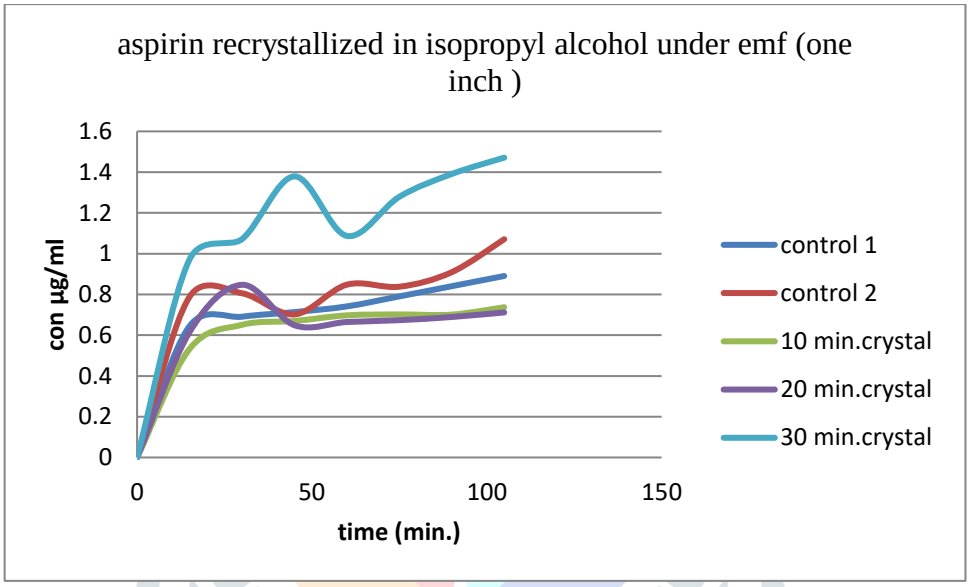


Fig.No.17: Dissolution of Aspirin Recrystallized Isopropyl alcohol (One inch) under emf

The drug concentration was monitored in every 15 minutes. It was observed that 30 minute crystals prepared (under emf) conc. at 10.8347pg/ml, 1.123µg/ml, t 1.317µg/ml maximum then control 2 (without m) 0.7001pg/ml, tu 0.7918µg/ml, to 0.9907µg/ml. Drug conc. of pure drug at f 0.6498µg/ml, 0.7487pg/ml and to 0.8977µg/ml. 20 minute crystals prepared (under emf) conc. at fy 0.7123µg/ml, 0.7491µg/ml, and at tros 0.8017pg/ml. 10 minute crystals prepared (under emf) shows minimum drug conc. at t 0.5417µg/ml, to 0.7074µg/ml and 0.8016µg/ml.

3.9.6 Dissolution of Aspirin Recrystallized Isopropyl alcohol (Two inch) under emf

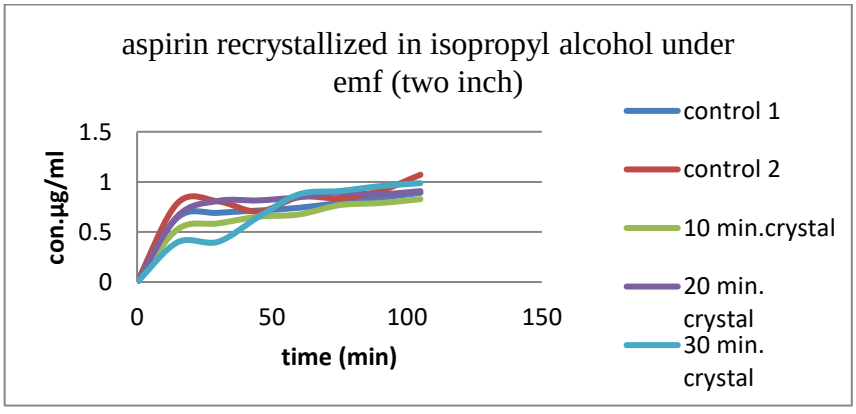


Fig.No.18: Dissolution of Aspirin Recrystallized Isopropyl alcohol (One inch) under emf

The drug concentration was monitored in every 15 minutes. It was observed that 30 minute crystals prepared (under emf) conc. at t15 0.6713µg/ml, t60= 0.7310µg/ml, t105 1.173µg/ml maximum then 20 minute crystals prepared (under emf) at tis= 0.5817µg/ml, too= 0.7189µg/ml, tios= 0.9991µg/ml. Drug conc. of control 2 crystals(without emf) prepared at tis= 0.7001µg/ml, t60= 0.7918µg/ml and tios 0.9907µg/ml. pure drug conc. at t15= 0.6498µg/ml, at too= 0.7487µg/ml. and at t105= 0.8977µg/ml. 10 minute crystals prepared (under emf) shows minimum drug conc. at tis= 0.5391µg/ml, t60= 0.7123µg/ml and tios= 0.7918µg/ml.

3.10 Particle Size

Tab.No.5: Particle Size of recrystallization Aspirin with mcc and their crystals

SL. No.	Drug	Mean Size (µm)	SD deviation (µm)	Particle Size range(µm)
1	Pure drug	42.1	±2.3	39.8- 44.4
2	Control 1 (Ethanol) without emf	34.91	±6.68	28.13- 4.69
3	Control 2 (Isopropyl alcohol) without emf	36.00	± 8.91	28.91- 34.91
4	Aspirin 10 min in ethanol Zero inch	30.86	±6.91	23.95- 37.77
5	Aspirin 20 min in ethanol Zero inch	29.12	±4.13	24.99-33.25
6	Aspirin 30 min in ethanol Zero inch	26.92	±7.01	19.91-33.93
7	Aspirin 10 min in Isopropyl alcohol Zero inch	33.71	±6.01	27.7-39.72
8	Aspirin 20 min in Isopropyl alcohol Zero inch	34.91	±4.03	30.88-38.94
9	Aspirin 30 min in Isopropyl alcohol Zero inch	38.91	±7.03	31.88-45.94
10	Aspirin 10 min in ethanol one inch	50.72	±4.63	46.09-55.35
11	Aspirin 20 min in ethanol one inch	42.71	±3.01	39.7-45.72
12	Aspirin 30 min in ethanol one inch	30.71	±5.2	25.51- 35.91
13	Aspirin 10 min in Isopropyl alcohol one inch	35.71	±3.98	31.73- 39.69
14	Aspirin 20 min in Isopropyl alcohol one inch	42.91	±4.11	38.8- 47.02
15	Aspirin 30 min in Isopropyl alcohol one inch	28.91	±4.98	23.93- 33.89

16	Aspirin 10 min in ethanol two inch	36.92	±5.01	31.91-4.93
17	Aspirin 20 min in ethanol two inch	50.12	±3.98	46.14-54.1
18	Aspirin 30 min in ethanol two inch	31.00	±5.41	25.59-36.41
19	Aspirin 10 min in Isopropyl alcohol two inch	32.71	±6.01	26.07- 38.72
20	Aspirin 20 min in Isopropyl alcohol two inch	39.71	±6.13	33.58-45.84
21	Aspirin 30 min in Isopropyl alcohol two inch	24.9	±3.78	21.12-26.68

4. CONCULSION:

It is obvious that the solvent plays an important role in recrystallization of any drug material or chemical moiety. Even the changes in ratio of solvents alter the physicochemical properties of the recrystallized material. In the present work it is an attempt to observe the effect electromagnetic field on recrystallization moreover emphasized on preparation of desired crystal under electromagnetic field. Change in time of electromagnetic radiation or field which alters the environment and quality of drug.

4.1 Evaluation of physicochemical parameter of aspirin in ethanol (zero inch)

Tab.No.6: Evaluation of physicochemical parameter of aspirin in ethanol (zero inch)

S no.	parameter	Pure drug	Crystal drug	10 min. crystal	20 min. crystal	30 min. crystal
1	pH	3.74	3.84	3.25	3.26	3.20
2	Melting point	141-142	134-135	137	135	133

4.2 Evaluation of physicochemical parameter of aspirin in isopropyl alcohol (zero)

Tab.No.7: Evaluation of physicochemical parameter of aspirin in isopropyl alcohol (zero)

S no.	parameter	Pure drug	Crystal drug	10 min. crystal	20 min. crystal	30 min. crystal
1	pH	3.74	3.76	3.93	3.75	3.75
2	Melting point	141-142	138-139	137	138	136

4.3 Evaluation of physicochemical parameter of aspirin in ethanol (one inch)

Tab.No.8: Evaluation of physicochemical parameter of aspirin in ethanol (one inch)

S no.	parameter	Pure drug	Crystal drug	10 min. crystal	20 min. crystal	30 min. crystal
1	pH	3.74	3.84	3.59	3.72	3.61
2	Melting point	141-142	134-135	138	137	137

4.4 Evaluation of physicochemical parameter of aspirin in isopropyl alcohol (one inch)

Tab.No.9: Evaluation of physicochemical parameter of aspirin in isopropyl alcohol (one inch)

S no.	parameter	Pure drug	Crystal drug	10 min. crystal	20 min. crystal	30 min. crystal
1	pH	3.74	3.76	3.86	3.90	3.72
2	Melting point	141-142	138-139	139	138	138

4.5 Evaluation of physicochemical parameter of aspirin in ethanol (two inch)

Tab.No.10: Evaluation of physicochemical parameter of aspirin in ethanol (two inch)

S no.	Parameter	Pure drug	Crystal drug	10 min. crystal	20 min. crystal	30 min. crystal
1	pH	3.74	3.84	3.88	3.91	3.82
2	Melting point	141-142	134-135	137	137	135

4.6 Evaluation of physicochemical parameter of aspirin in isopropyl alcohol (two inch)

Tab.No.11: Evaluation of physicochemical parameter of aspirin in isopropyl alcohol (two inch)

S no.	Parameter	Pure drug	Crystal drug	10 min. crystal	20 min. crystal	30 min. crystal
1	pH	3.74	3.76	3.72	3.68	3.32
2	Melting point	141-142	138-139	137	138	136

Recrystallization of aspirin increasing the pH to basic side here as ,recrystallizing in the presence of electromagnetic field exhibited decreasing the pH trend than control ,because the H -atom get involved in crystal lattice structure giving rise to hydrogen bonding since H-bond have higher energy levels, the melting point of crystal also increased by an enormous amount, whereas recrystallization under electromagnetic field resulted in lowering of

pH indicating release of more H-atom to the solution /release of H-atoms during crystal lattice formation. When crystal of aspirin were prepared under electromagnetic field it taken less time for nucleation which result less time for crystal formation .so crystal in the presence of electromagnetic field gives better crystal in morphology and crystal formation start within 2 -3 minute. Even though it difficult to conclude any firm explanation or interpretation to the variation in data at this stage ,since the work is at its preliminary level and need exhaustive experimentation and meticulous observation .hence future aspect of the work would be designed accordingly to acquire some probable explanation for change in various physicochemical parameter.

5. REFERENCES

1. Aalto S, Haarala C, Brück A, Sipilä H, Hämäläinen H, Rinne JO (July 2006). "Mobile phone affects cerebral blood flow in humans". Journal of cerebral blood flow and metabolism 26 (7): 885–90.
2. Blank, Martin; Goodman, Reba (2009). "Electromagnetic fields stress living cells".Pathophysiology 16 (2–3): 71–8.
3. Cvs subrahmanyam pharmaceutical engineering 2008 principles and practices,vallabh prakashan ,page no. 361-165
4. Lönn, Stefan et al 2005 Swedish Interphone Study Group . "Long-Term Mobile Phone Use and Brain Tumor Risk". American journal of epidemiology **161** (6) page no. 526–35.
5. Linet ms *et al.* july 1997 "Residential exposure to magnetic fields and acute lymphoblastic leukemia in children". The new England journal of medicine 337 (1): 1–7.
6. Jacobsen R; Olsen, JH; Boice, JD; McLaughlin, JK; Johansen, C (December 2006).” cellular telephone use and cancer risk:update of nation wide danish cohart” journal of the national cancer institute 98 (23): 170.
7. Linet MS *et al.* july 1997 . "Residential exposure to magnetic fields and acute lymphoblastic leukemia in children". The new England journal of medicine page no.337 (1): 1–7.
8. Baan R, et al July 2011 , "Carcinogenicity of radiofrequency electromagnetic fields". The lancet oncology 12 (7): 624–6. .
9. "What are the health risks associated with mobile phones and their base stations?" December 5, 2005 World Health Organization..
10. Rohani S, Horne S, Murthy K S K. 2005 Control of the product quality in batch crystallization of pharmaceuticals and fine chemicals. Part 1: design of the crystallization process and the effect of solvent.119(2) :263 -290
11. McKie D, McKie C. 1986 Essentials of Crystallography. London: Blackwell Scientific. Publications.
12. Mirmehrabi M, Rohani S 2005. An approach to solvent screening for crystallization of polymorphic pharmaceuticals and fine chemicals. J Pharm Sci, 94(7): 1560–1576.

13. Chibowski E, Holysz L, Szcześ A, Chibowski M. 2004 Some magnetic field effects on in situ precipitated calcium carbonate. Water Sci Technol; 49(2):169-76.
14. Mettler, Fred A., Jr., M.D., and Upton, Arthur C., M.D. 2005 Medical Effects of Ionizing Radiation, Second Edition, Philadelphia..
15. Hande, W.R. and Edwards, 1996 F.M., Editors, "Health Effects of Exposure to Low-Level Ionizing Radiation" Bristol, UK,
16. K Vishnu et al 2011 "study on effect of mobile phone radiation on DNA using laser induced fluorescence technique" received December 29 2010 published online September.
17. Enma V. Paez Espinosa 2012, Aspirin: Pharmacology and Clinical Applications, Hindawi Publishing Corporation, Volume 2012, 15.
18. Cadavid Angela 2017, Aspirin: The Mechanism of action Revisited in the Context of Pregnancy Complication Frontiers of Immunology, vol; 8, 261.