THE EFFECT OF RELATIVE HUMIDITY ON THE DISSOLUTION PROFILES OF CERTAIN BRANDS OF ASPIRIN TABLETS IN THE NIGERIAN MARKET.

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CERTIFICATION

We hereby certify that this work was carried out by **OBASOGIE OSARENMWINDAMWEN HARRY** in the department of Pharmaceutics and Pharmaceutical Technology , Faculty of Pharmacy, University of Benin, Nigeria as a project in partial fulfilment of the requirements for the award of Doctor of Pharmacy degree by the University.

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DEDICATION

This work is dedicated to God , for His guidance, love, protection and mercies throughout my undergraduate days. To my parents Mr and Mrs Obasogie and Dr Juliet Ese-Onakewhor whose enviable assistance ,love and unparalleled efforts have kept me on the path of success.

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TABLE OF CONTENTS

ABSTRACT

Ensuring that medications are effective is crucial for the pharmaceutical industry. Factors like humidity can have undesirable impact on the Dissolution Profiles of these drugs, which could affect their therapeutic efficacy. This study explores the frequently disregarded connection between humidity and the Dissolution Profiles of aspirin tablet for five popular brands in the Nigerian market. It is essential to understand this relationship to guarantee both patient safety and standard drug performance.

Aim and objectives: the aim of this study was to investigate how varying relative humidity affects the dissolution profiles of the various brands aspirin tablets after prolonged storage under these conditions.

Methods: The dissolution profiles of five well-known brands of aspirin tablets available in Nigeria were investigated using standard pharmacopeial methods. Two humidity levels, 0% and 70%, were used for the dissolution studies to replicate typical Nigerian ambient conditions. Dissolution Profiles were produced, and the rates and extents of dissolution under various humidity levels were compared.

Results : the results from the experiment showed that Elevated relative humidity seems to quicken the process of dissolution for the five brands of aspirin used in the study which could result in quicker drug release and absorption. On the other hand, reduced humidity can hinder drug disintegration and cause a delayed release of the medication.

Conclusion : This study confirmed that changes in the dissolution profiles occur when Aspirin tablets are stored under varying relative humidity conditions of 0% Relative humidity and 70%Relative humidity. This study revealed that there is an undesired reduction in the percentage of the drug released when stored at 0% relative humidity and also an undesired increase in the percentage of drug released when stored at 70% relative humidity as seen from the results over the 10 week period. It is imperative that patients, caregivers and even manufacturers are educated on the need to store tablets in facilities and areas of optimum relative humidity in order to preserve the efficacy of these drugs.

CHAPTER ONE

1.0.INTRODUCTION AND LITERATURE REVIEW

1.1.INTRODUCTION

The safety and efficacy of drugs is crucial to the healthcare industry. Drug use carries the risk of adverse events and other unintended outcomes, which can seriously injure patients and raise the expense of healthcare. It is the duty of healthcare professionals and pharmacists to guarantee and ensure that the medications they recommend and dispense to their patients are both efficacious and safe. The effectiveness of treatment can be impacted by slight variations in the rate of API disintegration,dissolution or release.(Lalić-Popović *et al.*, 2022)

An important concern in drug safety is the possibility of side effects from medicine use. The severity of adverse reactions might vary and can be attributed to multiple factors, including the stability of the medication. The safety and effectiveness of pharmaceutical products are significantly influenced by drug stability. The most beneficial medications are often safe and effective.

Drug stability is the degree to which a drug substance or product maintains the same qualities and attributes that it had when it was first manufactured, within predetermined bounds and during the course of its storage and usage. In other words, parameters related to its physical, chemical, microbiological, medicinal, and toxicological properties should remain unchanged from its initial state of production.

The possibility of side effects from medicine use is one of the main concerns in drug safety. Drug stability is one of the factors that might induce adverse effects, which can range in severity from mild to severe. Due to a decrease in dosage form concentration, unstable active pharmaceutical ingredients might result in undermedication of the drug.(*Tembhare, et al., 2019*)

Maintaining the stability, safety, and effectiveness of pharmaceutical medicines requires appropriate storage settings that protect them from external influences.

Stability testing is a crucial step in the development of any drug product. The main focus of stability testing is on assessing the chemical degradation to ensure that the product remains safe throughout the duration of its shelf-life.(Maclean *et al.*, 2022)

The outcomes of the stability testing include the prediction of the shelf life and the ideal storage conditions in addition to the assurance of the API quality. (Alhamdanv and Alfahad, 2021) The drugs must be subjected to high strains during the stability testing. This is an attempt to simulate the implications of extended storage under short time constraints.

Some of these high stresses include :

- Humidity
- Temperature
- Light Intensity.

In the context of chronic therapy, where daily, weekly, or monthly therapy can be separated, humidity is an intriguing component that should frequently not be disregarded since patients employ dose administration aids (DAAs). DAAs provide variable degrees of safeguarding against humidity to repackaged medication because they lack hermeticity. Dosage forms are taken out of their original packaging during this modification, an aspect that is not included in a typical stability research, which lasts for six months.

1.2.1. SHELF LIFE

The term "shelf life" describes the amount of time that, when stored properly, a product should stay stable, safe, and effective. The method of predicting shelf life is intricate and entails evaluating a number of variables that may have an impact on the product's stability over time. In order to predict the shelf life, several steps are involved. Presumably, during the designated storage step in certain store settings, the pharmaceutical manufacture matches for identification, purification, consistency, and hardness standards.(MAADH *et al.*, 2020)

- The product is first stored at varying degrees of these high stresses i.e Humidity, Temperature and Light Intensity in order to facilitate hastened degradation.
- Next, a reactant's concentration at each temperature, humidity and light intensity is determined.
- To determine the rate of reaction, samples are collected at various intervals of time.
- The concentration is plotted against time to establish a linear relationship.
- The reaction rate constant (k) for deterioration at each temperature, humidity and light intensity is shown by the slope of the line.
- The deterioration coefficient (k) at standard room temperature, humidity and moderate light intensity is then determined.
- The product's shelf life is then estimated by applying this value to the previously determined order of reaction.

The stability of pharmaceuticals is influenced by both product-related factors such as the active ingredient's chemical and physical properties, and environmental factors, such as temperature, humidity, and light. Pharmaceutical excipients, the dosage form and its composition, the production process, the nature of the container-closure system and the qualities of the packaging materials also play a role.

Only when strict storage guidelines as stated by the manufacturers are followed can the shelf-life of some preparations be guaranteed. Product integrity and shelf life are based on stability testing.(Wong and Datla, 2005)

In determining the stability of pharmaceutical products, certain aspects are key and they include :

1 Physical stability

1. Chemical stability
2. Microbiological stability
3. Accelerated stability study
4. Storage conditions

The stability of a drug product is related not only to the intrinsic chemical stability of the drug molecule, but also to the physical forms, manufacturing processes, interactions

among formulation components, container closure systems, and storage conditions (Guo, 2009)

1.2.2. PHYSICAL STABILITY

The ability of a pharmaceutical product to preserve its physical qualities, such as appearance, texture, and other features, over the course of its shelf life is referred to as physical stability in the context of pharmaceuticals. Ensuring the drug's usage, safety, and efficacy requires physical stability.

Physical stability is achieved by preserving a product's initial physical attributes, such as appearance, homogeneity, dissolution, and suspension properties. In addition to chemical stability, the physical stability of pharmaceutical products must also be evaluated to ensure that the product performance is not affected by storage. (Maclean *et al.*, 2022)

In addition to factors like solubility and hygroscopicity, it has also been shown that the mode of deformation of a material can influence the physical stability (Maclean *et al.*, 2022) . Several important factors are taken into account while evaluating the physical stability of medications in solid dosage forms, like tablets or capsules, in order to guarantee the effectiveness and quality of the pharmaceutical product and these include:

. For solid dosage forms to be accepted by patients, their appearance and integrity is essential. To maintain the integrity of the dosage form, it is crucial to keep an eye out for any changes in color, shape, size, or other physical flaws.

. Tablets in particular need to be kept at the proper hardness to prevent breaking or crumbling during handling and transit. Friability testing evaluates a tablet's propensity to shatter or chip when handled.

. Drug release from tablets and capsules depends on the disintegration time. By keeping track of the disintegration time, one can make sure that the medicine is released for absorption when the dosage form dissolves or fragments within the allotted period.

1.2.3. CHEMICAL STABILITY

Chemical stability, or the capacity of a pharmaceutical product to retain its chemical composition over time, is a crucial component in medication development and manufacture. In order to maintain the effectiveness, safety, and caliber of medications, it is imperative that variables that may cause chemical deterioration are observed and managed. Drug potency can be lost, and the drug's appearance can alter, as a result of chemical degradation events like hydrolysis, oxidation, isomerization, polymerization, and photochemical decomposition. (Florence and Attwood, 2006)

When the incident light's wavelength falls within the drug's absorption range, photolysis—where the drug molecule absorbs radiation and degrades—occurs (Florence and Attwood, 2006) . The solubility of the drug in suspension is influenced by temperature. (Florence and Attwood, 2006) . To determine a product's shelf life, testing must be conducted using the actual product at a realistic storage temperature, either in a refrigerator or at room temperature. The specific protocol for testing the photostability of new drugs and products is outlined in the ICH Guideline (ICH HARMONISED TRIPARTITE GUIDELINE, 2003).

1.2.4. MICROBIOLOGICAL STABILITY

Products lose their effectiveness through degradation, which causes them to no longer meet physical, chemical, microbiological, and therapeutic criteria. Microorganisms break down the product, making it dangerous for the patients. Therefore, it depends on the kind of microorganism and the potential amount of toxicity it produces. Contamination in ocular or parenteral formulations has the potential to be very harmful, but is not exactly harmful in other nonsterile products. The primary sources of microflora in medicines include workers, raw materials, processing equipment, and water utilized during manufacturing. Products lose their effectiveness through degradation, which causes them to no longer meet physical, chemical, microbiological, and therapeutic criteria. Microorganisms break down the product, making it dangerous for the patients. Therefore,

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1.2.5. CHEMICAL REACTIONS THAT CAUSE DRUG DEGRADATION

Many drugs are derivatives of carboxylic acid or contain functional groups based on this moiety, for example esters, amides, lactones, lactams, imides or carbamates (Florence and Attwood, 2006). As a result, the medication may degrade due to a variety of chemical interactions. Hydrolysis, oxidation, photochemical reactions, polymerization, isomerization, racemization, and dehydration are some examples of these reactions.

1.3. HYDROLYSIS AND SOLVOLYSIS

Since many medications contain hydrolysable functional groups, hydrolysis is the most prevalent method via which pharmaceuticals are broken down. It is the process by which water and medication molecules combine to produce breakdown products with distinct chemical compositions. In the liquid state, hydrolysis happens more easily than in the solid state. It can happen in aqueous medication solutions that are just partially soluble. There might be enough water in tablets and other solid dose forms to enable the drug hydrolyze.

The breakdown of chemical bonds in a solvated (dissolved) state is a common process in solvolysis reactions. In solvolysis, the solvent is essential to the reaction because it facilitates bond breakage and acts as a medium for interaction between the reactants. The speed of the reaction and the production of the product can be greatly influenced by the type of solvent used.

1.3.1. ESTER HYDROLYSIS

One of the most prevalent causes of drug instability is the hydrolysis of medications containing an ester functional group, such as procaine, atropine, etc. Usually, acyl-oxygen cleavage is involved in this bimolecular process. Ester hydrolysis is depending on the particular compound and the pH of the solution and is catalyzed by (H+) or (OH−) ions.

1.3.2. AMIDE HYDROLYSIS

Amides are generally more stable to hydrolysis than esters.(Remington, 2006).the amide bond in penicillins and cephalosporins is a portion of the strained four-membered ß-lactam rings. Numerous buffers, hydroxyl and hydrogen ions, and other ions catalyze their breakdown. These substances can't be combined to make solutions because they are too unstable.The amide bond in penicillins and cephalosporins is a portion of the strained four-membered ß-lactam rings. Numerous buffers, hydroxyl and hydrogen ions, and other ions catalyze their breakdown. These substances can't be combined to make solutions because they are too unstable.

1.3.3. OXIDATION

An electronegative atom or radical is added during oxidation, or an electropositive atom, radical, or electron is removed. The most frequent route of oxidative drug degradation is known as "autoxidation," and it occurs when a reaction involving molecular oxygen (O═O) takes place. Chain processes made up of three simultaneous reactions—initiation, propagation, and termination—may be involved in oxidative degradation by autoxidation. Free radicals, which are produced from organic molecules by the action of light, heat, or transition metals like copper and iron—which are found in tiny amounts in practically every buffer—can serve as an initial source. In general, first- or second-order kinetics govern oxidation in solution. Ascorbic acid, ferrous sulfate, adrenaline, and riboflavin are examples of oxidation reactions that are redox processes in which electrons are lost without oxygen being added. Numerous more degradative reactions, such as addition,

dehydration, polymerization, isomerization, acylation, transesterification, etc., have been explored in addition to oxidation and hydrolysis.

1.3.4. PHOTOCHEMICAL DEGRADATION

These are the processes that result from visible or ultraviolet light absorption. After absorbing photons of light, or energy, the reactant molecule becomes excited. The photodecomposition product is subsequently produced by the excited molecule. In many photochemical reactions, the energy of the incident radiation is absorbed by a mediator who then passes it to the reactant molecule, activating it, rather than the reactant molecule directly. A photosensitizer is one kind of mediator. At times, a molecule can act as a protector for the photolabile drug by preferentially absorbing the radiant energy and produce products. These compounds are referred to as screening agents.(Halbert, 2001)When a medication undergoes photodegradation, it is deemed practically significant if the compound absorbs light more than 300nm and the photodegradation manifests itself quickly.

1.3.4.1.SOURCES OF LIGHT FOR PHOTODEGRADATION STUDIES

Most medicinal chemicals have a white appearance, which indicates that, depending on their chemical makeup, they may absorb in the UV spectrum. These ultraviolet spectrum has been further subdivided into 3 subbands .(Creed, 1984)

1. UV-C: sometimes known as far UV or shortwave, is the spectrum between 200nm and 290nm. This band is absent from sunlight at the surface of the earth because it is absorbed by ozone and molecular oxygen in the upper atmosphere. UV-C sources that are employed in forced medication photodegradation research include welding arcs, discharge and germicidal lamps, and other artificial radiation sources (stress-conditions). These also seriously harm the cornea and skin.
2. The UV-B: band spans the wavelength range of 280nm to 320nm. It is the cause of many compounds' direct photoreaction in natural sunshine, as well as sunburn, skin cancer, and other biological impacts.

3. UV A: Since it is close to the visible zone, the UV-A band, also known as near-UV, is the long wavelength region between 320NM AND 400nm.

1.3.5. PHYSICAL PROPERTIES OF ASPIRIN

Usually, aspirin is seen as a solid or powder that is white and crystalline. Aspirin's appearance can change based on factors like crystal structure and particle size. It has a melting point range of about 135–136°C (275-277°F). it has a chemical formula or $C_9H_8O_4$. The purification and characterization of aspirin during the production process depend on this particular melting point. Aspirin dissolves more readily in organic solvents like ethanol and acetone than it does in water. Its solubility in water at room temperature is about 1 g/L, which may have an impact on how it dissolves and also, its bioavailability. Particle size variations in aspirin can affect characteristics like flowability and dissolving rate. Particle sizes can range from fine powders to bigger crystals.

1.3.5.1.PHARMACOLOGY OF ASPIRIN

Acetylsalicylic acid (ASA), another name for aspirin, is a nonsteroidal anti-inflammatory medication (NSAID) that acts as an antithrombotic and reduces fever, inflammation, and/or pain. Since its discovery in the late 19th century, aspirin is a medicinal substance that has been essential to healthcare. Aspirin, which was first recognized for its exceptional analgesic and antipyretic qualities, is now a vital component in the treatment of pain, inflammation, and cardiovascular disorders. Its cost and extensive use have helped make it one among the most widely used medications in the world. (Adina *et al.*, 1999) Aspirin is used to treat some inflammatory disorders, such as pericarditis, rheumatic fever, and in management of Arthritis. COX-1 is irreversibly inhibited by aspirin, whereas COX-2's enzymatic activity is altered. Prostanoids, which are mostly pro-inflammatory, are often produced by COX-2. (Adina *et al.*, 1999)

1.3.6. SYNTHESIS OF ASPIRIN

Aspirin production is categorized as an esterification reaction. When salicylic acid is treated with the acid derivative acetic anhydride, a chemical reaction occurs in which the hydroxyl group of salicylic acid becomes an ester group (R-OH → R-OCOCH3). Acetic acid, which is regarded as a byproduct of this reaction, and aspirin are produced during this procedure. Catalysts are nearly always small amounts of sulfuric acid (and sometimes phosphoric acid).

1.3.7. MECHANISM OF ACTION

Aspirin and other non-steroid anti-inflammatory drugs (NSAIDs) inhibit the activity of the enzyme now called cyclooxygenase (COX) which leads to the formation of prostaglandins (PGs) that cause inflammation, swelling, pain and fever. (Vane and Botting, 2003)

1.3.8. PHARMACOKINETICS OF ASPIRIN

1.3.8.1.ABSORPTION

There is a noticeable decrease in upper gastrointestinal (GI) tract platelet function within 60 minutes of aspirin absorption. This antiplatelet activity is associated with a prolonged bleeding duration and suppression of TXA2-dependent platelet aggregation.

Aspirin's absorption is considerably delayed by its enteric coating. Although the benefits of aspirin extend for around 10 days, the plasma half-life of the drug is barely 20 minutes. This is because platelets are unable to produce new COX. Platelet COX activity recovers by approximately 10% each day following an aspirin dose, depending on platelet turnover. Although it may take 10 days for the complete platelet population to be replenished, and therefore restore normal COX activity, it has been proven that if as low as 20 percent of platelets have normal COX activity, hemostasis may be normal. Enteric coating formulations have been developed in response to the observation of gastrointestinal intolerance to salicylate in certain patients.

1.3.8.2.DISTRIBUTION

Salicylate quickly permeates the bodily fluid reservoirs. In the plasma, it binds to albumin. The unbound proportion rises as overall plasma salicylate concentrations rise. Salicylate has the potential to pass through the placental barrier and into breast milk.

1.3.8.3.METABOLISM

Aspirin is quickly biotransformed into salicylate, an active metabolite. As a result, aspirin's half-life is extremely brief. The liver is primarily responsible for the metabolism of salicylate. The primary mechanism of this metabolism is hepatic conjugation with either glucuronic acid or glycin, which each need distinct metabolic pathways. The most common route is the saturable conjugation with glycin. This mechanism facilitates the metabolism of 90% of salicylate at low aspirin dosages. Salicylate's half-life lengthens with increasing dosage and is dependent on the primary metabolic pathway utilised at a particular concentration.Salicylate's half-life lengthens with increasing dosage and is dependent on the primary metabolic pathway utilised at a particular concentration.

1.3.8.4.ELIMINATION

Ten percent of the total amount of salicylate eliminated is excreted in the urine in its unaltered form. Salicylate excretion is the consequence of passive tubular reabsorption, active proximal tubular secretion via the organic acid transporters, and glomerular filtration. The amount of free ionized salicylate excreted increases from 3 percent of the total salicylate dose to more than 80 percent when the urinary pH climbs from 5 to 8. Urinary excretion is clearly pH dependent. Urine also contains salicylate metabolites that are expelled.(Vane and Botting, 2003)

1.3.9. CONTRAINDICATIONS

The contraindications of aspirin are classified as absolute or relative. (Mekaj *et al.*, 2015) . Active peptic ulcer, aspirin allergy, aspirin intolerance, thrombocytopenia, inherited bleeding disorders, recent history of gastrointestinal bleeding, recent history of cerebral

hemorrhage, renal impairment, and severe liver illness are among the absolute contraindications. Ages under 21 (increased risk of Reye syndrome), concomitant anticoagulation therapy, concurrent use of nonsteroidal anti-inflammatory medications, and poorly managed hypertension are among the relative contraindications of aspirin (risk of intracranial bleeding).

1.3.9.1.ASPIRIN TOXICITY

Salicylate ingestion continues to be a common cause of poisoning in children and adolescents. (Muhammad, 2022) . Since aspirin-containing analgesic medicines are so widely available and may be found in almost every home, they are frequent causes of accidental and suicidal intake. However, the introduction of child-resistant containers and reliance on other analgesics have reduced the frequency of salicylate poisoning in children. The link of salicylate with Reye syndrome has led to a major drop in its use, and repackaging has reduced the quantity of the drug that youngsters can access that can be fatal. (Muhammad, 2022) . A comprehensive review of the existing medical literature on methyl salicylate poisoning has determined that it is a relatively common source of pediatric exposures. (Davis, 2007) .

1.4.0. THE NEED FOR ACCELERATED STABILITY STUDY.

- All drugs break down with time. It is interesting to note that even seasoned formulators may encounter difficulties while assessing this breakdown procedure. This is due to the fact that a formulation with care will inherently take longer to break down.
- It is standard procedure to expose a formed product to "high stress" conditions—that is, particular combinations of temperature, humidity, and light intensity that encourage degradation—in order to assess the product's stability. (*ICH HARMONISED TRIPARTITE GUIDELINE*, 2003)
- Instability in most recent formulations frequently goes undetected until the items are stored for extended periods of time .

- Stability testing takes less time because of these high stress conditions, which speed up product deterioration.
- As a component of the official stability testing protocol, these investigations use fictitious storage circumstances in an effort to accelerate the pace of chemical deterioration and physical changes in a medicine.(*ICH HARMONISED TRIPARTITE GUIDELINE*, 2003)
- These studies speed up the time it takes for a successful product to hit the market by collecting more data in less time, which enables early detection of inadequate formulations.
- It is important to exercise caution when extrapolating the results of accelerated testing to standard storage settings.
- It is important to remember that the outcomes of accelerated testing tests do not necessarily indicate physical changes.
- Significant changes are observed under accelerated conditions, which are defined as a 5% potency loss from the initial assay value of a batch, exceeding the specified limits 27 of any specified degradants, exceeding pH limits, or exceeding specified dissolution limits for 12 capsules or tablets. (*ICH HARMONISED TRIPARTITE GUIDELINE*, 2003)

In the long run, well-formulated formulas will degrade more slowly than badly-formulated ones. Stability can be projected at recommended storage conditions once the best preparation has been determined.

1.4.1. GENERAL PRINCIPLES OF STABILITY TESTING

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity, and light,(*ICH HARMONISED TRIPARTITE GUIDELINE*, 2003)

A key component of evaluating pharmaceutical goods' stability in a shorter amount of time is accelerated stability testing, which involves subjecting them to high stress environments. In order to forecast a product's long-term stability more quickly, these

tests are intended to give information regarding the product's stability under accelerated conditions.The systematic method to stability evaluation includes information on the drug substance's stability as a fundamental component.

It is likely that a single batch of the pharmacological material will be used for stress testing. It should include the impact of humidity (e.g., 75 percent RH or above) and temperatures (in 10°C increments, e.g., 50°C, 60°C, etc.) above that for accelerated testing suitable levels of oxidation and photolysis on the medicinal ingredient. Stress testing should include photostability testing as a fundamental component. Use storage conditions that are greater than usual, usually 40°C/75 % relative humidity. Realistic temperatures should be used because Reaction at very high temperatures may not have any relevance, because they do not show ambient storage conditions.(Ebrahim *et al.*, 2021)

A shorter time frame for evaluation should be used. This shortened period of time makes it possible to evaluate possible stability problems more quickly.

The Arrhenius Equation serves as the foundational formula for the accelerated stability model. The relationship between a chemical reaction's rate constant, reaction temperature, and activation energy is expressed by this equation . Generally speaking, the reaction rate can double or quadruple for every 10 C increase in temperature (depending on the free energy of activation). This means that for every 10 C increase in solution temperature, we should expect twice as much deterioration. The Arrhenius equation is as follows:

$K = \frac{Ae-Ea}{RT}$ ----------(Equation 1)

$Log\ K = \frac{Log\ A - Ea}{2.303 \times RT}$ --------(Equation 2)

Where, K= rate constant

R= gas constant =1.987 cal/mole

T = absolute temperature A = frequency factor

Ea = energy of activation

T10% = (2.303/K)*(log100/90) T90% = (2.303/K)*(log100/10)

The activation energy can be found by conducting tests at various temperatures and calculating the slope of the resulting linear connection by graphing the natural logarithm of the reaction rate against the reciprocal of the absolute temperature (in Kelvin). Carrying out the experiment at too high temperature does not mirror real life ambient storage temperature and therefore becomes unrealistic.

1.4.2. METHODS OF DRUG ANALYSIS

Pharmaceutical testing and analysis can be used to examine the physical, chemical, and authentic qualities of pharmaceuticals as well as their active component content. This information helps to guarantee the drugs' stability and appropriate and efficient use.(Hussain and Saood, 2017)

1.4.3. CHEMICAL METHODS OF ANALYSIS

The primary application of chemical techniques in drug analysis is continuous analysis with great dependability and accuracy. They are not amenable to automation, though, and can be laborious and complex. However, because they are the easiest to carry out and need significantly less pricey in comparison to instrumental methods. The primary chemical analysis methods are pH, titrimetric, and gravimetric measurements.

1.4.4. TITRIMETRIC ANALYSIS

Acid-base titrimetry is the process of analyzing a drug's composition based on how much of a standard solution is consumed. It is done by measuring the volume of a solution containing a reagent that is added to the drug's solution until the chemical reaction is completed. The content of the measured component can be determined by measuring the volume and concentration of the reagent solution.

The chemical technique that is most frequently used to analyze drug samples is acid-base titration. the pharmaceutical sector since it is frequently utilized in the examination of raw materials, raw samples, intermediate goods, and final products.

1.4.5. DETERMINATION OF PH METHOD

pH is the negative logarithm of the hydrogen ion activity of a solution and it is used to indicate the acidity or alkalinity of a solution. The pH meter, sometimes referred to as the acidity meter, is a device consisting of an electrometer and an indicator used to detect pH. The glass electrode and the saturated calomel electrode comprise the main cell utilized in the pH measurement. and the solution prepared for measurement. The glass electrode is the indicating electrode, while the calomel electrode acts as a reference electrode to demonstrate the electrode's potential.

The pH value testing method is now a common practice for medications included in the pharmacopoeia of many countries worldwide.

1.5.0 INSTRUMENTAL METHODS OF DRUG ANALYSIS

1.5.1. SPECTROPHOTOMETRIC METHOD

1.5.1.1UV/VISIBLE SPECTROSCOPY

A chemical substance's molecules or atoms interact with electromagnetic radiation, and this interaction is measured using Absorption spectrophotometry. In pharmaceutical analysis, methods like UV, visible, infrared, and atomic absorption are commonly used. Colorimetry is the term used to describe spectrophotometric measurements in the visible spectrum.(Creed, 1984)

The primary idea behind spectroscopic technology is that various wavelengths and frequencies can be used to radiate the medicine that has to be detected. When the frequencies fall inside a specific range of wavelengths.

When a substance accepts wavelengths, vibration and rotation take place. A spectrum will be produced following the recording of information such as the

wavelength of maximum absorption which will allow the drug's absorbance values to be determined and its concentration examined. When doing medication examines by spectroscopy it is frequently important to set up a scope of groupings of a standard example of the analyte and measure the absorbance of every arrangement. (Shantier, 2020)

The molecular absorption of light by a drug substance in a solution increases with the concentration of the substance.(Creed, 1984) . By measuring the absorbance at a single wavelength, it is feasible to calculate the analyte's concentration. To find the wavelength of maximum absorption, first run a wavelength scan on the reference pure sample. The wavelengths of standard samples with known concentrations are measured and used to create a calibration curve. This calibration curve is then used to extrapolate the unknown quantity.

1.6.0. RATIONALE FOR THE STUDY

The following important factors serve as justification for examining how humidity affects aspirin stability, with a special emphasis on dissolution profiles:

1.6.1. ASPIRIN'S SIGNIFICANCE AS A THERAPEUTIC AGENT

1.6.1.1.ANALGESIC PROPERTY

As an analgesic, aspirin relieves mild to moderate pain, which is one of its main uses. Aspirin reduces pain perception by blocking the cyclooxygenase enzymes, which inhibits prostaglandin formation. This property makes aspirin an invaluable tool for treating headaches, toothaches, muscle pains, and other types of discomfort.

1.6.1.2.ANTIPYRETIC EFFECTS

Due to its antipyretic qualities, aspirin is a very useful medication for lowering fever, which is a common sign of inflammatory and viral diseases. Aspirin helps relieve fever and related symptoms by reducing increased body temperature by its

effect on the hypothalamus, improving patient comfort and speeding healing from diseases. (Weaver, *et al.*, 2011)

1.6.1.3.ANTI-INFLAMMATORY ACTIVITY

Aspirin has strong anti-inflammatory qualities in addition to its analgesic and antipyretic effects. Aspirin reduces inflammation, swelling, and redness associated with a variety of acute and chronic inflammatory illnesses, such as tendinitis, arthritis, and autoimmune disorders, by preventing the production of pro-inflammatory prostaglandins.(Chime *et al.*, 2020)

1.6.1.4.ANTIPLATELET ACTION

Aspirin's antiplatelet activity is arguably one of its most important functions in clinical practice because it helps prevent thrombotic events by irreversibly acetylating and inhibiting platelet cyclooxygenase-1 (COX-1), which in turn lowers the amount of thromboxane A2, a powerful platelet aggregator. (Bath *et al.*, 2018) Because of this mechanism of action, aspirin serves as a the core therapy for averting cardiovascular events like myocardial infarction and ischemic stroke. (Warner, *et al.*, 2011)

1.6.2. ASPIRIN'S ASESSIBILITY

The adaptability and accessibility of aspirin are among its most notable qualities. Because aspirin is a widely accessible and reasonably priced drug, people from a wide range of socioeconomic backgrounds can use it. Its proven safety profile when used appropriately and adaptability to treat a wide range of illnesses highlight its indispensable role in contemporary healthcare.

1.6.3. ENVIRONMENTAL FACTORS' EFFECT ON THE STABILITY OF PHARMACEUTICALS

Temperature, Humidity and Light are only a few of the environmental elements that affect pharmaceutical stability. Humidity is one of these that has been found to be

crucial and has a big influence on the physicochemical characteristics of medications. To ensure that aspirin remains safe and effective for the duration of its shelf life, it is crucial to comprehend how humidity affects its stability.

1.6.4. INSUFFICIENT KNOWLEDGE ABOUT HOW HUMIDITY AFFECTS ASPIRIN STABILITY

Aspirin's significance as a medication is widely known, but we still don't fully grasp how humidity influences the drug's stability. The effects of temperature, light, and other environmental conditions on pharmaceutical stability have been thoroughly studied; however, the specific impact of humidity on the stability of aspirin, especially in dissolving tests, has gotten relatively less attention. There are various variables that lead to this incomplete comprehension:(Raimi-Abraham *et al.*, 2017). In the past, temperature and light exposure have been the main factors in studies on the stability of medications. These elements have the potential to affect the safety and effectiveness of drugs by hastening processes of degradation like hydrolysis, oxidation, and photolysis. Because of this, studies on pharmaceutical stability have mostly focused on temperature and light as crucial variables, frequently ignoring humidity.In the past, temperature and light exposure have been the main factors in studies on the stability of medications. These elements have the potential to affect the safety and effectiveness of drugs by hastening processes of degradation like hydrolysis, oxidation, and photolysis. Because of this, studies on pharmaceutical stability have mostly focused on temperature and light as crucial variables, frequently ignoring humidity.

The effects of humidity on the stability of pharmaceuticals are intricate and varied. Humidity can affect stability through both chemical processes like hydrolysis and degradation as well as physical mechanisms like moisture absorption, in contrast to temperature and light, which predominantly cause chemical reactions. The complex interactions among moisture content, molecular interactions, and formulation features pose a challenge in identifying and characterizing the precise impacts of humidity on aspirin stability. (Alhamdanv and Alfahad, 2021) . In addition to

organoleptic parameters, mechanical properties are tracked throughout stability studies involving solid dose forms. Dissolution profile alterations are given special consideration when prescribing medications that are poorly soluble. Deprivation of therapeutic efficacy may result from modifications to the mechanical properties and rates of dissolution of some medications. (Lalić-Popović *et al.*, 2022)

1.6.5. VARIABILITY IN ENVIRONMENTAL CONDITIONS

Humidity levels and other environmental parameters can vary greatly based on a number of variables, including location, time of year, and storage environment. Additionally, during production, packing, distribution, and storage, pharmaceutical formulations could be subjected to varying humidity levels. A thorough and methodical examination is necessary to comprehend the combined effect of these varied settings on aspirin stability, as this has not been done in prior investigations.

1.6.6. LIMITED EXPERIMENTAL DATA

Although aspirin is widely used in clinical practice and humidity is known to have a significant role in pharmaceutical stability, there is deficiency of thorough experimental evidence explaining the precise effects of humidity on aspirin stability, especially in dissolving investigations. Because temperature, light, and pH are known to have a substantial impact on medication stability, these parameters have historically received the majority of attention in studies on pharmaceutical stability. Although it is known that humidity is a significant environmental characteristic, in experimental research, these other factors frequently take center stage. Because of this, there hasn't been much funding or research dedicated to examining how humidity affects the stability of aspirin. Because of the complex interactions between moisture content, molecular interactions, and formulation features, researching the effects of humidity on aspirin stability necessitates the use of advanced experimental settings and methodology. The technological difficulties in precisely controlling humidity levels, preserving consistent environmental

conditions, and precisely measuring variations in aspirin stability may discourage scientists from conducting in-depth experimental studies.

In a groundbreaking work, (Smith *et al.*, 2017) showed that aspirin hydrolyzes when exposed to high humidity, producing salicylic and acetic acids as a byproduct. It was discovered that this hydrolysis process was a major element regulating aspirin's rate of solubility and, consequently, its bioavailability. The results emphasized how crucial humidity management is to the production and storage of pharmaceuticals.

This research was furthered by (Sutcliffe *et al.*, 2013) , who emphasized the importance of humidity in pharmaceutical stability. Their research highlighted how important it is to maintain exact humidity control at every stage of the medication development process, from formulation to packing. The authors emphasized the possible repercussions of failing to maintain humidity management, such as alterations in medication strength and the deterioration of active components.

Together, these findings lay the groundwork for the current investigation, which emphasizes the negative effects of humidity upon the stability of aspirin. The extant literature, however, does not fully address the impact on dissolving kinetics and does not provide a thorough explanation about the molecular and chemical alterations that underlie these observations.

The incomplete knowledge of how humidity affects aspirin stability has real-world ramifications for quality assurance, production of pharmaceuticals, and compliance with regulations. Manufacturers may find it difficult to improve formulation procedures, create suitable packaging, and set up storage conditions that guarantee the stability and effectiveness of aspirin products if they lack a thorough understanding of the impact of humidity. Guidelines for humidity management in pharmaceutical facilities may be difficult for regulatory bodies to set, which could result in variations in the quality and safety of products.

These dissolution studies are essential for explaining the complex connection between aspirin stability and humidity. The purpose of the experimental setup was

to assess how humidity affects aspirin stability by means of a controlled environment and methodical sample preparation. To replicate the conditions of pharmaceutical manufacturing, storage, and actual real world use, a range of humidity levels was used. Reliability and reproducability of the results were ensured by carefully considering the exposure period, sample size, and replication.

1.7. AIM AND OBJECTIVES OF THE STUDY

The aim of this study was to investigate the effect of varying relative humidity on the dissolution profiles of aspirin tablets with time after storage under these conditions.

Specific objectives of this research are:

I. To assess and evaluate the organoleptic properties of the various brands of aspirin tablets.
II. To investigate if these brands of aspirin tablets meet the official standards.
III. To evaluate the physicochemical properties of each brand of aspirin tablets used in the study and ensure they fall within acceptable limits.
IV. To quantify the active pharmaceutical ingredient in each brand of aspirin tablets.
V. To evaluate the dissolution profiles of the various brands of aspirin tablets used in the study.
VI. To provide a suitable guide for industrial pharmacists, community pharmacists, healthcare practitioners and patients on the proper storage condition to protect aspirin tablets against the effects of humidity.

CHAPTER TWO

MATERIALS AND METHOD

2.1. MATERIALS

To ensure consistency and quality, JQC HUAYIN PHARMACEUTICAL CO. LTD, Huayin city, Shaanki, China. provided high-purity aspirin powder. All chemicals and reagents used in this study were of standard analytical grade.

Additional materials used also included:

- 0.1N hydrochloric acid in the dissolution medium to mimic normal physiological conditions
- Five different brands of aspirin tablets (four of which were 75mg tablets and one was 300mg) were purchased from pharmacy shops in Benin City.

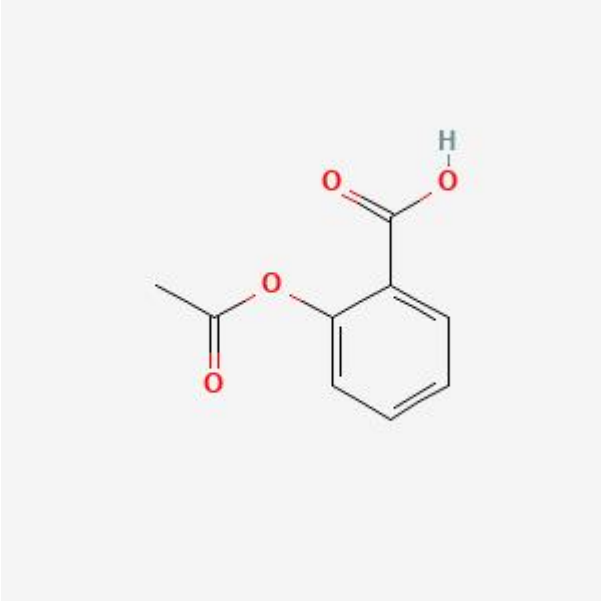

Figure 2.1 : The chemical Structure of Aspirin.

Its IUPAC name is 2-Acetoxybenzoic acid. The percentage purity of the reference sample used is 98%.

2.1.2. PHYSICAL APPEARANCE OF ASPIRIN TABLETS.

Aspirin tablets come as 75mg and 300mg , coated and uncoated tablets. Both strengths were employed in the study and were purchased from different registered pharmaceutical outlets in Benin City, Edo State. Information on validity, labeled strength, batch number, manufacture date, NAFDAC registration number and manufacturers address were recorded from the product label.

2.1.3. HUMIDITY CHAMBERS

Humidity chambers are used to study how humidity affects the stability of drugs. Two desiccators were used to simulate humidity chambers during this research. The first chamber was prepared by placing about 5g of salt (NaCl) into the desiccator and adding up to 2cm of water into the desiccator to simulate a 70% humidity environment for the research. The second chamber was prepared by adding desiccant (activated silica gel) into the desiccator in order to reduce the moisture in the chamber and simulate low/ zero humidity. (Freeman *et al., 2015).* A hygrometer was used to confirm that the relative humidity of the environments were as stated. 100 tablets of each brand of the drug were placed in each of these humidity chambers.

2.2. METHOD

2.2.1. SAMPLE PREPARATION

To guarantee purity, consistency, and quality, pharmaceutical-grade aspirin samples were procured from reliable companies. Pharmacopeial standards and regulatory regulations were fully met by the aspirin utilized in the study. To avoid mixing up samples and guarantee traceability throughout the experiment, each aspirin sample was precisely identified and tagged with necessary information, such as its batch number, expiry date, NAFDAC registration numbers, and other relevant details.

2.2.2. EVALUATION OF ORGANOLEPTIC PROPERTIES

Physical evaluation of the color, shape, presence or lack of surface coating, scoring, and manufacturer's imprints of the five (5) distinct brands of aspirin tablets utilized in the study were used to assess the organoleptic qualities of the tablets.

2.2.3. WEIGHT UNIFORMITY TEST

Ten (10) aspirin tablets from each of the several brands were chosen at random and weighed separately on a digital analytical balance. The entire weight was then added together and divided by the number of tablets used to get the average weight of the ten tablets.

find the average weight. The weight of each tablet was divided by its average (mean) weight to find the percentage variation. It is anticipated that the individual weight's percentage departure from the average weight won't go above the specified limit of ± 7.5%.(Zaid *et al.*, 2013)

2.2.4. FRIABILITY TEST

After carefully selecting and precisely weighing Ten (10) tablets from each brand, the pills were carefully placed in a Roche friabilator and set to rotate at 25 rpm for four minutes. The weight loss was determined by reweighing the tablets and calculating the variations in weight.

Between the starting and finishing weights. The percentage of weight loss was used to calculate the friability. This information was taken from the formula:

$$\text{Friability (\%)} = \frac{\text{Initial weight (W1)} - \text{final weight (W2)}}{\text{Initial weight (W1)} \times 10} \quad \text{----------(Equation 3)}$$

For tablets and capsules, the USP, IP, and BP state that an overall reduction in weight (percentage friability) of not higher than 1.0% is permitted for tablets and capsules. (Sangramsinh *et al.*, 2015)

2.2.5. HARDNESS TEST

Ten (10) tablets of each brand of Aspirin were individually placed in a vertical position on a fix anvil, and the plunger pushed to lock the tablet in between. This method was utilized with the Monsanto hardness tester. The plunger was kept moving until the tablet broke. The average force (calculated as kPa) as well as the standard deviation were measured, calculated and recorded.

2.2.6. DISINTEGRATION TEST

A Manesty disintegration tester with water as the disintegration medium was used for this test. This is to simulate conditions of the stomach at 37^{o}C The disintegration apparatus's tubes held six (6) tablets of the same brand of Aspirin, which were shaken continuously in water kept at 37°C. Using a stopwatch, the time it took for each tablet to fully breakdown and pass through the mesh of the disintegration tube was recorded. The other brands underwent the same process again. Each brand's result was computed and given as mean standard deviation.

2.2.7 DISSOLUTION TEST

First, a standard calibration plot (also known as a Beer-Lambert's Plot) was calculated using the pure (reference) Aspirin sample in O.1N HCl. A series of Aspirin solutions, ranging in concentration from 0 µg/ml to 100 µg/ml, were made, and the corresponding absorbance were recorded using a UV/Visible spectrophotometer with two stations that was set to record at a wavelength where the maximum absorbance was 265 nm. The amount of drug contained was determined by creating a graph of its respective concentrations versus the acquired absorbance values.

Next, each tablet brand's in vitro dissolution study was conducted using the USP apparatus for dissolving (Paddle technique). One tablet of each Aspirin brand was added to a beaker that contained 900 milliliters of 0.1N HCl, the leaching or dissolving fluid,

and was submerged in a water bath with a thermostat set to maintain a temperature of 37 ± 0.50 degrees Celsius.

The device was calibrated to rotate at 50 revolutions per minute (rpm). Ten milliliters of the solution were withdrawn and put into appropriate sample containers for examination at different intervals. To keep the dissolution condition consistent, the precise volume of the sample that was removed was replaced with the leaching fluid (O.INHCL) at the same temperature after each withdrawal. A UV/Visible spectrophotometer was used to measure the absorbances of the extracted solutions at 265 nm (United States Pharmacopoeia 2009).

2.2.8 CONTENT UNIFORMITY TEST

In a dry, clean mortar, ten (10) pills of each brand were ground into a fine powder. To achieve a concentration of 1 mg/ml solution, an equivalent of 100 mg of the active drug ingredient was weighed and put into a 100 ml volumetric flask with a solution of distilled water and ethanol. After that, the mixture was filtered through Whattman filter paper, and 10ml of the filtrate were taken out and subjected to a spectrophotometric measurement at 265 nm to determine the solution's absorbance (United States Pharmacopoeia 2011). This was done before exposing the tablets to relative humidity.

2.2.9. ANALYTICAL METHOD AND STATISTICAL ANALYSIS

Descriptive statistical analysis and data presentation was done using Microsoft excel 21 for windows. Same weight uniformity, friability, disintegration, hardness and dissolution studies and UV Spectrophotometric analysis were carried out on the tablets subjected to different humidities in the humidity chambers at weekly intervals for 10 weeks to determine if the behaviour of the tablets for the time period especially the dissolution profile and extent of drug released were affected by subjecting these tablets to the various humidity conditions over time.

CHAPTER THREE

3.0. RESULTS AND DISCUSSION

3.1. LABELLING INFORMATION

Results of the labelling information gathered from the samples evaluated are shown in Table 3.1. Based on the information gathered, all five (5) brands were within their designated validity periods and shelf life. Additionally, it demonstrated that every sample gathered for the research had the necessary NAFDAC approval numbers, which are needed to ascertain the products' authenticity. The packaging and labellings for all brands employed in this study conformed to NAFDAC specified guidelines. (NAFDAC 2019)

Table 3.1: Labeling Information of the Different Brands of Aspirin Tablet.

Code	Brand name	Batch no	Manufacturing date	Expiry date	Labelled strength	NAFDAC No	Country Of Origin
ASA 1	Vasoprin®	1907	08/2023	07/2026	75mg	04-1797	Nigeria
ASA 2	Emprin®	4537A	09/2021	09/2024	75mg	04-8344	Nigeria
ASA 3	Microprin® (film coated)	2202124	02/2022	02/2025	75mg	04-7193	Nigeria
ASA 4	Anacin®	A2256	11/2022	11/2025	300mg	04-2225	Nigeria
ASA 5	Shalina ® (film-coated)	2374535	09/2022	08/2025	75mg	A4-100136	India

3.2.Organoleptic Properties Of The Different Brands Of Aspirin Tablet.

The organoleptic characteristics of the various aspirin tablet brands that were evaluated are presented in Table 3.2.

All tablets ranged from white to off-white except one (i.e ASA 1) which was orange in colour. Tablets are often coloured to add aesthetics , enhance patients' acceptance and compliance , for easy identification and sometimes to protect against photodegradation for such light sensitive drugs.

All tablets of the various brands were circular bi-convex (i.e for three brands) while two brands were oblong in shape.

Only one brand was scored. Scoring of tablets enables the patient to obtain lower doses of the drug especially in certain situations when lower doses may be required for peadiatric patients (Shaharia *et al., 2020).*

Out of the five brands of aspirin evaluated, two were film coated as indicated by the product label while the remaining brands were conventional tablets. By implication, the conventional uncoated tablet brands are expected to release their content in the stomach for maximum absorption while the film coated were expected to have maximum release in the small intestine.

All brands evaluated had company logo/ inscription which is relevant for easy identification especially in conditions of poisoning.

Table 3.2 : Showing the organoleptic properties of the different aspirin tablets

Code	Colour	Shape	Scored	Coating	Inscriptions
ASA 1	Orange	Circular bi-convex	No	No	V/JHL
ASA 2	Off white	Circular bi-convex	Yes	No	Emzor
ASA 3	White	Oblong	No	Yes	-----
ASA 4	White	Circular bi-convex	No	No	▲
ASA 5	White	Oblong	No	Yes	S/75

3.3.Effects of Relative Humidity on the Physicochemical Properties of the brands of Aspirin.

The effects of relative humidity on the physical properties of the tablets from the different brands are detailed below:

3.3.1. Effects of Relative Humidity on the Weight Uniformity of the Aspirin tablets

The effects of relative humidity on the weight uniformity is shown in table 3.8.2 and 3.8.3.

This characteristic (i.e weight uniformity) is important since it makes sure that every batch of tablets is within the proper range of sizes. (Al-Dujaili, *et.al.*, 1986) It also indicates content homogeneity, which clarifies the drug's effectiveness. not more than two of the individual weight by more than 5% and none should deviate by more than 10% of the average weight.('The British Pharmacopoeia', 2007)

Tables 3.3.1 displays the result of the uniformity of weight, of the 5 distinct brands of Aspirin before subjection to storage under the varying humidity conditions. The weight fluctuation and uniformity of the five brands were observed. The standard deviations from the mean weight, when expressed, were determined to be within acceptable specification of less than ± 5%. Tables 3.3.1.2 amd 3.3.1.3 show results for the weight uniformity test for the five brands of aspirin stored under 0% relative humidity and 70% relative humidity. For the tablets stored under 70% relative humidity , it was observed that there was increase in weight of the tablets over the 10 week period while for the tablets stored at 0% there was decrease in the average weight of the tablets over the 10-week period.

N.B: All weights are computed in grams(g)

Table 3.3.1 : showing the mean weight of tablets for the different brands and the standard deviation before subjection to accelerated relative humidity.

S/N	ASA 1	ASA 2	ASA 3	ASA 4	ASA 5
1	0.170	0.128	0.265	0.428	0.268
2	0.155	0.129	0.275	0.429	0.274
3	0.175	0.125	0.280	0.430	0.258
4	0.160	0.126	0.280	0.430	0.272
5	0.190	0.124	0.290	0.424	0.271
6	0.165	0.130	0.265	0.430	0.265
7	0.150	0.128	0.295	0.428	0.263
8	0.175	0.125	0.270	0.425	0.257
9	0.182	0.127	0.291	0.426	0.282
10	0.145	0.126	0.289	0.432	0.278
MEAN WEIGHT	0.168	0.127	0.275	0.427	0.267
STANDARD DEVIATION	0.0680	0.0016	0.019	0.0022	0.0216

Table 3.3.1.2: Weight uniformity readings for tablets stored under relative humidity of 0%

NB:All weights are computed in grams(g)

Weights are recorded for 10 tablets each for each brand

Date	Vasoprin	Emprin	Microprin	Anacin	SHALINA
Day 1	1.558	1.270	2.761	4.284	2.678
Day 2	1.556	1.268	2.753	4.280	2.677
Day 3	1.552	1.265	2.730	4.275	2.675
Week 1	1.547	1.262	2.623	4.266	2.660
Week 2	1.546	1.262	2.534	4.252	2.654
Week 3	1.541	1.260	2.482	4.251	2.651
Week 4	1.535	1.257	2.300	4.249	2.649
Week 5	1.531	1.256	2.232	4.246	2.643
Week 6	1.529	1.253	2.203	4.241	2.635
Week 7	1.528	1.249	2.170	4.224	2.632
Week 8	1.525	1.247	2.168	4.213	2.632
Week 9	1.519	1.248	2.161	4.201	2.626
Week 10	1.517	1.243	2.157	3.993	2.624

Table 3.3.1.3: Weight uniformity readings for tablets stored under relative humidity of 70%

NB: 1. All weights are measured in grams(g)

2 . weights recorded are for 10 tablets of each brand

Date	Vasoprin	Emprin	Microprin	Anacin	SHALINA
Day 1	1.650	1.192	2.774	4.290	2.671
Day 2	1.662	1.208	2.774	4.293	2.682
Day 3	1.669	1.208	2.775	4.295	2.682
Week 1	1.678	1.209	2.775	4.327	2.688
Week 2	1.695	1.212	2.775	4.339	2.692
Week 3	1.696	1.212	2.775	4.341	2.692
Week 4	1.696	1.215	2.774	4.341	2.692
Week 5	1.698	1.215	2.775	4.345	2.693
Week 6	1.698	1.215	2.776	4.346	2.693
Week 7	1.701	1.215	2.776	4.348	2.693
Week 8	1.701	1.216	2.776	4.348	2.693
Week 9	1.703	1.216	2.776	4.348	2.693
Week 10	1.704	1.217	2.776	4.352	2.694

3.3.2. Effects of Relative Humidity on the Friability of the tablets.

The results of the friability test carried out on the tablets before subjection to relative humidity are shown in Tables 3.4.1 while the results for the effect of 70% relative humidity and 0% humidity are shown in Table 3.4.3 and 3.4.4. The percentage friability result revealed that all five brands had extremely low levels of friability, demonstrating the tablets' excellent compactness and ability to endure mechanical stress during handling, packaging, and transportation without experiencing any kind of capping or damage to the tablet's surface. This technique is used to assess the physical strength of uncoated tablets after they are subjected to mechanical shock and wear and tear. The results of a friability test indicate the level of mechanical stress that tablets can tolerate during production, handling, and distribution and also by the patients. As stated in the United States Pharmacopoeia and the British Pharmacopoeia from 2007, the maximum percentage of friability should not exceed 0.8% and 4%, respectively. Every brand passed the test based on the B.P as seen in tables 3.4.1 and 3.4.2. at the end of the 10 week period, it was observed that there was no significant change in the friability of the tablets subjected to both 0% and 70% relative humidity.

Table 3.4.1: Result for Friability Test for the tablets before subjection to relative humidity.

NB: 1. All weights are measured in grams(g)

S/N	ASA 1	ASA 2	ASA 3	ASA 4	ASA 5
1	0.149	0.124	0.282	0.430	0.256
2	0.151	0.117	0.279	0.428	0.263
3	0.149	0.118	0.270	0.420	0.253
4	0.152	0.121	0.278	0.427	0.264
5	0.150	0.125	0.271	0.422	0.260
6	0.148	0.120	0.272	0.432	0.265
7	0.153	0.121	0.276	0.425	0.258
8	0.150	0.123	0.277	0.418	0.268
9	0.147	0.116	0.268	0.426	0.261
10	0.149	0.121	0.272	0.429	0.254
MEAN	0.1506	0.1206	0.275	0.424	0.262

Table 3.4.3: Result for bi-weekly Friability Test for tablets stored under relative humidity of 70%. The results show the mean weight for 10 tablets for each brand.

NB: all weights are computed in grams(g)

S/N	ASA 1	ASA 2	ASA 3	ASA 4	ASA 5
Week 2	0.149	0.124	0.282	0.430	0.256
Week 4	0.151	0.117	0.279	0.428	0.263
Week 6	0.149	0.118	0.270	0.420	0.253
Week 8	0.152	0.121	0.278	0.427	0.264
Week 10	0.150	0.125	0.271	0.422	0.260

Table 3.4.4: Result for bi-weekly Friability Test for tablets stored under relative humidity 0%. The results show the mean weight for 10 tablets for each brand.

NB: all weights are computed in grams(g)

S/N	ASA 1	ASA 2	ASA 3	ASA 4	ASA 5
Week 2	0.155	0.128	0.273	0.423	0.259
Week 4	0.149	0.123	0.281	0.421	0.261
Week 6	0.156	0.121	0.278	0.416	0.258
Week 8	0.148	0.130	0.271	0.419	0.257
Week 10	0.153	0.124	0.280	0.417	0.260

3.3.3. Content Uniformity of the tablets.

The results of the content uniformity test for the different aspirin brands are shown in table 3.4.5. From the results seen in table 3.4.5, all five brands of aspirin tablets used passed the test and met the pharmacopoeia specification.

When a product has the same amount of the active ingredient in the same dosage formulation and gets administered at the same molar doses under similar conditions, with no variation in the drug's availability at the site of action, it is deemed pharmaceutically equivalent to the innovator brand. (Shams *et al.*, 2011)

tablets should contain not less than 95% and not more than 105% of the label strength.(‘The British Pharmacopoeia’, 2007) .

Table 3.4.5 : Result for Content Uniformity Test for the various aspirin brands using a uv spectrophotometer.

Brand Code	Percentage Content (%)
ASA 1	102.05
ASA 2	102.40
ASA 3	99.90
ASA 4	101.35
ASA 5	99.60

3.3.4. Effects of Relative Humidity on the Hardness of the tablets.

The results of the mean hardness of aspirin for each brand is displayed in Table 3.4.6. according to the results from tables 3.4.7 and 3.4.8, When a Monsanto hardness tester applied pressure to the tablets with varying crushing strengths, it was found that all of the tablets suffered from diametric fracture. It is important to note that the higher humidity content had a negative influence on the tablets' breaking resistance, although almost insignificantly given the brief testing period. Analogous data have been achieved by other research. concluded that tablets soften when there is a 70% rise in humidity. The presence of humidity within the aspirin tablet pores can function as an internal lubricant, so reducing friction, facilitating sliding, improving the transmission of compression force through the compact, and decreasing the adhesion of the tablets to the tablet matrix. (Al-Dujaili, *et al.*, 1986)

Table 3.4.6: Result for Hardness Test

1. Note that hardness is measured in kPa

S/N	ASA 1	ASA 2	ASA 3	ASA 4	ASA 5
1	3.00	4.00	9.00	4.00	4.00
2	4.00	4.00	9.00	4.00	5.00
3	4.00	4.00	8.00	4.00	5.50
4	4.00	4.50	10.00	4.00	7.00
5	3.50	5.00	9.00	4.50	6.00
6	4.00	4.00	8.00	4.00	7.50
7	4.00	5.00	9.50	4.50	7.00
8	4.00	4.50	8.00	4.00	5.00
9	4.50	4.00	9.00	4.00	6.00
10	4.00	4.00	8.00	4.00	4.00
MEAN	3.90	4.30	8.75	4.10	5.70

Table 3.4.7 Result for bi-weekly Hardness Test performed on tablets stored under relative humidity of 70%

1. Note that hardness is measured in kPa

S/N	ASA 1	ASA 2	ASA 3	ASA 4	ASA 5
Week 2	4.00	4.00	11.00	4.00	8.00
Week 4	4.00	4.00	10.00	4.00	8.00
Week 6	4.00	3.50	10.00	4.00	7.50
Week 8	3.50	3.50	10.00	4.00	7.00
Week 10	3.00	3.00	9.00	3.50	6.00

Table 3.4.8 Result for bi-weekly Hardness Test performed on tablets subjected to relative humidity of 0%

1. Note that hardness is measured in kPa

S/N	ASA 1	ASA 2	ASA 3	ASA 4	ASA 5
Week 2	4.00	4.00	9.00	4.00	8.00
Week 4	4.00	4.00	10.00	4.00	8.00
Week 6	4.00	4.00	9.00	4.00	8.50
Week 8	4.00	4.00	8.00	4.00	7.00
Week 10	4.00	3.50	9.00	3.50	7.00

3.3.5. Effects of Relative Humidity on the Disintegration profile of the tablets

The results of the disintegration test for the various brands of aspirin tablet before exposure to relative humidity are shown in table 3.5.1.

The results of disintegration test carried out on tablets subjected to 70% and 0% Relative Humidity are shown in tables 3.5.2 and 3.5.3. Both humidity conditions increased the disintegration rate of the tablets.

Drugs must initially be in solution in order for the body to absorb them easily. For the majority of tablets, the disintegration process which breaks the tablet down into tiny particles or granules is the first and most crucial step toward a solution. (Bamgbola et al, 2018) . For uncoated tablets, the maximum disintegration time is fifteen minutes. ('The British Pharmacopoeia', 2007)

Disintegration is influenced by the kind, method, and caliber of binding agent utilized in the formulation. According to the results in table 3.5.1, every brand passed the test, with the exception of ASA 3 and ASA 5, which took more than fifty-five minutes. However, given that both brands are slow-release tablets, this may have something to do with it. According to USP and BP, the disintegration time of an uncoated tablet is 15 minutes, whereas that of a coated tablet is 30 minutes.

Table 3.5.1 Results For The Disintegration Test

Note that the results for the disintegration test were computed in Seconds

	ASA 1	ASA 2	ASA 3	ASA 4	ASA 5
Tab 1	32	40	>45mins	309	>45mins
Tab 2	33	40	>45mins	300	>45mins
Tab 3	33	42	>45mins	307	>45mins
Tab 4	35	40	>45mins	310	>45mins
Tab 5	35	41	>45mins	305	>45mins
Tab 6	35	41	>45mins	311	>45mins
MEAN	33	40	>45mins	307	>45mins
STANDARD DEVIATION	1.744	0.66	-	3.96	-

Table 3.5.2 Results For The bi-weekly Disintegration Test for tablets subjected to relative humidity of 70%

Note that the results for the disintegration test were computed in Seconds

	ASA 1	ASA 2	ASA 3	ASA 4	ASA 5
Week 2	30	37	>45mins	298	>45mins
Week 4	28	34	>45mins	287	>45mins
Week 6	27	26	>45mins	272	>45mins
Week 8	21	24	>45mins	268	>45mins
Week 10	17	20	>45mins	253	>45mins

Table 3.5.3 Results For The bi-weekly Disintegration Test for tablets subjected to 0% humidity environment with desiccant.

Note that the results for the disintegration test were computed in Seconds

	ASA 1	ASA 2	ASA 3	ASA 4	ASA 5
Week 2	32	36	>45mins	303	>45mins
Week 4	29	36	>45mins	297	>45mins
Week 6	27	28	>45mins	284	>45mins
Week 8	25	27	>45mins	273	>45mins
Week 10	22	25	>45mins	262	>45mins

3.3.6. Effects of Relative Humidity on the dissolution profiles of the Problets

Table 3.6.1 shows the results of the dissolution profiles of tablets of the different aspirin brands before subjection to relative humidity while tables 3.6.2 to 3.7.3 shows the results of the dissolution profile of the various brands of aspirin after subjecting them to relative humidity over a 10 week period. Figures 3.2 to 3.7.2 illustrate the changes in dissolution profiles of the five aspirin brands which occurred during the 10-week test period on the tablets stored at 0% relative humidity and 70% humidity.

From the results obtained in table 3.6.1, three of the brands assayed ASA1 ASA 2 and ASA 4 passed the dissolution test according to USP (2007) which stipulates that at least 70% of the content would have been released by 30 minutes. ASA 3 and ASA 5 failed the test because both tablets are slow release tablet formulations.

From the results obtained, in tables 3.6.2 to 3.7.3, there is a trend of decrease in the percentage of drug released with time for the aspirin tablets stored at 0% humidity over the 10 week period and a progressive increase in amount and percentage of drug released with time for the tablets stored at relative humidity of 70% over the same period.

When a medication dissolves, it releases its dose form and becomes accessible for later gastrointestinal absorption. Pharmaceutical solid dosage forms' dissolution analysis is a crucial quality control technique that can be used as a delicate technique for distinguishing between different drug formulations. (Shams *et al.*, 2011) A medication's ability to dissolve from its dosage form depends on a variety of factors, including the drug's physicochemical characteristics, the dosage form's formulation, and the manufacturing process. As a result, regular dissolution testing of pharmaceuticals in the market is vital to guarantee the availability of high-quality medications (Raimi-Abraham *et al.*, 2017) .

In order to ascertain the degree to which humidity influences Aspirin release profile if the tablet is exposed to these circumstances which is conceivably possible if the drug is removed from its original packaging, which might happen during the course of weekly or monthly therapy the impact of humidity over a brief ten-week period was studied.

Table 3.6.1: Result for the Dissolution Test on the different Aspirin Brands before Subjection to various Humidity conditions

DATE: 29/01/2024 **WAVELENGTH:265nm**

Brand	Time(min)	Absorbance(nm)	Concentration (mcg/ml)	Amount released(mg)	Percentage released(%)
Vasoprin (ASA 1)	5	0.029	10.71	9.64	12.85
	10	0.059	21.43	19.28	25.71
	15	0.075	27.14	24.42	32.57
	20	0.081	29.29	26.35	35.14
	25	0.105	37.85	34.07	45.42
	30	0.168	60.35	54.32	72.42
	45	0.215	77.14	69.42	92.57
	60	0.226	81.07	72.96	97.20
Emprin (ASA 2)	5	0.032	11.79	10.61	14.15
	10	0.059	21.43	19.27	25.71
	15	0.073	26.43	23.79	31.71
	20	0.086	31.07	27.96	37.29
	25	0.099	35.71	32.14	42.86
	30	0.183	65.71	59.14	78.86
	45	0.212	76.07	68.46	91.29
	60	0.224	80.36	72.32	96.43
Microprin (ASA 3)	5	0.001	0.710	0.643	0.86
	10	0.001	0.710	0.643	0.86
	15	0.004	1.786	1.607	2.14
	20	0.005	2.142	1.929	2.57
	25	0.005	2.142	1.929	2.57
	30	0.008	3.210	2.890	3.86
	45	0.017	6.420	5.786	7.71
	60	0.022	8.21	7.393	9.86

Anacin (ASA 4)	5	0.092	33.21	29.89	9.96
	10	0.221	79.28	71.36	23.79
	15	0.472	168.92	152.04	50.67
	20	0.679	242.86	218.57	72.86
	25	0.728	260.35	234.32	78.12
	30	0.862	308.20	277.39	92.46
	45	0.868	310.36	279.32	93.10
	60	0.900	321.78	289.60	96.54
Shalina	5	0.001	0.710	0.643	0.86
Aspirin	10	0.001	0.710	0.643	0.86
(ASA 5)	15	0.001	0.710	0.643	0.86
	20	0.005	2.142	1.929	2.57
	25	0.005	2.142	1.929	2.57
	30	0.010	3.930	3.536	4.71
	45	0.021	7.860	7.071	9.42
	60	0.028	10.36	9.320	12.43

Table 3.6.2: Result for the bi-weekly Dissolution Test on the different Aspirin Brands subjected to relative Humidity of 70%

DATE: week 2 **TIME: 3:30PM** **WAVELENGTH:265nm**

Brand	Time(min)	Absorbance(nm)	Concentration (mcg/ml)	Amount released(mg)	Percentage released(%)
Vasoprin (ASA 1)	5	0.030	10.84	9.75	13.20
	10	0.061	21.71	19.54	26.10
	15	0.076	27.51	24.74	32.96
	20	0.081	29.72	26.62	35.47
	25	0.106	38.35	34.53	45.98
	30	0.170	61.22	55.00	73.27
	45	0.218	78.32	70.31	93.66
	60	0.229	82.23	73.90	98.26
Emprin (ASA 2)	5	0.032	11.79	10.61	14.15
	10	0.059	21.43	19.27	25.71
	15	0.074	26.79	24.11	32.14
	20	0.087	31.52	28.31	37.72
	25	0.111	36.17	32.53	43.42
	30	0.186	66.59	59.88	79.89
	45	0.215	77.00	69.34	92.40
	60	0.227	81.26	73.22	97.87
Microprin (ASA 3)	5	0.001	0.710	0.643	0.86
	10	0.001	0.710	0.643	0.86
	15	0.004	1.786	1.607	2.14
	20	0.005	2.142	1.929	2.57
	25	0.005	2.142	1.929	2.57
	30	0.008	3.210	2.890	3.86
	45	0.017	6.420	5.786	7.71
	60	0.022	8.21	7.393	9.86

Anacin (ASA 4)	5	0.093	33.63	30.26	10.00
	10	0.230	80.27	72.21	24.14
	15	0.478	171.00	153.81	51.31
	20	0.687	245.82	221.41	73.92
	25	0.737	263.58	237.22	79.22
	30	0.869	311.97	280.72	93.81
	45	0.879	314.12	282.94	94.41
	60	0.920	325.74	293.92	97.78
Shalina	5	0.001	0.710	0.643	0.86
Aspirin	10	0.001	0.710	0.643	0.86
(ASA 5)	15	0.001	0.710	0.643	0.86
	20	0.005	2.142	1.929	2.57
	25	0.005	2.142	1.929	2.57
	30	0.010	3.930	3.536	4.71
	45	0.021	7.860	7.071	9.42
	60	0.028	10.36	9.320	12.43

Table 3.6.3: Result for the bi-weekly Dissolution Test on the different Aspirin Brands subjected to relative Humidity of 70%

DATE: week 4 **WAVELENGTH:265nm**

Brand	Time(min)	Absorbance(nm)	Concentration (mcg/ml)	Amount released(mg)	Percentage released(%)
Vasoprin (ASA 1)	5	0.030	10.92	9.86	13.34
	10	0.062	21.91	19.78	26.40
	15	0.075	27.84	25.12	33.34
	20	0.079	30.08	26.93	35.87
	25	0.107	38.78	34.95	46.55
	30	0.170	61.87	55.12	74.11
	45	0.221	79.12	70.82	94.73
	60	0.230	82.41	74.68	99.44
Emprin (ASA 2)	5	0.032	11.89	10.72	14.31
	10	0.060	21.67	19.51	26.10
	15	0.072	27.14	24.45	32.51
	20	0.084	31.90	28.63	38.15
	25	0.113	36.62	32.90	43.93
	30	0.191	67.39	60.63	80.84
	45	0.219	77.90	70.19	93.52
	60	0.230	82.21	74.20	99.04
Microprin (ASA 3)	5	0.001	0.712	0.646	0.89
	10	0.001	0.713	0.649	0.90
	15	0.004	1.784	1.605	2.13
	20	0.005	2.144	1.928	2.56
	25	0.005	2.145	1.923	2.57
	30	0.008	3.212	2.892	3.87
	45	0.017	6.421	5.786	7.79
	60	0.022	8.213	7.391	9.87

Anacin (ASA 4)	5	0.094	34.00	30.62	10.14
	10	0.234	81.20	73.03	24.43
	15	0.482	173.06	155.72	52.01
	20	0.692	248.92	224.23	74.95
	25	0.743	266.74	240.18	80.18
	30	o.882	315.76	284.23	94.73
	45	0.892	317.74	286.18	95.40
	60	0.930	328.63	297.27	98.82
Shalina	5	0.001	0.709	0.642	0.88
Aspirin	10	0.001	0.710	0.643	0.90
(ASA 5)	15	0.001	0.710	0.643	0.90
	20	0.005	2.143	1.934	2.56
	25	0.005	2.145	1.938	2.59
	30	0.010	3.937	3.538	4.76
	45	0.021	7.862	7.074	9.51
	60	0.028	10.365	9.325	12.49

Table 3.6.4: Result for the bi-weekly Dissolution Test on the different Aspirin Brands subjected to relative Humidity of 70%

DATE: week 6 **WAVELENGTH:265nm**

Brand	Time(min)	Absorbance(nm)	Concentration (mcg/ml)	Amount released(mg)	Percentage released(%)
Vasoprin (ASA 1)	5	0.031	10.97	9.91	13.45
	10	0.063	22.02	19.87	26.54
	15	0.076	27.98	25.25	33.51
	20	0.079	30.23	27.07	36.15
	25	0.108	39.00	35.12	46.80
	30	0.171	62.18	55.40	74.49
	45	0.221	79.52	71.18	95.21
	60	0.231	82.82	75.06	99.93
Emprin (ASA 2)	5	0.033	11.95	10.72	14.38
	10	0.062	21.78	19.51	26.17
	15	0.073	27.25	24.45	32.64
	20	0.084	31.98	28.75	38.44
	25	0.113	36.62	32.90	43.93
	30	0.191	67.39	60.63	80.84
	45	0.219	77.90	70.19	93.52
	60	0.230	82.21	74.20	99.30
Microprin (ASA 3)	5	0.0011	0.721	0.652	0.89
	10	0.0012	0.723	0.653	0.91
	15	0.0041	1.797	1.621	2.145
	20	0.0053	2.164	1.940	2.59
	25	0.0053	2.164	1.940	2.59
	30	0.0081	3.241	2.917	3.91
	45	0.0173	6.475	5.833	7.87
	60	0.0224	8.280	7.464	9.96

Anacin (ASA 4)	5	0.095	34.29	30.86	10.20
	10	0.237	81.78	73.49	24.60
	15	0.487	174.28	156.92	52.43
	20	0.698	250.87	226.15	75.62
	25	0.750	268.51	241.90	80.81
	30	0.891	318.98	287.16	95.40
	45	0.901	320.67	288.44	96.10
	60	0.940	330.66	298.90	99.61
Shalina	5	0.0011	0.715	0.647	0.89
Aspirin	10	0.0012	0.717	0.648	0.908
(ASA 5)	15	0.0012	0.717	0.648	0.908
	20	0.0051	2.164	1.954	2.64
	25	0.0051	2.164	1.954	2.64
	30	0.0101	3.973	3.568	4.81
	45	0.0211	7.931	7.131	9.59
	60	0.0281	10.450	9.420	12.59

Table 3.6.5: Result for the bi-weekly Dissolution Test on the different Aspirin Brands subjected to relative Humidity of 70%

DATE: week 8 **WAVELENGTH:265nm**

Brand	Time(min)	Absorbance(nm)	Concentration (mcg/ml)	Amount released(mg)	Percentage released(%)
Vasoprin (ASA 1)	5	0.0312	11.00	9.92	13.53
	10	0.0632	22.12	19.94	26.63
	15	0.0764	28.15	25.35	33.57
	20	0.0795	30.31	27.18	36.26
	25	0.1090	39.14	35.24	46.95
	30	0.1720	62.38	55.60	74.74
	45	0.2218	79.78	71.38	95.49
	60	0.2320	83.20	74.92	99.32
Emprin (ASA 2)	5	0.031	10.97	9.91	13.45
	10	0.063	22.02	19.87	26.54
	15	0.076	27.98	25.25	33.51
	20	0.079	30.23	27.07	36.15
	25	0.108	39.00	35.12	46.80
	30	0.171	62.18	55.40	74.49
	45	0.221	79.52	71.18	95.21
	60	0.231	82.82	75.06	99.93
Microprin (ASA 3)	5	0.0011	0.721	0.652	0.89
	10	0.0012	0.723	0.653	0.91
	15	0.0043	1.799	1.624	2.19
	20	0.0055	2.167	1.942	2.62
	25	0.0056	2.168	1.944	2.64
	30	0.0081	3.241	2.917	3.91
	45	0.0173	6.475	5.833	7.87
	60	0.0224	8.280	7.464	9.96

Anacin (ASA 4)	5	0.098	34.72	31.31	10.34
	10	0.242	82.97	74.93	24.99
	15	0.494	176.99	159.58	53.28
	20	0.708	254.50	229.90	77.00
	25	0.761	272.24	246.00	81.92
	30	0.904	323.79	291.95	96.36
	45	0.905	323.92	292.00	96.89
	60	0.953	331.00	299.18	99.71
Shalina	5	0.0011	0.715	0.647	0.89
Aspirin	10	0.0012	0.717	0.649	0.910
(ASA 5)	15	0.0012	0.717	0.649	0.910
	20	0.0051	2.164	1.954	2.64
	25	0.0051	2.164	1.957	2.64
	30	0.0101	3.973	3.568	4.81
	45	0.0211	7.931	7.131	9.60
	60	0.0281	10.450	9.420	12.59

Table 3.6.6: Result for the bi-weekly Dissolution Test on the different Aspirin Brands subjected to relative Humidity of 70%

DATE: week 10 **WAVELENGTH:265nm**

Brand	Time(min)	Absorbance(nm)	Concentration (mcg/ml)	Amount released(mg)	Percentage released(%)
Vasoprin (ASA 1)	5	0.0314	11.05	9.92	13.58
	10	0.0632	22.15	19.94	26.63
	15	0.0765	28.19	25.35	33.59
	20	0.0798	30.38	27.18	36.28
	25	0.1092	39.14	35.25	46.95
	30	0.1726	62.38	55.67	74.78
	45	0.2218	79.78	71.37	95.49
	60	0.2324	83.27	74.98	99.76
Emprin (ASA 2)	5	0.031	10.97	9.91	13.45
	10	0.063	22.02	19.87	26.54
	15	0.076	27.98	25.25	33.51
	20	0.079	30.23	27.07	36.15
	25	0.108	39.00	35.12	46.89
	30	0.171	62.18	55.40	74.70
	45	0.223	79.52	71.18	95.36
	60	0.234	82.96	75.10	99.98
Microprin (ASA 3)	5	0.0011	0.721	0.652	0.89
	10	0.0012	0.723	0.653	0.91
	15	0.0043	1.799	1.624	2.19
	20	0.0055	2.167	1.942	2.62
	25	0.0056	2.168	1.944	2.64
	30	0.0084	3.243	2.914	4.20
	45	0.0173	6.475	5.833	7.87
	60	0.0226	8.287	7.53	9.99

Anacin (ASA 4)	5	0.100	35.38	21.94	10.58
	10	0.247	84.64	76.50	25.51
	15	0.510	179.57	161.92	54.36
	20	0.725	260.50	234.49	77.56
	25	0.779	278.72	251.93	83.47
	30	0.926	330.62	297.78	98.31
	45	0.926	330.64	298.84	98.41
	60	0.963	337.61	299.93	99.97
Shalina	5	0.0011	0.715	0.647	0.89
Aspirin	10	0.0012	0.717	0.649	0.910
(ASA 5)	15	0.0012	0.717	0.649	0.910
	20	0.0051	2.164	1.954	2.64
	25	0.0051	2.164	1.957	2.64
	30	0.0101	3.973	3.568	4.81
	45	0.0211	7.931	7.131	9.60
	60	0.0281	10.450	9.420	12.59

Table 3.6.7: Result for the bi-weekly Dissolution Test on the different Aspirin Brands subjected to relative Humidity 0%

DATE: week 2 **WAVELENGTH:265nm**

Brand	Time(min)	Absorbance(nm)	Concentration (mcg/ml)	Amount released(mg)	Percentage released(%)
Vasoprin (ASA 1)	5	0.0280	10.40	9.38	12.48
	10	0.0570	20.79	18.72	24.92
	15	0.0730	26.38	23.68	31.63
	20	0.0784	28.36	25.57	34.14
	25	0.1017	36.79	33.10	44.12
	30	0.1630	58.52	53.04	70.34
	45	0.2083	75.05	67.36	89.79
	60	0.2191	78.65	70.78	94.31
Emprin (ASA 2)	5	0.0310	11.47	10.30	13.74
	10	0.0574	20.80	18.70	24.98
	15	0.0710	25.63	23.10	30.78
	20	0.0837	30.12	27.09	35.81
	25	0.096	34.60	31.18	41.56
	30	0.178	63.77	57.39	76.49
	45	0.218	73.79	66.46	88.51
	60	0.2176	78.0	70.16	93.50
Microprin (ASA 3)	5	0.000996	0.707	0.64	0.87
	10	0.000996	0.707	0.64	0.87
	15	0.00399	1.777	1.61	2.13
	20	0.004995	2.133	1.93	2.60
	25	0.004996	2.134	1.95	2.60
	30	0.00799	3.196	2.89	3.85
	45	0.0171	6.390	5.77	7.70
	60	0.02184	8.167	7.36	9.82

Anacin (ASA 4)	5	0.0894	32.188	29.04	9.68
	10	0.2147	76.95	69.32	23.11
	15	0.4587	163.98	147.56	49.16
	20	0.6587	235.40	211.93	70.79
	25	0.7075	252.73	227.22	75.89
	30	0.8369	298.74	269.13	89.73
	45	0.8424	301.12	270.96	90.30
	60	0.8731	312.23	280.85	93.64
Shalina	5	0.000995	0.706	0.63	0.87
Aspirin	10	0.000996	0.707	0.64	0.87
(ASA 5)	15	0.00400	1.779	1.64	2.36
	20	0.004995	2.133	1.97	2.65
	25	0.004996	2.138	1.98	2.69
	30	0.00799	3.196	2.89	3.85
	45	0.0171	6.390	5.77	7.70
	60	0.02186	8.167	7.35	9.86

Table 3.6.8: Result for the bi-weekly Dissolution Test on the different Aspirin Brands subjected to relative Humidity 0%

DATE: week 4 **WAVELENGTH:265nm**

Brand	Time(min)	Absorbance(nm)	Concentration (mcg/ml)	Amount released(mg)	Percentage released(%)
Vasoprin (ASA 1)	5	0.0277	10.34	9.33	12.41
	10	0.0570	20.79	18.72	24.92
	15	0.0730	26.38	23.68	31.63
	20	0.0784	28.36	25.57	34.14
	25	0.1017	36.79	33.10	44.12
	30	0.1630	58.52	53.04	70.11
	45	0.2083	75.05	67.36	89.73
	60	0.2174	78.65	70.56	93.97
Emprin (ASA 2)	5	0.0307	10.98	10.12	12.90
	10	0.0574	20.80	18.70	24.98
	15	0.0710	25.63	23.10	30.78
	20	0.0837	30.12	27.09	35.76
	25	0.096	34.60	31.18	41.54
	30	0.178	63.77	57.39	76.49
	45	0.218	73.79	66.46	88.51
	60	0.2172	77.70	70.02	93.00
Microprin (ASA 3)	5	0.000996	0.707	0.64	0.87
	10	0.000996	0.707	0.64	0.87
	15	0.00399	1.777	1.61	2.13
	20	0.004994	2.133	1.93	2.57
	25	0.004994	2.134	1.95	2.57
	30	0.00799	3.196	2.89	3.85
	45	0.0170	6.390	5.77	7.70
	60	0.02183	8.167	7.36	9.82

Anacin (ASA 4)	5	0.0892	32.142	28.89	8.49
	10	0.2147	76.95	69.32	23.11
	15	0.4587	163.98	147.56	49.16
	20	0.6587	235.40	211.93	70.79
	25	0.7075	252.73	227.22	75.89
	30	0.8369	298.74	269.13	89.73
	45	0.8424	301.12	270.96	90.30
	60	0.8200	308.23	279.85	92.64
Shalina	5	0.000995	0.706	0.63	0.87
Aspirin	10	0.000996	0.707	0.64	0.87
(ASA 5)	15	0.00400	1.779	1.64	2.36
	20	0.004995	2.133	1.97	2.65
	25	0.004996	2.138	1.98	2.69
	30	0.00799	3.196	2.89	3.85
	45	0.0171	6.390	5.77	7.70
	60	0.02186	8.167	7.35	9.86

Table 3.6.9: Result for the bi-weekly Dissolution Test on the different Aspirin Brands subjected to relative Humidity 0%

DATE: week 6 **WAVELENGTH:265nm**

Brand	Time(min)	Absorbance(nm)	Concentration (mcg/ml)	Amount released(mg)	Percentage released(%)
Vasoprin (ASA 1)	5	0.0275	10.29	9.27	12.35
	10	0.056	20.56	18.52	24.67
	15	0.0720	26.12	23.40	31.34
	20	0.0780	28.10	25.30	33.80
	25	0.1001	36.40	32.80	43.72
	30	0.1600	57.86	52.31	69.68
	45	0.2062	74.28	66.59	88.88
	60	0.2173	77.78	70.02	93.18
Emprin (ASA 2)	5	0.0286	10.23	9.78	12.30
	10	0.0574	20.80	18.70	24.98
	15	0.0710	25.63	23.10	30.78
	20	0.0837	30.12	27.09	35.76
	25	0.096	34.60	31.18	41.54
	30	0.178	63.77	57.39	76.49
	45	0.218	73.79	66.46	88.51
	60	0.212	77.21	69.99	91.00
Microprin (ASA 3)	5	0.000996	0.707	0.64	0.87
	10	0.000996	0.707	0.64	0.87
	15	0.00399	1.777	1.61	2.13
	20	0.004994	2.133	1.93	2.57
	25	0.004994	2.134	1.95	2.57
	30	0.00799	3.196	2.89	3.85
	45	0.0170	6.390	5.77	7.70
	60	0.02183	8.167	7.36	9.82

Anacin (ASA 4)	5	0.873	31.48	28.26	8.33
	10	0.210	75.30	68.10	22.50
	15	0.449	161.20	145.36	48.04
	20	0.646	231.1	208.13	69.16
	25	0.693	246.89	222.60	74.00
	30	0.8192	292.16	264.29	87.37
	45	0.826	294.97	266.10	88.96
	60	0.804	300.94	273.30	90.06
Shalina	5	0.000995	0.706	0.63	0.87
Aspirin	10	0.000996	0.707	0.64	0.87
(ASA 5)	15	0.00400	1.779	1.64	2.36
	20	0.004995	2.133	1.97	2.65
	25	0.004996	2.138	1.98	2.69
	30	0.00799	3.196	2.89	3.85
	45	0.0171	6.390	5.77	7.70
	60	0.02186	8.167	7.35	9.86

Table 3.7.1: Result for the bi-weekly Dissolution Test on the different Aspirin Brands subjected to relative Humidity 0%

DATE: week 8 **WAVELENGTH:265nm**

Brand	Time(min)	Absorbance(nm)	Concentration (mcg/ml)	Amount released(mg)	Percentage released(%)
Vasoprin (ASA 1)	5	0.0107	10.98	10.12	12.90
	10	0.0574	20.80	18.70	24.98
	15	0.0710	25.63	23.10	30.78
	20	0.0837	30.12	27.09	35.76
	25	0.096	34.60	31.18	41.54
	30	0.178	63.77	57.39	76.49
	45	0.218	73.79	66.46	88.51
	60	0.2172	77.70	70.02	93.00
Emprin (ASA 2)	5	0.0286	10.23	9.10	12.20
	10	0.0574	20.80	18.16	23.14
	15	0.0710	25.63	22.80	30.12
	20	0.0837	30.12	27.00	34.20
	25	0.096	34.60	31.18	41.12
	30	0.178	63.77	57.39	76.23
	45	0.218	73.79	66.46	88.20
	60	0.209	76.21	69.19	90.70
Microprin (ASA 3)	5	0.000996	0.707	0.64	0.87
	10	0.000996	0.707	0.64	0.87
	15	0.00399	1.777	1.61	2.13
	20	0.004994	2.133	1.93	2.57
	25	0.004994	2.134	1.95	2.57
	30	0.00799	3.196	2.89	3.85
	45	0.0170	6.390	5.77	7.70
	60	0.02183	8.167	7.36	9.82

Anacin (ASA 4)	5	0.873	31.48	28.24	8.32
	10	0.210	75.30	68.00	22.48
	15	0.449	161.20	145.22	48.00
	20	0.646	231.1	208.00	69.10
	25	0.691	246.89	222.29	73.93
	30	0.817	292.16	264.02	87.29
	45	0.824	294.97	265.80	88.86
	60	0.803	300.94	272.80	90.05
Shalina	5	0.000995	0.706	0.63	0.87
Aspirin	10	0.000996	0.707	0.64	0.87
(ASA 5)	15	0.00400	1.779	1.64	2.36
	20	0.004995	2.133	1.97	2.65
	25	0.004996	2.138	1.98	2.69
	30	0.00799	3.196	2.89	3.85
	45	0.0171	6.390	5.77	7.70
	60	0.02186	8.167	7.35	9.86

Table 3.7.2: Result for the bi-weekly Dissolution Test on the different Aspirin Brands subjected to relative Humidity 0%

DATE: week 10 **WAVELENGTH:265nm**

Brand	Time(min)	Absorbance(nm)	Concentration (mcg/ml)	Amount released(mg)	Percentage released(%)
Vasoprin (ASA 1)	5	0.0099	10.23	9.78	12.30
	10	0.0554	20.10	18.20	24.98
	15	0.0710	25.63	23.10	30.78
	20	0.0837	30.12	27.09	35.76
	25	0.096	34.60	31.18	41.54
	30	0.178	63.77	57.39	76.49
	45	0.218	73.79	66.46	88.51
	60	0.212	77.21	69.99	91.00
Emprin (ASA 2)	5	0.0286	10.23	9.10	12.20
	10	0.0574	20.80	18.16	23.14
	15	0.0710	25.63	22.80	30.12
	20	0.0837	30.12	27.00	34.20
	25	0.096	34.60	31.18	41.12
	30	0.178	63.77	57.39	76.23
	45	0.218	73.79	66.46	88.20
	60	0.2154	77.28	69.55	92.7
Microprin (ASA 3)	5	0.00994	0.7060	0.640	0.86
	10	0.00993	0.7060	0.639	0.86
	15	0.0040	1.777	1.610	2.127
	20	0.00420	2.134	1.940	2.56
	25	0.00423	2.135	1.950	2.55
	30	0.00800	3.192	2.890	3.85

	45	0.0170	6.400	5.770	7.69
	60	0.0219	8.159	7.360	9.81
Anacin (ASA 4)	5	0.873	31.48	28.24	8.32
	10	0.210	75.30	68.00	22.48
	15	0.449	161.20	145.22	48.00
	20	0.646	231.1	208.00	69.10
	25	0.691	246.89	222.29	73.93
	30	0.8038	287.14	258.42	86.14
	45	0.817	292.14	262.92	87.60
	60	0.819	292.86	263.57	87.85
Shalina	5	0.000995	0.706	0.63	0.87
Aspirin	10	0.000996	0.707	0.64	0.87
(ASA 5)	15	0.00392	1.779	1.54	2.20
	20	0.004995	2.133	1.97	2.65
	25	0.004996	2.138	1.98	2.69
	30	0.00799	3.196	2.89	3.85
	45	0.0171	6.390	5.77	7.70
	60	0.02175	8.167	7.10	9.12

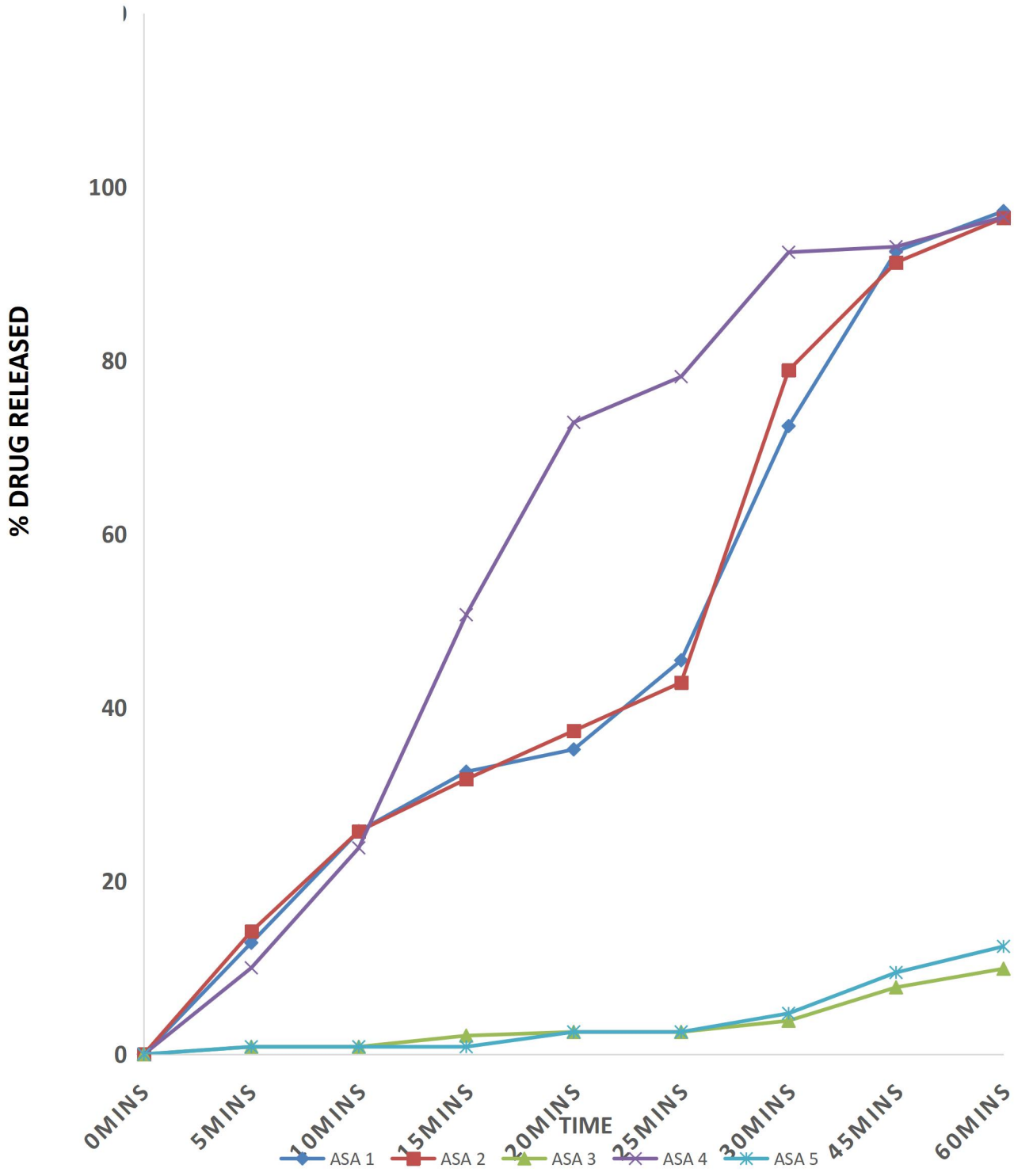

Figure 3.2 : A graph of percentage drug released (%) versus time (min) for brands ASA 1 – ASA 5 before subjection to humidity

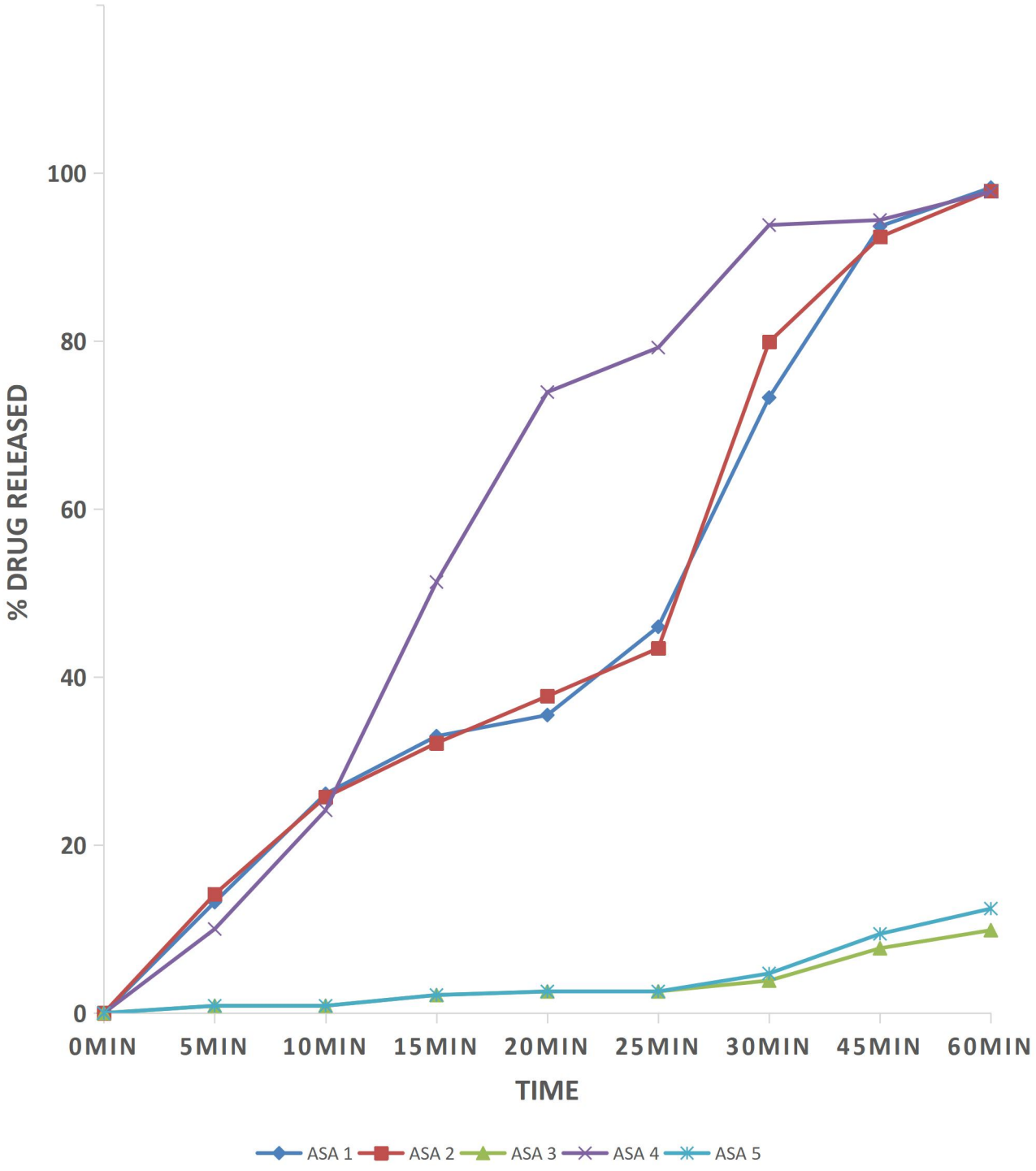

Figure 3.3.1 : A graph of percentage drug released (%) versus time (min) for brands ASA 1 – ASA 5 after two weeks of storing at 70% relative humidity

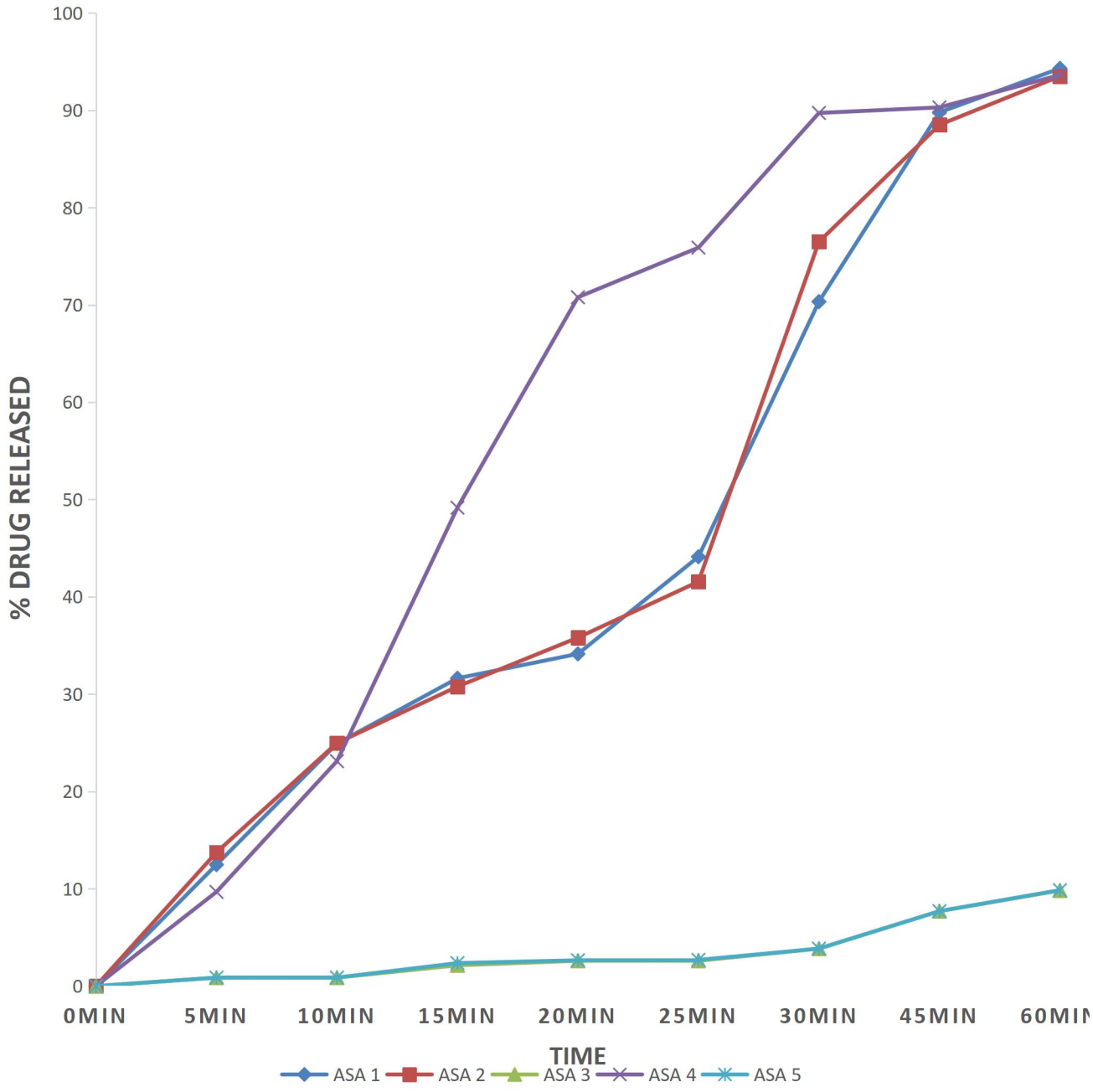

Figure 3.3.2 : A graph of percentage drug released (%) versus time (min) for brands ASA 1 – ASA 5 after two weeks of storing at 0% relative humidity

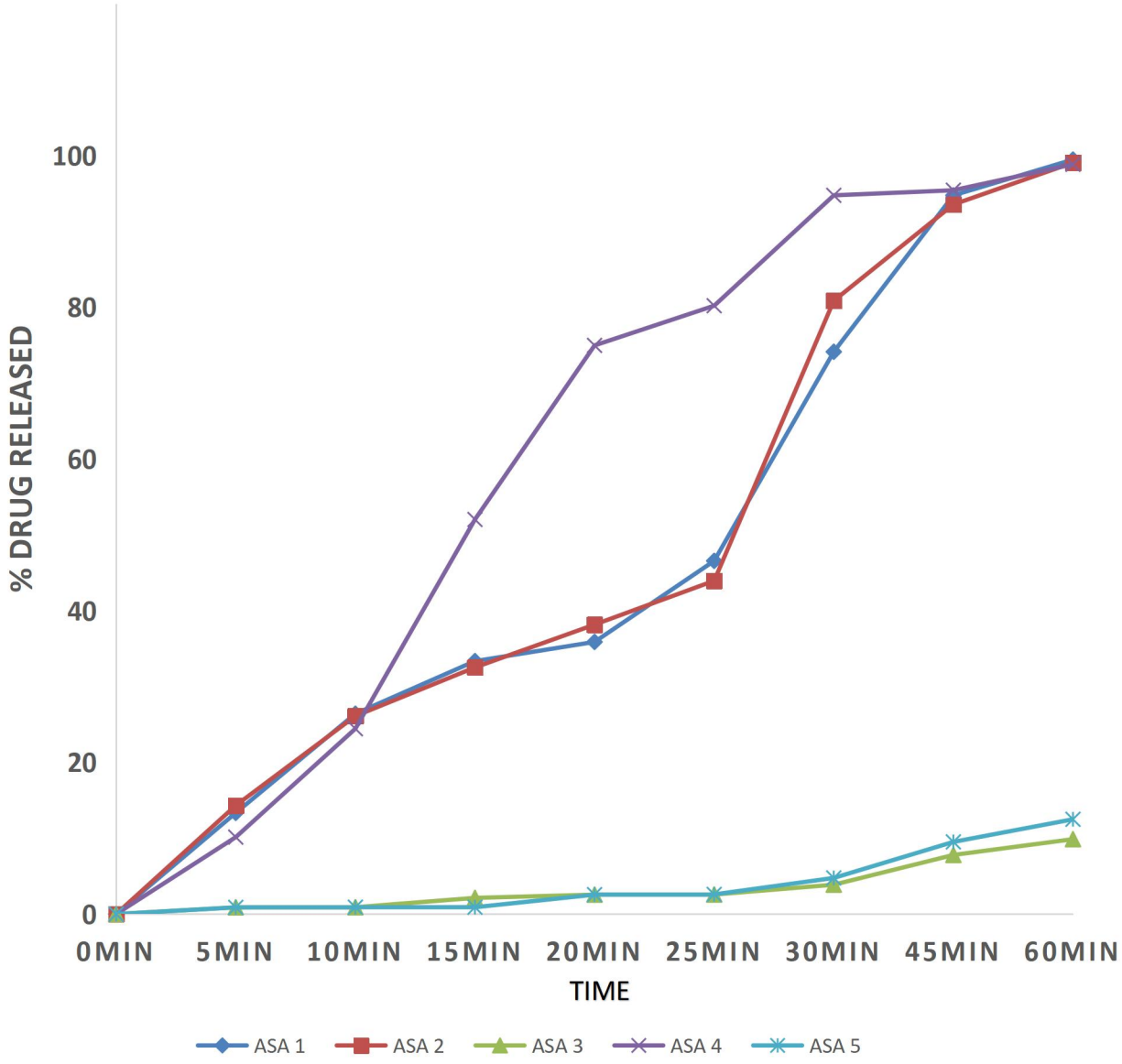

Figure 3.4.1 : A graph of percentage drug released (%) versus time (min) for brands ASA 1 – ASA 5 after four weeks of storing at 70% relative humidity

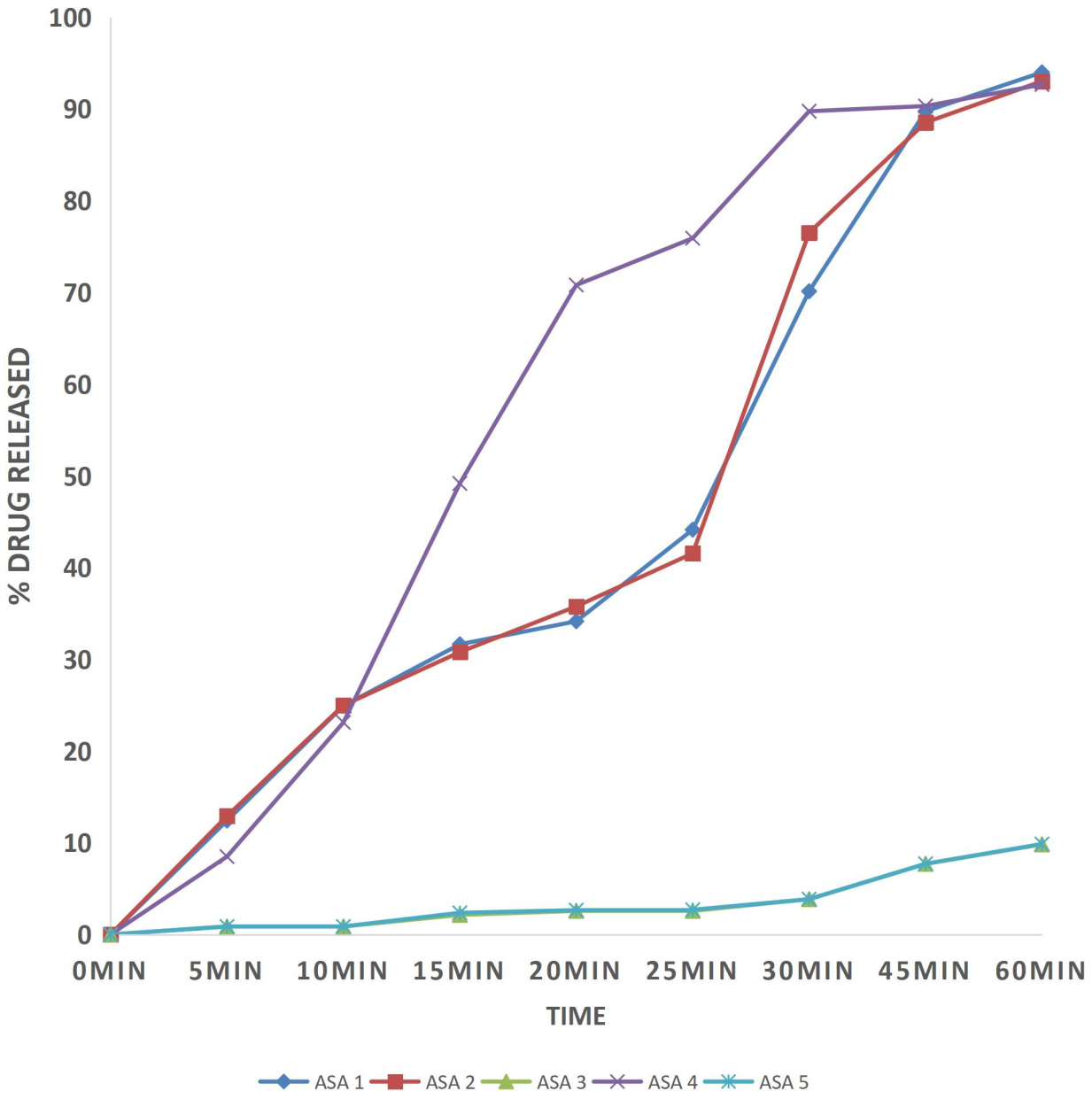

Figure 3.4.2 : A graph of percentage drug released (%) versus time (min) for brands ASA 1 – ASA 5 after four weeks of storing at 0% relative humidity

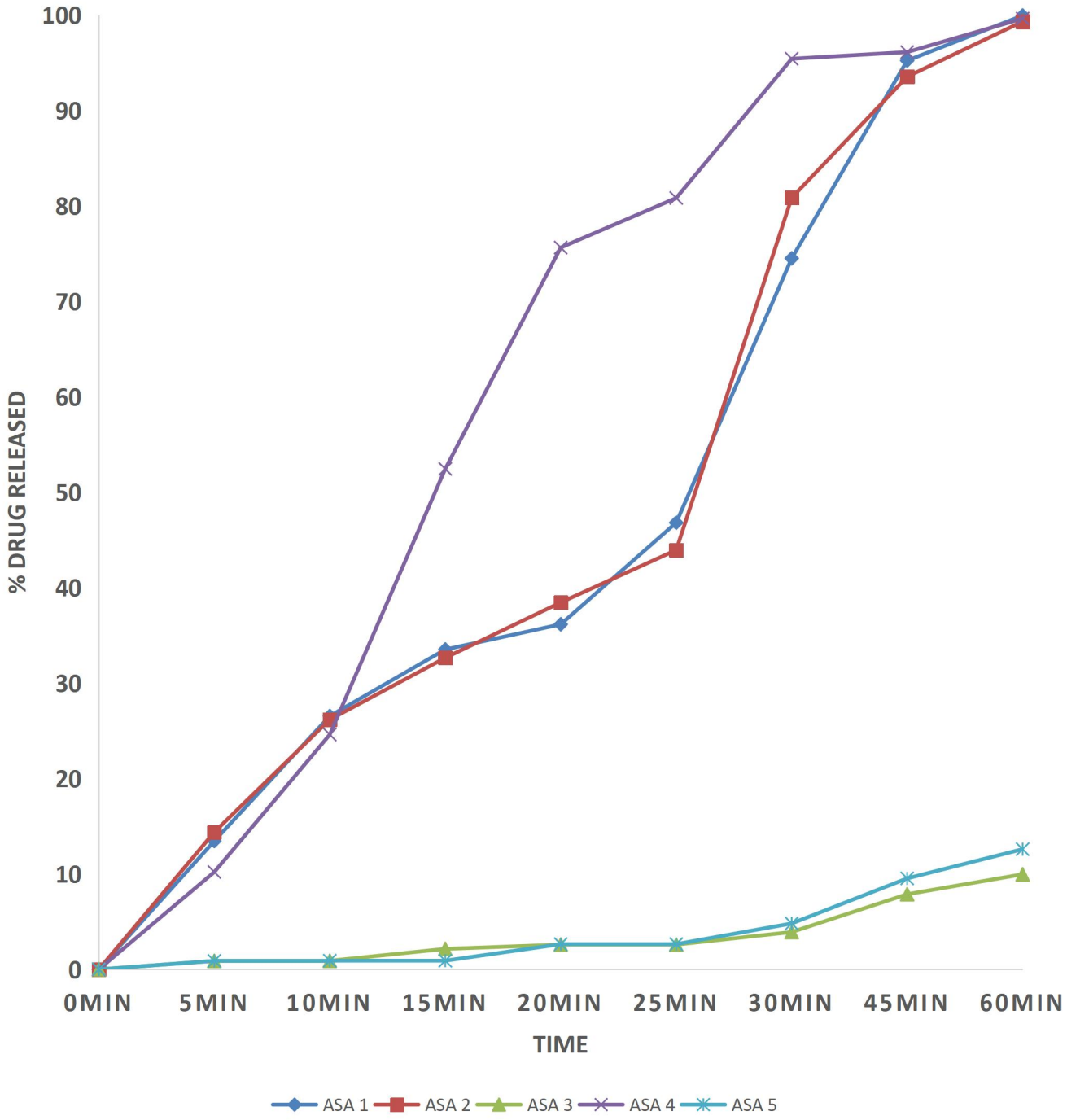

Figure 3.5.1 : A graph of percentage drug released (%) versus time (min) for brands ASA 1 – ASA 5 after six weeks of storing at 70% relative humidity

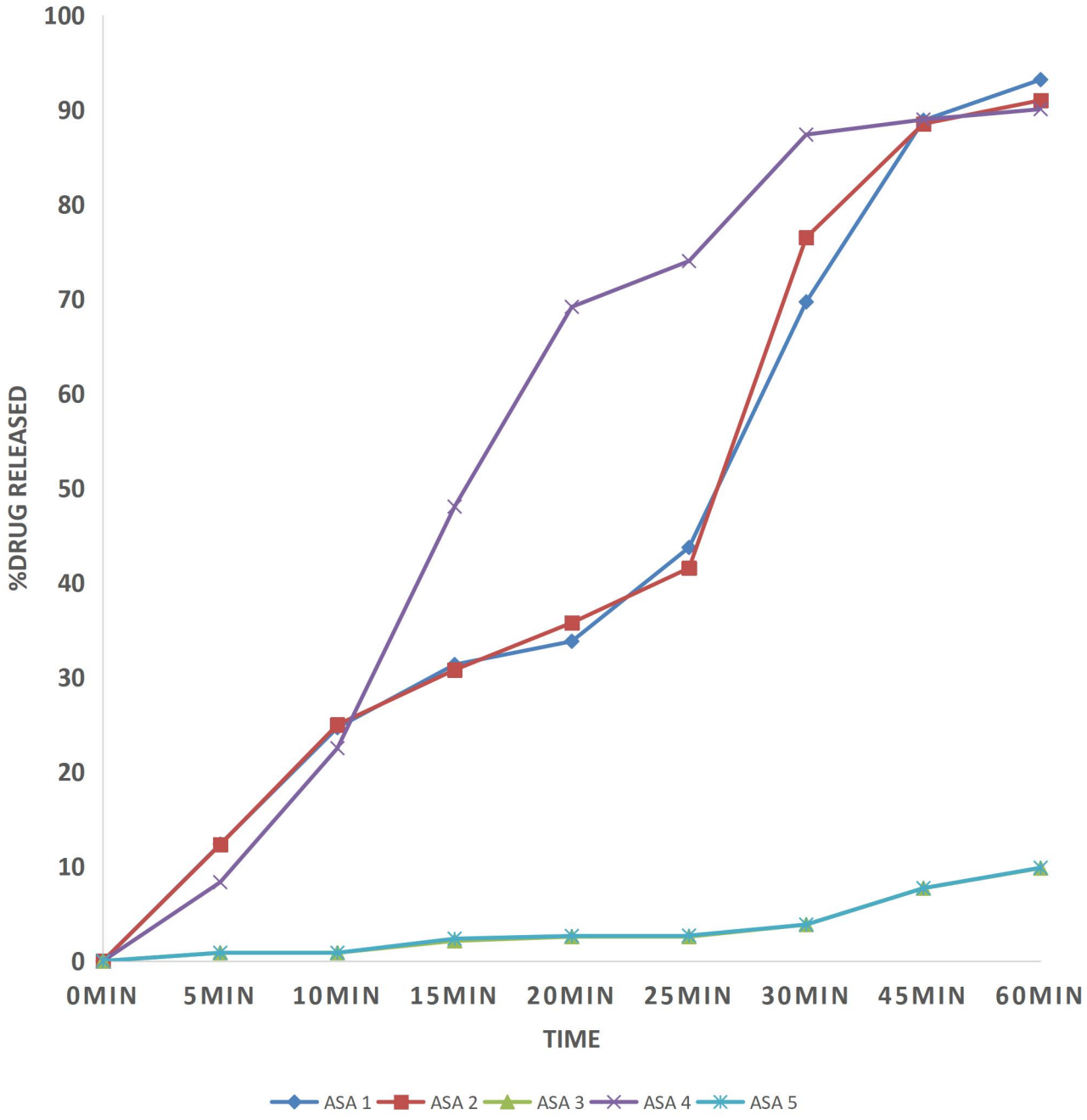

Figure 3.5.2 : A graph of percentage drug released (%) versus time (min) for brands ASA 1 – ASA 5 after six weeks of storing at 0% relative humidity

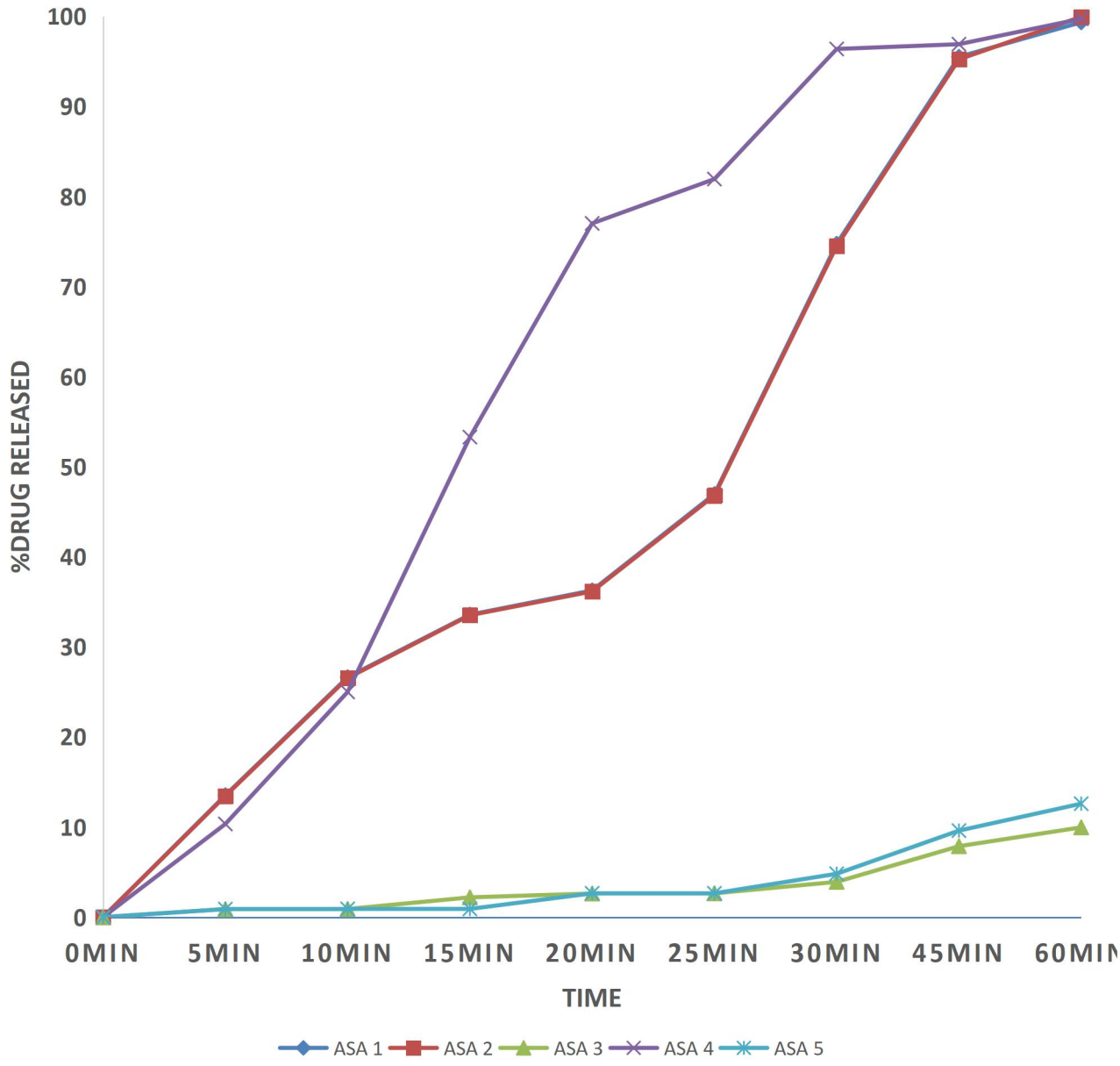

Figure 3.6.1 : A graph of percentage drug released (%) versus time (min) for brands ASA 1 – ASA 5 after eight weeks of storing at 70% relative humidity

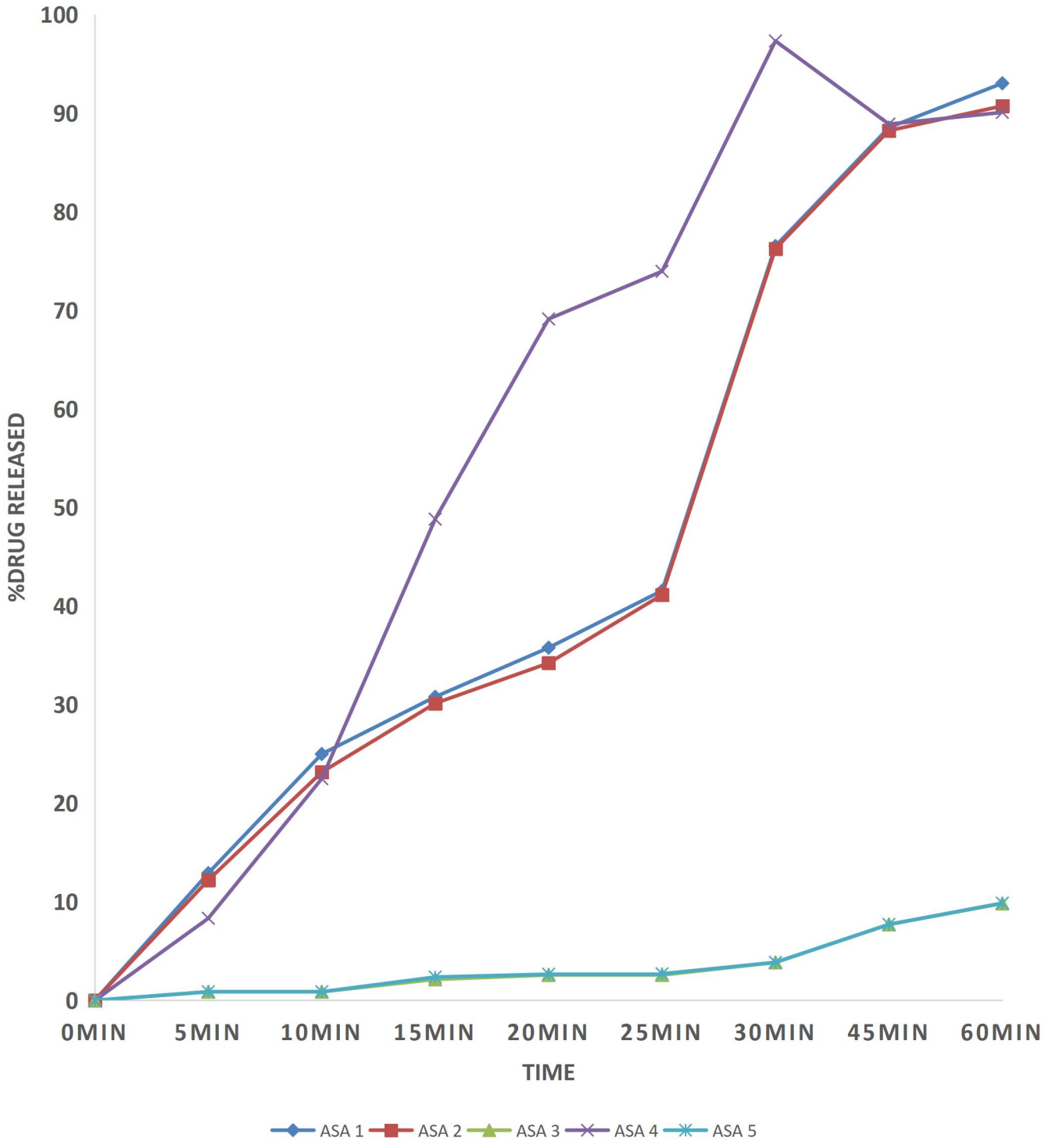

Figure 3.6.2 : A graph of percentage drug released (%) versus time (min) for brands ASA 1 – ASA 5 after eight weeks of storing at 0% relative humidity

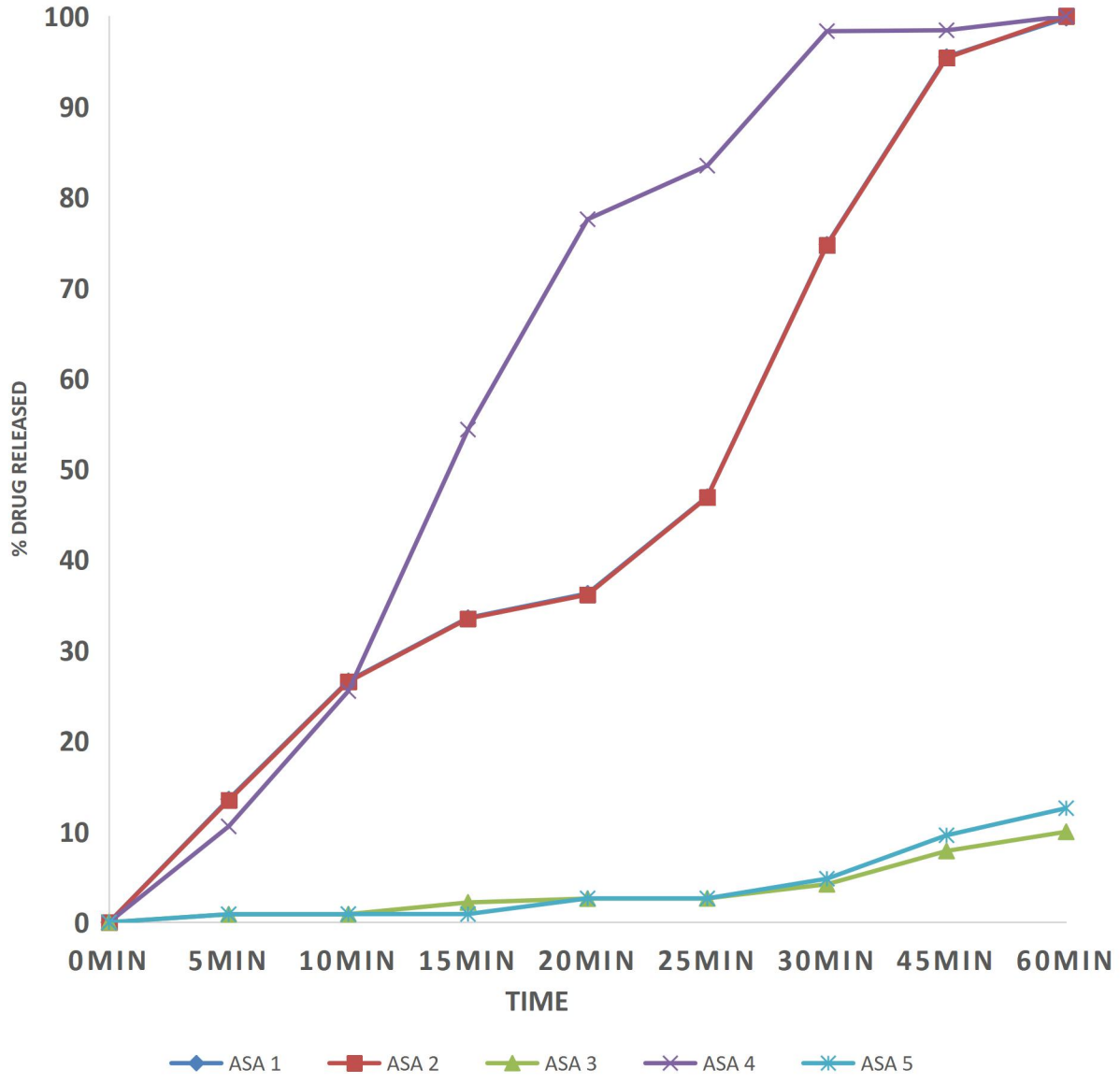

Figure 3.7.1 : A graph of percentage drug released (%) versus time (min) for brands ASA 1 – ASA 5 after ten weeks of storing at 70% relative humidity

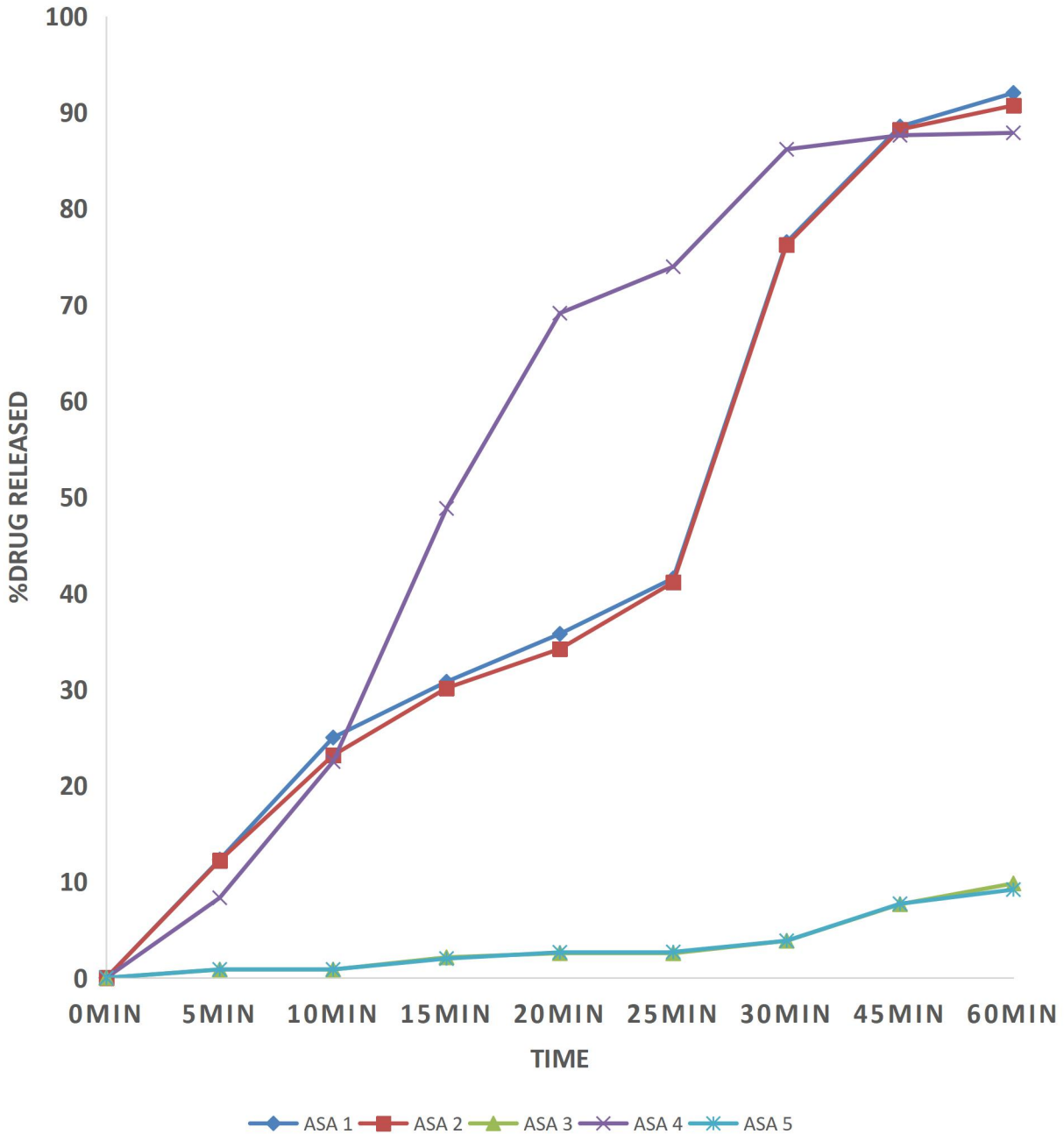

Figure 3.7.2 : A graph of percentage drug released (%) versus time (min) for brands ASA 1 – ASA 5 after ten weeks of storing at 0% relative humidity

CHAPTER FOUR

CONCLUSION AND RECOMMENDATION

4.1. CONCLUSION

This study confirmed that changes in the dissolution profiles occur when Aspirin tablets are stored under varying relative humidity conditions of 0% RH and 70%RH. This study revealed that there is an undesired reduction in the percentage of the drug released when stored at 0% relative humidity and also an undesired increase in the percentage of drug released when stored at 70% relative humidity as seen from the results over the 10 week period. It is imperative that patients, caregivers and even manufacturers are educated on the need to store tablets in facilities and areas of optimum relative humidity in order to preserve the efficacy of these drugs. According to preliminary research, aspirin tablet dissolving kinetics are significantly impacted by humidity. Elevated relative humidity seems to quicken the dissolution process, which could result in quicker drug release and absorption than is intended for the drug. On the other hand, reduced humidity can hinder drug disintegration and cause a delayed release of the medication than is intended for the drug. These findings highlight how crucial it is to take environmental variables like humidity into account when formulating and storing pharmaceuticals and conducting quality control procedures to guarantee consistent therapeutic performance and efficacy.

4.2. RECOMMENDATION:

I would recommend that the information obtained from the study be made available to manufacturers, patients , pharmacists and other medical practitioners so as to improve and ensure effective utilization of this drug by ensuring the drug is stored at optimum humidity. Manufacturers, community pharmacists, patients and other health care practitioners should adopt storing these tablets in controlled humidity environments. Dehumidifiers can be used in storage facilities of manufacturing companies to control the humidity of the environment within the storage facility in order to preserve the integrity of the tablets. Patients especially those using dose administration aids can store their tablets with dehumidifiers like small bags of silica gel in

order to also control the humidity of the storage environment. Further studies should be carried out on Aspirin for an extended period and across different humidity conditions to ascertain the optimum humidity condition for storage of the drug across different regions.

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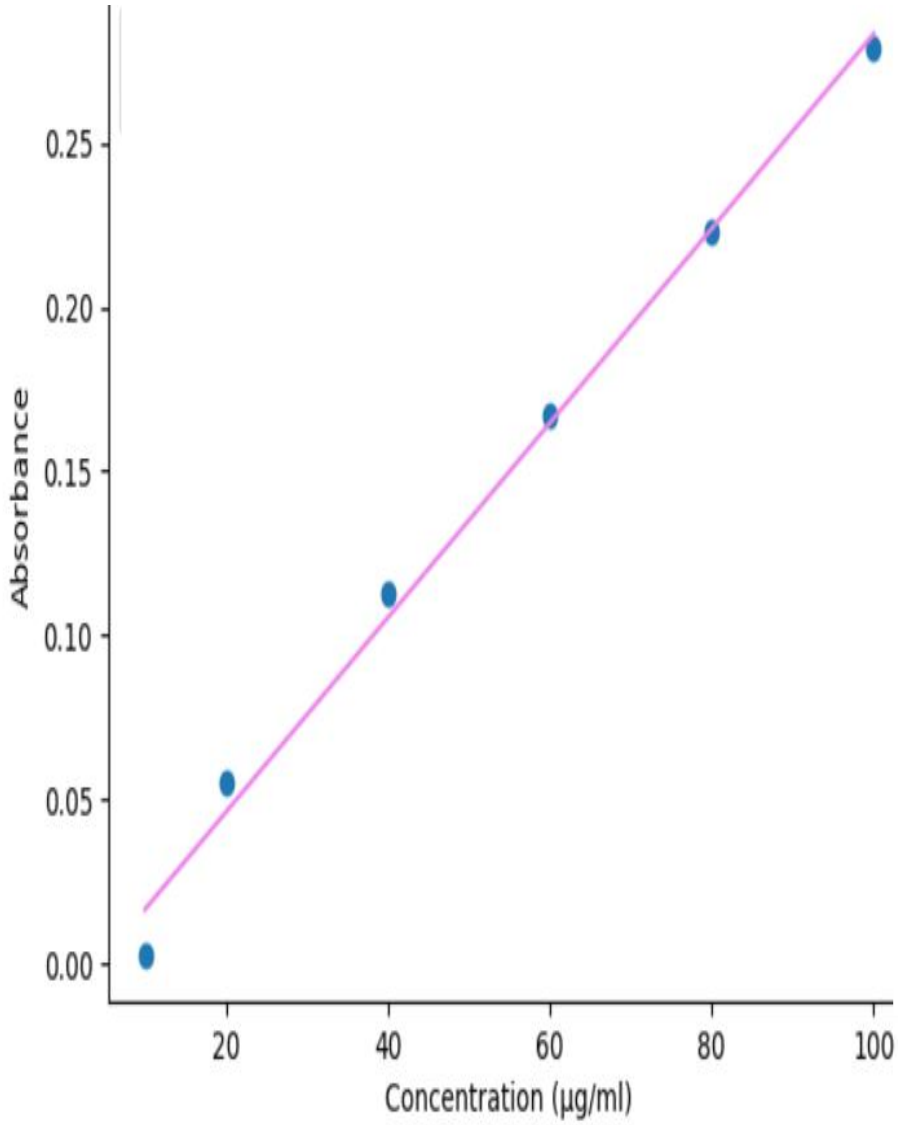
APPENDIX

Table 3.8.1: DISSOLUTION TEST RESULTS

Table for Standard Aspirin Powder

Concentration(ug/ml)	Absorbance(nm)
0	0
10	0.0027
20	0.0550
40	0.1130
60	0.1670
80	0.2230
100	0.2790

Figure 3.1: Calibration Curve for Pure Aspirin Sample



3.1: Calibration Curve for Pure Aspirin Sample

Slope: 0.0029626027397260278

Intercept: -0.01311780821917810

R^2 Value :0.9934734048735858

Equation of the line: y = 0.0028x – 0.0010