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

PREPRATION AND EVALUTION OF ASPIRIN

MOHD AYYUB, B.PHARM, GURU NANAK COLLEGE OF PHARMACEUTICAL SCIENCE DEHRADUN, UTTARAKHAND, 248007

MS SHIVALI SAGAR, ASSISTANT PROFESSOR, GURU NANAK COLLEGE OF PHARMACEUTICAL SCIENCE, DEHRADUN, UTTARAKHAND, 248007

CORRESPONDING EMAIL

ayyubmohd010@gmail.com

ABSTRACT

Aspirin is a nonsteroidal anti-inflammatory medication (NSAID). . Easily absorbed from the digestive system is aspirin. Aspirin functions in a manner similar to other NSAIDs but also inhibits platelet activity normally. To create acetylsalicylic acid for the first time, scientist Charles Frédéric Gerhardt combined sodium salicylate with acetyl chloride in 1853.

Formulations with improved physicochemical qualities is a difficult issue for pharmaceutical researchers and industry. Acetylsalicylic Acid, better known as aspirin, In solutions of ammonium acetate or the acetates, carbonates, citrates, or hydroxides of the alkali metals, aspirin decomposes very quickly. We constructed two-phase enteric-coated granules of aspirin and L-glutamate compound by extrusion spheronization method and fluidized bed coating. Aspirin is classified as a bcs classification ii tablet, which are solid dosage forms manufactured by compression and containing one or more medicines with or without excipients. It offers the least content fluctuation and good dosage accuracy. Tablet additives refer to inert substances used in addition to active components.This aspirin product is collected, refined by recrystallization, and its purity is assessed by measuring its melting temperature. Utilizing a Büchner filtration device, separate the crystals from the liquid while completely removing the aspirin from the flask using tiny amounts of the ice-cold deionized water. The monsanto hardness test equipment was used to measure the hardness of the tablets. Instead, we switched to another piece of equipment and discovered that salicylic acid, which has a molecular weight of 0.330 g, was synthesised by reacting excessively with acetic amhydride. The amount of aspirin product that is theoretically feasible is determined by the amount of salicylic acid utilised because too much aceticanhydride was used. The molecular weight of aspirin is 0.635 g.

INTRODUCTION

Acetylsalicylic acid (ASA), generally known as aspirin, is a nonsteroidal anti-inflammatory medication (NSAID) used to treat inflammation, fever, and/or discomfort as well as a blood thinner. Aspirin is used to treat a variety of inflammatory disorders, including Kawasaki illness, pericarditis, and rheumatic fever. Although aspirin has antipyretic and analgesic qualities, it does not have any practical anti-inflammatory characteristics. Easily absorbed from the digestive system is aspirin.

Long-term usage of aspirin can also aid in the prevention of blood clots, ischemic strokes, and further heart attacks in high-risk individuals. Effects usually start to take action for pain or fever within 30 minutes. Aspirin functions in a manner similar to other NSAIDs but also inhibits platelet activity normally.

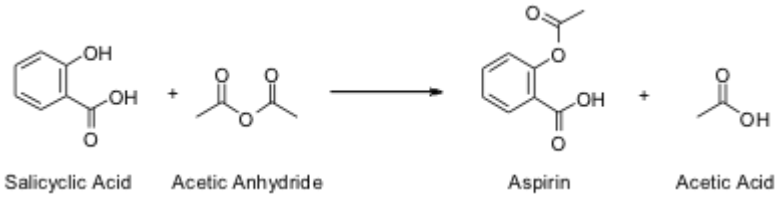
For at least 2,400 years, a forerunner to aspirin found in the willow tree's (genus Salix) bark has been utilised for its medicinal properties. To create acetylsalicylic acid for the first time, scientist Charles Frédéric Gerhardt combined sodium salicylate with acetyl chloride in 1853. Other scientists developed more effective manufacturing techniques and determined the chemical structure throughout the course of the following 50 years.

The creation of appropriate formulations with improved physicochemical qualities is a difficult issue for pharmaceutical researchers and industry. An organic ester is aspirin. When an acid and an alcohol containing a -OH group interact, an ester is the resultant chemical. Salicylic acid and acetic anhydride react to produce the ester (aspirin).

A particular class of carbon-containing chemicals are called organic compounds. The term "organic" comes from the presumption that they could only be manufactured from ingredients originating from such organic sources, such as plants, or separated from plants.

Acetylsalicylic Acid, better known as aspirin, is the chemical compound that was really created in this experiment. Salicylic acid, which is used to make Acetylsalicylic Acid, interacts with Acetyl Anhydride in the manner shown in Figure 1.1 below:

Figure 1.1: Reaction



Reaction of Salicylic Acid and Acetic Anhydride to form Aspirin and Acetic Acid

Non-steroidal anti-inflammatory medicines (NSAIDs) are among the most often prescribed medications in the world and are readily accessible to treat fever, pain, and arthritis [1]. NSAIDs work by preventing cyclooxygenase from doing its job (COX). COX-1 and COX-2 are the two subtypes of common COX. COX-1 plays a role in the production of the prostatic (PGs) essential for proper cell activity and is required to maintain some basic bodily functions. COX-2 contributes in the manufacture of mediators of inflammation, pain, and PGs, and its expression rises in response to tissue damage and inflammation. NSAIDs reduce COX-2 activity to produce antipyretic, analgesic, and anti-inflammatory actions, whereas COX-1 inhibition produces antithrombotic benefits.

Aspirin and indomethacin are examples of COX-1 high-selection inhibitors. Ibuprofen and acetaminophen are examples of COX-1 low-selection inhibitors. Naproxen and diclofenac are examples of COX non-selection inhibitors. COX-2 selection inhibitors include celecoxib and rofecoxib. However, long-term usage of NSAIDs might result in serious gastrointestinal side effects. According to epidemiological research, between 20 and 30 percent of patients develop gastric ulcers, and 2 percent experience serious side effects such stomach bleeding or perforation or even death. High-risk groups can occur with an incidence of up to 10%.Those who do not use medications had a 1.5–2 times higher prevalence of dyspepsia. Rheumatoid arthritis sufferers who experience gastrointestinal side effects in the range of 5–15% stop taking their medications. It is clear that the stomach damage impact of NSAIDs has become a significant barrier to the clinical use of such medications, making the discovery of a safe and effective method to stop gastric injury induced by NSAIDs of enormous therapeutic value.

MOLECULAR COMPOSITION

In solutions of ammonium acetate or the acetates, carbonates, citrates, or hydroxides of the alkali metals, aspirin decomposes very quickly. It is stable in dry air but progressively hydrolyzes into acetic and salicylic acids when it comes into contact with moisture. The hydrolysis happens quickly in alkali solutions, and the clear solutions that result may only include acetate and salicylate.

Similar to flour mills, aspirin tablet makers must regulate the quantity of powder that is allowed to get airborne inside the structure since the combination of powder and air might be explosive. A 5 mg/m3 recommended exposure limit has been established by the National Institute for Occupational Safety and Health (NIOSH) for use in the United States (time-weighted average). 5 mg/m3 was the legal allowed exposure limit for aspirin imposed by the Occupational Safety and Health Administration (OSHA) in 1989, however this was overturned in the 1993 AFL-CIO v. OSHA ruling.

PHYSICAL PROPERTIES

Salicylic acid's acetyl derivative, aspirin, is a white, crystalline compound with a modest acidity that melts at 136 °C (277 °F) and decomposes at 140 °C (284 °F). At 25 °C (77 °F), it has an acid dissociation constant (pKa) of 3.5.

PROCEDURE

In this process, phosphoric acid (H3PO4) serves as a catalyst while an excess of acetic anhydride (C4H6O3) reacts with a precisely calculated quantity of salicylic acid (C7H6O3). The mixture is heated to create acetic acid and acetylsalicylic acid (C9H8O4) (C2H4O2). Following the reaction, water is added to the product to remove any extra Acetic Anhydride and induce the aspirin product to crystallise. This aspirin product is collected, refined by recrystallization, and its purity is assessed by measuring its melting

temperature. The product is dissolved in a tiny, precisely measured amount of water, and the diluted solution is then examined using UV-Spectroscopy.

MATERIALS AND TOOLS

Acetate Anhydride

Aspirator

Beakers (100ml, 200ml, 400ml)

Catheter Tubes

Cuvette

Desi-Cooler

Distilled Water

The Eye Dropper

Crutch For Filters

Paper Filters

Fuming Hood

Stirrer Made Of Glass

The Glass Stopper

The Glass Vial

Graduation Cylinders (10ml And 50 Ml)

The Hot Plate

Ice

Lab Journal

Watch Glass Label

Melt-Temp Equipment

Pestle And Mortar

Oven

Acid Phosphoric

Acid Salicylate

Scoopula

Spritzer Bottle

Balane With Top Loading

Uv-Vis Absorbance Meter

The Vacuum Hose

Glass Watch

Measure Bottle

Tablet punching machine

Hot air oven

CHEMICALS:

Aspirin, lactose, dry starch, magnesium stearate, and talc.

All chemicals and equipment collected by guru nanak college laboratory for preparing aspirin.

PREPRATION OF ASPIRIN

Salicylic acid should be measured out to 1 gram in a 25 mL Erlenmeyer flask. To the test tube, add 3.5 mL of acetic anhydride. The pipette dispenser for this reagent, referred to as a "repipette," is installed in the fume hood in the lab and is programmed to provide precisely 3.5 mL. After the acetic anhydride has been added, avoid pointing the flask's open end at anyone or anything.

3–4 drops of strong (18M) sulfuric acid should be cautiously added to the flask before being well mixed with a glass rod. Add one or two additional drops of strong sulfuric acid and mix vigorously if the solid does not dissolve. Discard the solid if it still does not dissolve.

Finally, throw out the mixture, and start over with a fresh, dry flask.

Give the reaction around ten minutes to complete. Cool around 50 mL of deionized water in an ice water bath while you wait.Following the 10-minute period, add 5 mL of cold deionized water SLOWLY (0.5 mL at a time, stirring with a glass rod after each addition), followed by 5 minutes in an ice water bath.Any unreacted acetic anhydride will be destroyed by the addition of water, producing heat in the process.Even though there is far less acetic anhydride left over after the reaction, you should still proceed with caution.

In the ice water bath again, leave the flask for roughly 15 minutes. You could then notice the solid aspirin's white crystals. Stir the solution and scrape the inside of the flask with a glass rod to trigger precipitation if you don't observe a sizable amount of white solid. After the first 15 minutes of precipitation, keep cooling for an additional 15 minutes.

Utilizing a Büchner filtration device (Figure 1), separate the crystals from the liquid while completely removing the aspirin from the flask using tiny amounts of the ice-cold deionized water.

Draw air through your product for a few minutes after washing it with a tiny amount of additional ice-cold deionized water.

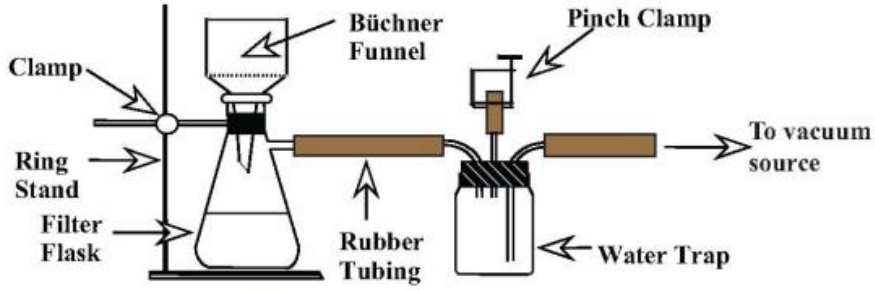


Figure1. Buchner filtration apparatus

When the aspirin crystals are dry, weigh them and record the mass. Assuming the reaction goes to completion, determine the percent yield for your synthesis. Salicylic acid (MW = 138 g/mol) Acetic anhydride (MW = 102 g/mol, density = 1.08 g/mL) Acetylsalicylic acid (MW = 180.16 g/mol).

For a TLC test, set aside roughly 100 mg of the crude product. The remainder of your crude product should be dissolved in a minimum amount of ethanol in a 125 mL Erlenmeyer flask while the alcohol is being warmed in water.

to affect the dissolving, bath. Based on the aspirin dosage, 10 to 30 mL of ethanol should be required. If any undissolved solids are present, filter the mixture to get rid of them.

25 mL of warm (approximately 50o C) water should be added to the clear alcohol solution. At this stage, if any crystals form, heat the flask's contents to cause them to dissolve.

Place the flask aside to chill while keeping a close eye on it. Cool the flask by covering it with cold water as crystals begin to form. After that, the crystallisation will have finished. Vacuum filter the crystals and collect them. Save your aspirin sample for future examination and let the crystals dry.

TLC EVALUATION

Your recrystallized product, your crude product, the salicylic acid starting material, and a sample of a brand-name aspirin tablet will all be subjected to a TLC analysis. Just a few milligrammes of each should be dissolved in 0.1 mL of ethanol. The commercial acid tablet must be crushed using a mortar and pestle before being dissolved.

Mark a piece of Silica/UV paper that is 7 cm × 2 cm, and then spot the paper with each solution. To make the dots visible under ultraviolet lighting, UV paper is utilized. In the wide mouth developing 4 chamber, add roughly 5 mL of the 80/10/10 petroleum ether/ethanol/ethyl acetate solution. To make the medium acidic, add a few drops of acetic acid. All of the acids ought to protonate as a result. Light the paper with the 254 nm Hg-UV lamp while developing the TLC plate and softly marking the spots. Determine the Rf for every component you can see.

ASPIRIN'S SPECTROSCOPIC ANALYSIS

It should be fascinating to examine how contemporary instrumental methods of analysis may reveal the identification and purity of a reaction product, even though some of the specifics of the spectroscopic techniques you will use to evaluate your aspirin are outside the purview of this course. You will get a vibrational spectrum for your purified product using a Fourier transform infrared spectrometer (FTIR) fitted with an attenuated total reflection (ATR) crystal, a gas chromatogram and mass spectrum using a gas chromatography mass spectrometer, and a proton nuclear magnetic resonance (NMR) spectrum for your purified product. These instrument located in BFIT institute laboratory. The laboratory incharge, will help run my sample.

For each assay, get your samples ready as follows:

NMR In a tiny sample vial, combine 50 mg of your aspirin with 1 mL of the deuterated chloroform/TMS solvent. Your solution can be a bit hazy; if so, filter it through a little plug of glass wool before putting it in the NMR tube.

FTIR For this study, a solid sample weighing around 10 mg will be used.

GCMS Fill a tiny sample vial with 0.5 mL of dichloromethane and 10 milligrammes of your aspirin.

Attached at the end of this document are an NMR spectrum, an FTIR-ATR spectrum, a GCMS chromatogram, and a spectrum of pure acetylsalicylic acid. The exact equipment that you will be utilising was used to collect this statistics.

METHOD FOR MAKING A FEW FLAVORING ESTERS

You can create a few typical esters if you have some extra time after the aspirin synthesis or while you're waiting.

The following steps should be followed in order to prepare flavoured esters:

• In a large test tube, combine 2 mL of alcohol and 2 g of carboxylic acid (or 2 mL if the material is a liquid). The test tube should be placed in a hot water bath (80 °C) for 5 to 10 minutes after adding 5 to 7 drops of concentrated (18 M) sulfuric acid and thoroughly swirling the mixture with a glass stirring rod. The water bath temperature shouldn't go over 65 °C for test tube #1.

- Take the test tube out of the hot water bath, then carefully pour the contents into a small beaker filled with 15 mL of saturated sodium bicarbonate. A sodium Any unreacted acid will be neutralised by bicarbonate.

• Pay attention to the scent that is given off by the end result of each esterification reaction. Create balanced equations for the esterification and the acid/sodium bicarbonate reactions as well as the structure of the generated esters.

SAFETY AND DISPOSAL

Both glacial acetic acid and 18 M H2SO4 are corrosive substances. After being in contact with these chemicals for at least 15 minutes, wash any exposed skin with water. Take off any clothes that has been exposed to these corrosive substances. Consult a medical expert if blistering happens.

Many organic substances can irritate the respiratory system, including glacial acetic acid. Do not inhale deeply from these items! You will work with the chlorinated hydrocarbons in the hood because they are known carcinogens.

When handling sulfuric acid, acetic acid, or acetic anhydride, as well as when cleaning up any spills that happen during this laboratory time, gloves must be used.

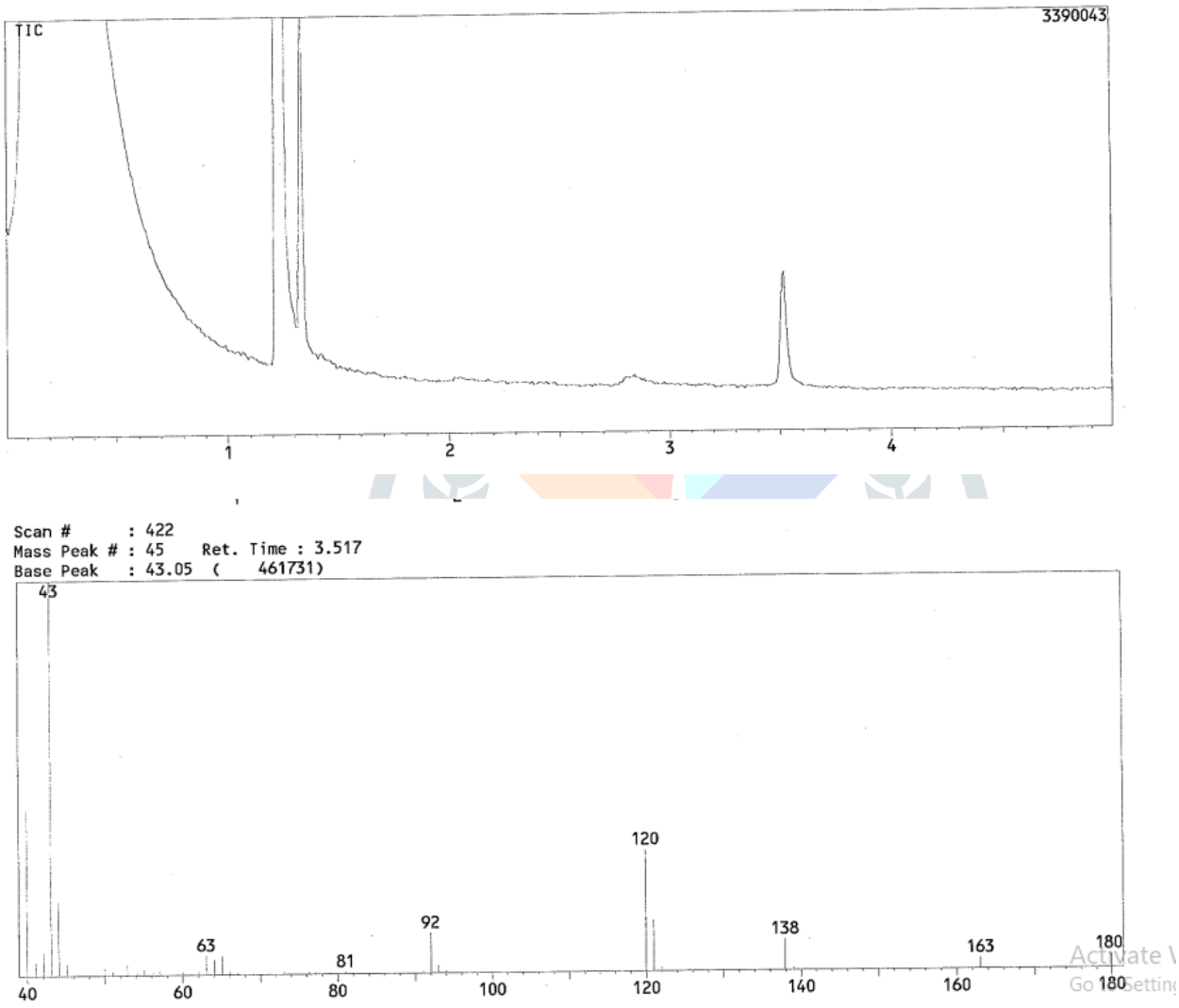
In acid solutions, acetic anhydride and water react violently. Make sure the test tubes are dry, and add strong acid at the reaction's initial stage. Acids that are diluted Don't add acetic anhydride to a diluted acid since it will result in unfavourable strong reactions (acetic anhydride is mainly water).

The experiment employed only organic substances, all of which are combustible. To heat organic solutions, use a hot plate instead of a Bunsen burner with a water bath.i can dispose of any watery chemicals in the sink.By adding more water to the sink, 18M H2SO4, glacial acetic acid, and acetic anhydride should be diluted and disposed of gently.

Aspirin and any other solid esters must be discarded in the jars for solid chemical waste.

In the organic waste carboy, organic liquids (liquid esters, alcohols, and TLC mobile phases) must be poured. Chloroform and dichloromethane, which contain halogens, must be poured into the carboy designated for halogen waste.

Used filter paper ought to be disposed of with other garbage.Used TLC plates should be placed in the container with the corresponding label.



EVALUTION OF ASPIRIN

The monsanto hardness test equipment was used to measure the hardness of the tablets.20 pills are weighed separately as part of a weight variation test. The average weight has been calculated, and each person's weight is contrasted with the average weight.

Test for friability

Friability is a measure of a tablet's mechanical toughness. If a tablet is more friable, it could not stay intact during handling, shipping, or packing. The following approach is performed to determine the friability using the Roche friabilator. The friabilator receives pre-weighed pills. With each rotation, the plastic chamber of the friabilator, which rotates at 25 revolutions per minute, drops the tablets six inches away. For at least 4 minutes, the tablets are rotated in the friabilator. At the conclusion of the test, the tablets are dusted and reweighed; the percentage loss in weight is the measure of friability and is stated as: % friability is equal to 1 x 100 (weight loss / starting weight).

ASSAY

20 pills are pulverised and weighed for the assay. An amount of powder weighing approximately 0.15g of aspirin is precisely weighed, 50ml of 0.1m sodium hydroxide is added, diluted with 100ml of water, shaken for 15 minutes, and then enough water is added to make 250ml. They are combined, filtered, and 10ml of the filtrate is diluted with 100ml of water. 10ml of the resultant solution is combined with 10ml of sodium hydroxide 0.1m, which has been diluted to 100ml with water. Using UV-visible spectroscopy, the absorbance of the resultant solution was measured at its highest at around 257nm.

Experimental setup

The disintegration investigation was as follows: medium: 30 cycles per minute for the water 37.50 degrees Celsius One tablet was placed into each of the device' six tubes, and the assembly was suspended in a water-filled beaker while the time it took for each tablet to dissolve was recorded. The average disintegration time was calculated from this.

Dissolution research: A type-2 paddle-type USP apparatus was used for the investigation. 900 ml of 6.8 ph phosphate buffer were used as the set condition, and 5 ml of samples were taken out every five, fifteen, and forty-five minutes. These samples were then replaced by The sample was appropriately diluted in a new equal amount of dissolving liquid before being measured at 280 nm using UV-visible spectroscopy. The drug concentration per ml was calculated using the calibration curve. Using a calibration curve, the quantity of medication release was determined.

Amount of drug release = $conc.\times vol.of.dissolutionmedium\times dilfactor$ 1000 percentage drug release = $amountofdrugreleasestrength$ x 100 report the formulation and a comparative analysis of commercially available aspirin pills was carried out.

CONCLUSION

While the pure aspirin had a less puffy, crystalline powder and is whiter, the impure (crude) aspirin was powered and fluffy with tiny clumps. This revealed clear parallels as well as noticeable variances between the two compounds, demonstrating that aspirin was manufactured to some extent. Before being recrystallized, the crude aspirin may have had contaminants like acetic acid (a product of the reaction process).

First, we attempted to synthesise aspirin by crystallising a commercial sample, but this experiment was unsuccessful because aspirin never crystallised and we were unable to complete the entire process on our own. Instead, we switched to another piece of equipment and discovered that salicylic acid, which has a molecular weight of 0.330 g, was synthesised by reacting excessively with acetic amhydride. The amount of aspirin product that is theoretically feasible is determined by the amount of salicylic acid utilised because too much acetic anhydride was used. The molecular weight of aspirin is 0.635 g.

This study demonstrates that NSAIDs like aspirin can induce persistent stomach damage, while L-glutamate has a clear protective effect. L-glutamate must be administered at a minimum dosage of 100 mg/kg. The extrusion spheronization process and fluidized bed coating can be used in tandem to create two-phase complex enteric granules. The produced pellets' test findings demonstrated that they have a white, spherical look. Additionally, yield might exceed 85%. The free salicylic acid release complies with the standard for quality.

The hydrogen bonding between the carboxylic acids of the two components was discovered to be the mechanism through which the medicine and coformer interacted.

REFERENCES

Jones A (2015*). Chemistry: An Introduction for Medical and Health Sciences*. John Wiley & Sons. pp. 5–6.

Ravina E (2011). *The Evolution of Drug Discovery: From Traditional Medicines to Modern Drugs*. John Wiley & Sons. p. 24.

"ASPIRIN"*American Society of Health-System Pharmacists*. 29 November 2021. On 25 April 2017.

effreys D (2008). Aspirin the remarkable story of a wonder drug. Bloomsbury Publishing USA. from the original on 8 September 2017.:PP 46-48

Hansen JM, Hallas J, Lauritsen JM, Bytzer P. Non-steroidal anti-inflammatory drugs and ulcer complications: a risk factor analysis for clinical decision-making. *Scand J Gastroentero.* 1996;31:126–30.

Laine L. GI risk and risk factors of NSAIDs. *J Cardiovasc Pharm.* 2006;47:60–S66.

Trask AV (2007) An overview of pharmaceutical cocrystals as intellectual property. *Mol Pharm* 4(3):301-309.

Kale DP, Zode SS, Bansal AK (2016) Challenges in translational development of pharmaceutical cocrystals. *J Pharm Sci* 2:1–14.

Chaudhari FM, Puttewar TY, Patil RY (2015) Solubility enhancement of aspirin by solid dispersion method. *Int J Pharm Pharm Res* 5(1):208–218

United States Pharmacopeia and National Formulary (2016) Rockville, MD*: United States Pharmacopeial Convention.*

Aspirin and tension-type headache - Ivano Farinelli , Paolo MartellettiJ - *Headache Pain* (2007) 8:49–55

Review Article The mechanism of action of aspirin J.R. Vane, R.M. Botting *; Thrombosis Research 110* (2003) 255–258.

Aspirin the novel antiplatelet drug D Pawar, S Shahani, S Maroli *HKMJ* 1998;4:415-8.

Steering Committee of the Physicians' Health Study Research Group. Final report on the aspirin component of the ongoing Physicians' Health Study. *N Engl J Med* 1989;321(3):129–135.

Walter Sneader, The discovery of aspirin: a reappraisal, *BMJ*. 2000 Dec 23; 321(7276): 1591–1594.