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Synthesis of Green Nano – Organic Compounds By Using Analytical Method and Study Their Biological Activity

A thesis

Submitted to the Department of Chemistry, College of Science, University of Kerbala In partial fulfillment of the requirements for the degree of Master in Chemistry

By

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Dedication

To the souls of my dear

father and mother, and to the martyrs of the leaders of the

victory, I dedicate my humble work

Acknowledgement

First of all, I would like to thank God Almighty for granting me success in completing my studies and bearing the difficulties that I faced. I would also like to thank my supervisors , Dr.BakerA.Joda and Dr.Alaa H. Khalaf for their guidance, directions and scientific advice , which were very helpful.

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بسم الله الرحمن الرحيم

صدق الله العلي العظيم

فاطر (28)

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We, the examining committee, certify that we have read this thesis "Synthesis of Green Nano – Organic Compounds By Using Analytical Method and Study Their Biological Activity" and *examined the student* (Zeina Mohammed Abed Al kadhom) *in its contents and that in our opinion, it is adequate as a thesis for the degree of Master of Science in chemistry.*

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Abstract

The aim of the work reported in this thesis is to develop methods suitable for the green analytical synthetic method of valuable materials of Nano-organics cleanly and efficiently. The use of organic nanoparticles derived from biomass in the medical and pharmacological studies has increased in terms of published research studies. The main aim of this study was to validate the use of edible fresh potato for the synthesis of Nano cellulose. In this procedure, there are no chemicals were used in any step. This method was performed to prepare nanoparticles extracted from potato through natural extraction and physical technical steps.

It was found that the FTIR spectra confirmed the presence of amorphous (Nano crystalline) cellulose's structure by detecting several functional groups such as (-OH) broad (3100-3600 cm^{-1}), (C-H) (2800-3000 cm^{-1}), (C-H) symmetric bending (1400 cm^{-1}), and (C–O–C) stretching (856 cm^{-1}).

AFM measurements and SPM analysis reports were proved the Nano scale of prepared cellulose particles by showing the average diameter was (23.44 nm) and median diameter was (18 nm) of Nano cellulose according to granularity cumulation distribution chart, while the average height was (12.714 nm) according to the height cumulation distribution chart. Surface topology and roughness analysis and parameters were discussed.

At applicable scale, different equivalent ratios of Nano cellulose were used with the medicines to find out the best quantity of nanoparticles that can be used for the purpose of encapsulating the medicine and keeping it from liberating and losing quantities of it in the acidity of the stomach, and then transferring it to the safest area of greatest absorption in the human body (small intestine, alkaline medium).

The retention ability reaches up to (70 %) for aspirin; the retention ability reaches up to (54 %) for paracetamol; the retention ability reaches up to (44 %) for Flagyl by using 4 equivalents of Nano cellulose.

The order of medicine response to the controlled Nano carrier system (Nano cellulose) statistically was in the following order:

Aspirin > Paracetamol >Flagyl

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Abbreviation

AS	Aspirin
AA	Acrylic acid
AFM	Atomic force Microscopic
BC	Bacterial Cellulose NC
CNFs	Cellulose Nano fibers
CNCs	Cellulose Nano crystal
COX	Cyclooxygenase
CLO	Clopidogrel
DDS	Drug delivery systems
EGDMA	Ethylene glycol dimethyl acrylate
MAA	Methyl methacrylic acid
NSAID	Non steroidal anti-inflammatory drugs
PGs	prostaglandins
SPM	Scanning Probe Microscopy
TRIM	Tri methyl propane tri methacrylate

Chapter One

General Introduction

1. Introduction

1.1 Green Chemistry

The economy of the chemical industry and the improvement of environmental protection require new chemistry. The concept of green chemistry presents an attractive technology for novel chemistry research to help chemists, academics, and industrialists. Green chemistry is used primarily to reduce the environmental damages which are accompanied by material production. Furthermore, it can use to minimize and remove waste generated during various chemical processes. Green chemistry is another definition of a new procedure utilized for the synthesis and dispensation of chemical resources in such a way as to decrease the risks in the world. Therefore, chemistry will improve either by using eco-friendly materials or by reducing the use and production paths of conventional energy sources of poisonous substances [1].

1.2 Basic Principles of Green Chemistry

A previous study was investigated that there are twelve laws discussed the fundamental of Green chemistry, which are the fundamental principles of it [2]. The following examples show the new chemical materials, new synthesis, and new techniques.

1.2.1 The Prevention of Wastes is Better Than Treatment or Purification Which are Discarded after its Formation.

This process explains chemists' ability to re-create chemical conversions to reduce hazardous waste generation. Thus, pollution is eliminated by avoiding the generation of waste [3]. In addition, the risks associated with the collection, transport and treatment of wastes may be decreased. In general, waste generation and prevention involve modernizing industrial processes by using clean

manufacturing technology. These techniques are designed to reduce gassy releases, effluents, solid residues, and noise generation; they are generally developed to contribute to climate protection and the most auspicious strategy to avoid discarded formation would simply not be to produce the wanted product [4]. It would not be feasible in most situations; however, it may be rational to create entirely new goods instead, which show greater value and longer longevity. Higher volumes of these new, superior goods [3].

1.2.2 Increase the Economy of Atoms

The atomic economy is a term that was established in the primary 1990s to determine the effectiveness of chemical transformations on a component-by-component basis [5]. In contrast with well-recognized produce estimates, the "atom economy" principle is founded on the relation of the whole mass of atoms in the target product to the total mass of atoms in the starting materials. One strategy for reducing waste generation is to design certain chemical transformations that optimize the incorporation of all materials used in the process into the final product, resulting in the lowest possible number of wasted atoms [6].

1.2.3 Less Dangerous Chemical Synthesis Design

standards of green chemistry matter in imitation biological chemistry to successfully transform them in a novel way, with a new molecule or in a new order. Different investigators clearly showed how toxic, and the linked dangers and risks related to chemical responses to the material matrix current in the reaction vessel are directly connected to them An immunity is defined where a molecule is generated to demonstrate toxicity and/or biological activity by intent [7].

1.2.4 Model Healthy Materials and Chemicals

Chemical yields should be engineered for their desired purpose and their toxicity should be reduced at once. New, intrinsically safer products that are highly efficient for mark submission can be developed. In immobilizing hazardous organic waste in very low-cost resources as well as natural clay, for example, the desperate incorporation in the concrete of radioactive spent waste liquid scintillation with clay is considered to create a safe steadied product that is easy to handle, manufacture and disposal [8-9].

1.2.5 Safer and Complementary Solvents

It encourages the use of healthier solvents and auxiliary materials. It applies to any materials that do not donate directly to the construction of the reaction product to occur a chemical or process reaction. Many chemical compound reactions occur in liquid environments, where the solvent behaves in various ways: it can allow reactant interaction, steady, or unsettle produced intermediates, or it can affect transition conditions. transitory conditions. The applied solvent also controls the collection of suitable downstream and renewal progressions and techniques for recycling or disposal [10].

1.2.6 Energy Efficiency Development

Power is typically used in essential ways to enhance human life. The supply and combustion of commonly used sources of fuel, including coal, oil and gas, is limited. Both the push towards renewable energy and energy management design are required to enhance the quality of life continuously. In conjunction with the selection of sufficient energy sources, the design of more effective processes by selecting the right technologies and operations. The use of an electric motor with

sun and wind energy sources is more ecologically viable than fossil fuel. How energy is turned into useful and the main questions for engineers and inventors are where it gets lost to help society use energy more efficiently [11].

1.2.7 Utilization of Renewable Feedstocks

Under Green chemistry principles underdone material or feedstock should not be depleted if mechanically and efficiently feasible and should rather be renewable. It represents an effective way for the sustainable development and transformation of functional bio products using renewable supplies like microscopic plant biomass that are integrated into a nature-locked carbon round [12].

1.2.8 Reduce Bypasses

Many processes could be planned so that additional components and waste can be reduced. A derivative of a compound that contains groups that are not required in the ending outcome must often be synthesized, but which permit for more easy creation or refining steps. Yet these alternatives lead to a lower nuclear economy as they add nuclear energy that is not used in the finished product yet eventually becomes waste; they clash with the concept of nuclear efficiency. Chemists are presently engaged in research to identify alternatives for several reactions traditionally required for protective groups [13].

1.2.9 Catalytic

Catalysis is the chemical reaction that a catalyst facilitates or speeds up. Ostwald says that catalysts are substances that allow a strongly supportive transitional status between reactants to speed up the reaction, but which have no consumption and no net reaction equivalence [14]. In new manufacturing economies, in our

environmental management, and in all biological processes, catalysts play an important role. Saleh and others establish that the mechanism of celluloses peroxide oxidative degradation was strengthened with iron and copper sulphate as catalysts. Synthesis has recently been advanced to allow easy movement of specific Nano-catalysts in magnitude and figure the reaction phase materials and the regulation of nanostructure morphology to change its physical and chemical characteristics. The paramagnetic core Nano –catalyst organizations allow speedy and discerning chemical changes with outstanding product performance combined with easy catalyst splitting and retrieval [15].

1.2.10 Degradation Feature

Some of the main aims of green chemistry are to maximize production and minimize undesirable by- yields. yields and courses which show a lower effect on humans and the surroundings, for instance the creation of sustainable composites for mortar which can be considered as a value-added product for different applications, are reported as the inactive form to immobilize low and middle level radioactive waste, decorative slates, building blocks and light concrete. In this situation, greatly reactive hydroxyl radicals react to the organic moisture content of waste fibers by either subtracting hydrogen ions or adding organic radicals that are readily corroded by oxygen to their unsaturated location. Therefore, only carbon dioxide and water were final yields of the deteriorating cycle [16-17]

1.2.11 Pollution Mitigation Real-Time Study

The development of various toxic chemicals with improvement in chemistry is a major environmental issue. Green chemistry practitioners are familiar with one of the main principles. For several years, less toxic products have been heard in

chemical constructions and waste reduction. Green chemistry is consequent in developing enhanced mechanized procedures for chemical matter with minimal discarded production by tracking operating processes in real time, the removal of the use and creation of dangerous substances. This makes an early response right before waste or toxins are genetically modified [18].

1.2.12 Safer Chemical for the Avoidance of Injuries

Avoiding extremely reactive chemicals which could theoretically reason mistakes during the reaction is of exceptional importance. The composition and type of a material used in a chemical process should be selected in a manner that minimizes the risk for chemical incidents, including releases of toxins, bangs, and fire. Intrinsically, healthy chemistry can also be done in flow mode, using tube-like micro reactors with tiny diameter reaction channels. These flow chemistry schemes significantly reduce the volume of the reaction, the reaction time, and the catalyst requirement by improving the space/time. Returns open new procedure frames with respect to extreme temperatures and pressures to be applied. In addition, flow chemical applications in micro reactors are also an advocate of a tactic to address traditional microwave driven process drawbacks such as restricted permeation depth of microwaves to the absorbing media [19-20] In recent years, there have been many trends of the quest method, including the application of green chemistry techniques, and applications for Nanotechnology. The Nano materials are valuable devices dependent on toxic heavy metal for instance particles from CdS and Ru composites. The recent TiO_2/anthocyanin catalyst showed effective catalyzed photo degradation under solar radiation than the previously used systems. While escaping their harmful character and the probability of improving their effectiveness and facility of recovery from catalytic reaction by supporting on

active carbon molecule. But the procedure needs to revitalize the improved catalyst by re-treatment with fresh anthocyanin dye due to their degradation These days, researchers have concentrated on developing viable green mechanisms utilized in the making of nanomaterials, such as: Nano-catalysis, self-syntheses, use of solid state-solvent less process, non-poisonous starting materials viable starting materials. The preparation of biopolymers from natural supplies, such as corn plant and sugar beet roots where starch is obtained from these plants, has become a phenomenon specialist scientists and established materials as green Nano catalysts are directly interested in lowering reaction period and temperature in a secure reactor compared to conventional business processes [21].

1.2.13 Nanotechnology

Nano materials have been extensively used in many of valuable purposes to humankind; still,the greatest of these Nano materials are not natural and are produced by complex manufacturing procedures with the problem of being costly, poisonous, energy ineffective and their apparent conservational crash. Thus, around an increasing need to incorporate green renewable natural supplies as antecedents in nanoparticles creating (nano-organics) by using green schemes. The created nanoparticles by green renewable procedures are naturally gentle and harmless to custom in several purposes. A global push to create a mix of nanotechnology and organic chemistry [22]. Build and apply green technologies for smart materials synthetization. Nano-organics were created from cellulose and vegetables by poor green procedures in the green chemistry laboratory and used for many important purposes, including desertification management, pollutant degradation and drug delivery [22]

1.3 Nano Cellulose

Cellulose is the major component of planets fibers and most abundant polymer on earth while Nano cellulose is a term referring to structured cellulose with diameter less than 100 nm in one dimension. It is unique promising material naturally extracted its advantages due to physical properties, high surface area, its biological properties, lack of toxicity, alignment and orientation, and barrier properties [23].

There are three type of Nano cellulose, namely Nano crystalline cellulose, Nano fibrillated cellulose, and bacterial Nano cellulose. The main difference between each other is in morphology although they are sharing in the same chemical composition. [24]. The hydroxylic surface groups of cellulose can become readily accessible and provide rich chemistry possibilities. Therefore, it is possible to deals with innovative approaches to prepare new sustainable usable materials in terms of super colloidal and super molecular modifications [25].

It is well known that cellulose has been successfully used in FDA-approved medicines in the United States. Previous studies have reported that a Nano cellulose can use for drug delivery systems due to its critical properties, such as high crystallinity, biocompatibility, biodegradability, high surface area, special mechanical and rheological properties, morphology, and geometrical measurements in terms of chemical functionality, and the possibility for multi functionality [16]. It was found that various therapeutic agents can be bound and released using some modifications. Therefore, Nano cellulose has been used in several drug delivery experiments. The CNFs, CNCs, and BC are the same, but each one use for specific drug delivery mechanism based on unique variations and characteristics. In addition, the delivery time of NC-based systems ranges between several months and a few minutes. [26].

It was found that wood, fungi, bacteria, and algae can use to make Nano cellulose. Amorphous and crystal components of cellulose are mostly known to be sequentially located in a row along the fiber path. While amorphous components are split between Nano fibrils. Since the heavy hydrogen connection between hydroxyl groups in cellulose is almost impossible to sever the crystal pieces. In the other side, it is simple to split amorphous pieces of cellulose. Thus, the separation of NCs from natural resources comprises the pre-treatment and breaking down of amorphous cellulose sections to derive NCs in CNF Composites [27].

1.3.1 Smart Materials

Intelligent structures and materials NC show an intelligent behavior to design intelligent materials for many applications in response to environmental factors including illumination, temperature, electrical input, pH and magnetic power. Cellulose-driven stimulatory materials have demonstrated tremendous promise in electro-stimulation targeted drug delivery systems because of their biocompatible and biodegradable nature. high-aspect CNCs with a mechanically rugged fiber can be used in Nano composites as sustainable enhancers as well as a handle to incorporate sensations. CNF photo-responsive design can act in a soft polymer matrix as the adaptive filler and can act as a photo-switchable gelato, as well. The characteristics of NC such as low density, thermal stability, chemical resistance, high mechanical strength, biocompatibility, and biodegradability have made it a versatile material for pH, organic vapors, ions and humidity detection systems. In the last five years, nanostructured products such as CNC, CNF and BC have widely been used in the literature. Cellulose has minimal versatility in intelligent materials and systems, but the 3D hierarchy system comprising nanofibers or nanoparticles has increased its opportunity in this field [28].

In general, energy generation, transportation, and processing, water purification, food packaging, fire retardant design, and form memory devices are all promising industrial applications for these materials [29]. They also use for biomedical applications such as radical scavenging, photodynamic and photo thermal therapy of tumors and microbial infections, drug delivery, biosensors, isolation of various biomolecules, electrical stimulation of damaged tissues. In addition, it can use for other applications such as neural and bone tissue engineering, blood vessel engineering, and advanced wound dressing. However, there is a risk of cytotoxicity and immunogenicity [29].

1.4 Extraction

To separate the required natural products from their raw materials, the first step used is extraction, and the most important extraction method is by solvent, pressure, sublimation, and the method of distillation according to the principle of extraction [30].

Green chemistry involves eliminating or reducing the use of hazardous materials through the innovation and design of new chemical methods. As for vegetable extraction, it can be defined as reducing energy consumption and using alternative solvents and renewable natural materials by discovering and innovating new extraction methods, which must include obtaining a high-quality product. In order to reduce the use of energy, solvents and raw materials, three solutions have been proposed for their laboratory and industrial use, including:

1- Improving and developing the processes currently used.

2- Use of non-specific materials and equipment

3- Creating new methods and processes that include the use of an alternative solvent [31-32].

The use of organic compounds in the commercial and industrial fields such as the pharmaceutical and food industries necessitates finding new early methods side by side for current methods of extracting organic materials. The effectiveness of the methods depends on understanding the nature of the plant, knowledge of input information, understanding of the chemistry of organic compounds in addition to scientific experience [33].

The necessity of using green chemistry in the extraction process since the 1990s to reduce energy consumption and reduce environmental pollution using alternative solvents. New green techniques for extracting materials from herbal materials are ultrasound techniques, microwave assisted extraction, supercritical fluid extraction and mechanical stress. As well as a breakthrough technology of instant monitoring [34].

1.5 Drag Deliver

In recent years, interest has increased in using nanoparticles to deliver drugs inside the human body to diseased cells. These particles are designed in a way that makes them attract to diseased cells so that the drugs can directly treat and improve their effectiveness and reduce the side effects of drugs. Thus, lead to improved health where the benefit was made from the 12 principles of green chemistry which are employed in drag delivery application to treat the problem of dosing traditional medicine [35].

Drug delivery systems (DDS) are extensively studied and proliferated to ameliorate the efficacy and administration of active pharmaceutical compounds, such as drugs, vaccines, antibodies, enzymes, peptides, proteins, etc to achieve targeted delivery and to avoid rapid degradation of drugs or protection from clearance. Therefore, a plethora of controlled DDS has been developed [36].

Conventional chemotherapeutic drug delivery systems present a number of critical

issues related to sensitive toxicity, poor specificity, and drug resistance induction, all of which significantly reduce the therapeutic efficiency of many drug systems. Nano carrier-based platforms are dedicated systems for transporting chemotherapeutic active drugs that are made up of colloidal nanoparticles Characterized by a high surface area to volume ratio in general. These nanostructured prototypes have allowed for the efficient delivery of active (including anticancer) drugs into diseased tissues. The overall goal of using Nano carriers in drug delivery applications is to treat a disease effectively while minimizing side effects, aiming for a sensitive improvement in therapeutic outcomes [37].

1.6 Applications

In 2013 a report demonstrated the feasibility of using many of the techniques available for Nano scale packaging for organic compounds, such as Cellulose. For example, self-assembly or aggregation, high homogeneous pressure, Nano scale emulsification, supercritical liquids, etc. The lamellar micro scale can be converted to the spherical Nano scale of dissolved Cellulose particles in ethyl acetate solvent by using the supercritical fluid technique, using the CO2 (supercritical fluid) pressure rise at 40 °C [21].

1.6.1 Aspirin

The structural formula and molecular weight of aspirin are C9H8O4 and 180.157, respectively. Aspirin is the oldest synthetic drug which originally used as an anti-inflammatory medication and because of its antiplatelet properties become used in preventing cardiovascular and cerebrovascular disease [38]. Cyclooxygenase (COX) activity which results in the formation, inflammation,

swelling, pain, and fever of prostaglandins (PGs). However, aspirin like medicines has prevented physiologically essential PGs from being developed by inhibiting this important enzyme in PG synthesis to protect human stomach mucosa against damage caused by hydrochloric acid, preserve kidney function and add platelets where appropriate. This conclusion was a standard interpretation of the medicinal behavior and common adverse effects of aspirin-like medications. Twenty years later, it became apparent with the discovery of a second COX gene that two COX isoforms exist. The constituent isoform COX-1 promotes beneficial homeostatic function, while the inducible isoform, COX-2 is up regulated by inflammatory mediators and its products contribute to various symptoms such as rheumatoid and osteoarthritis inflammatory disorders [39]. Aspirin is prepared by the acetylation of salicylic acid using anhydride or acetyl chloride (proton H would be present) because (-OH) is less stable than (-COOH). and acidic. Aspirin hydrolyses lead to rise acidity this in turn lead to more blood flow [40]. More acetic acid and salicylic acid form as a result from aspirin hydrolyses in wet conditions, as shown in Figures 1-4.

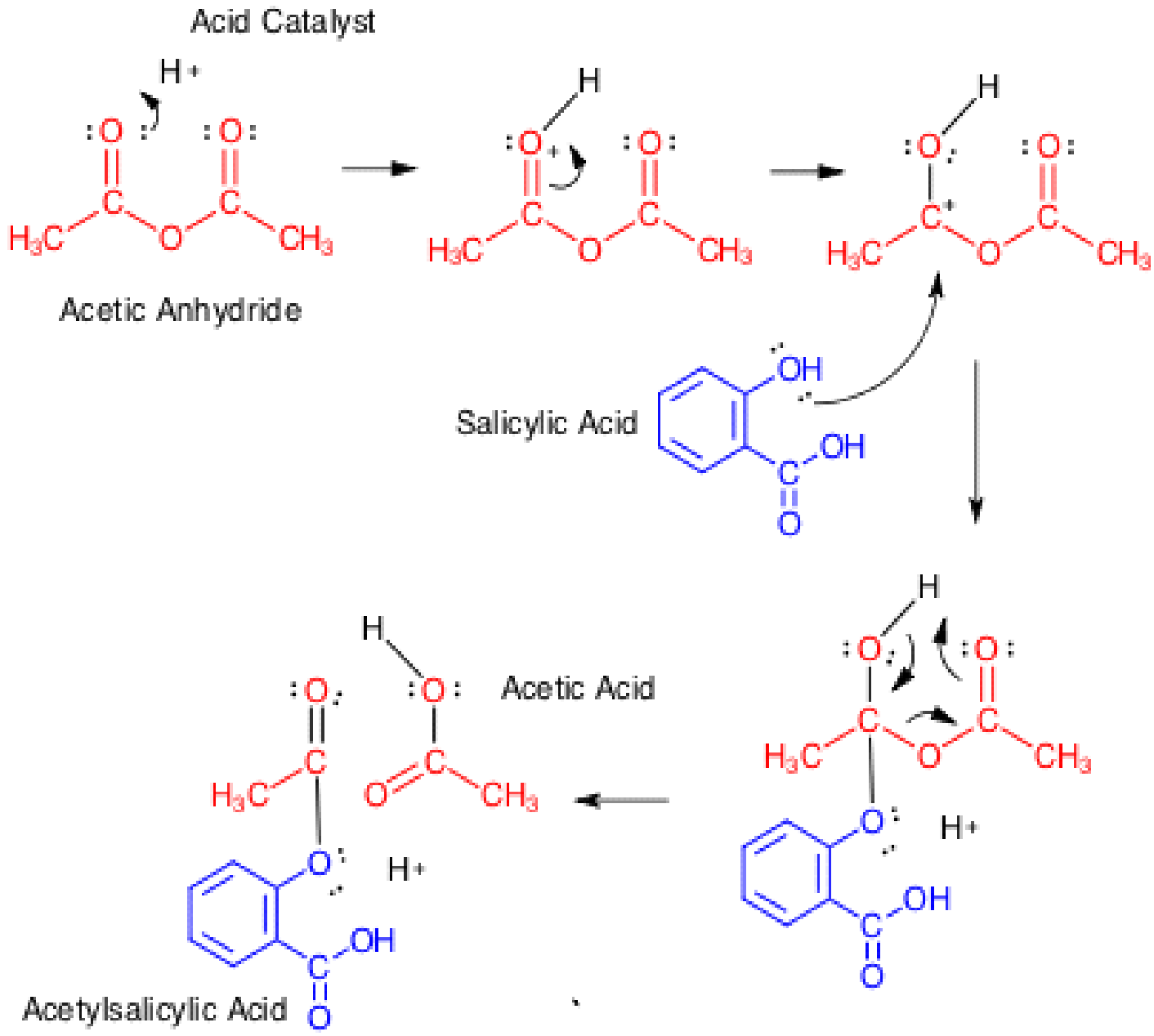


Figure 1.1: The mechanism of esters synthesis (synthesis of aspirin)

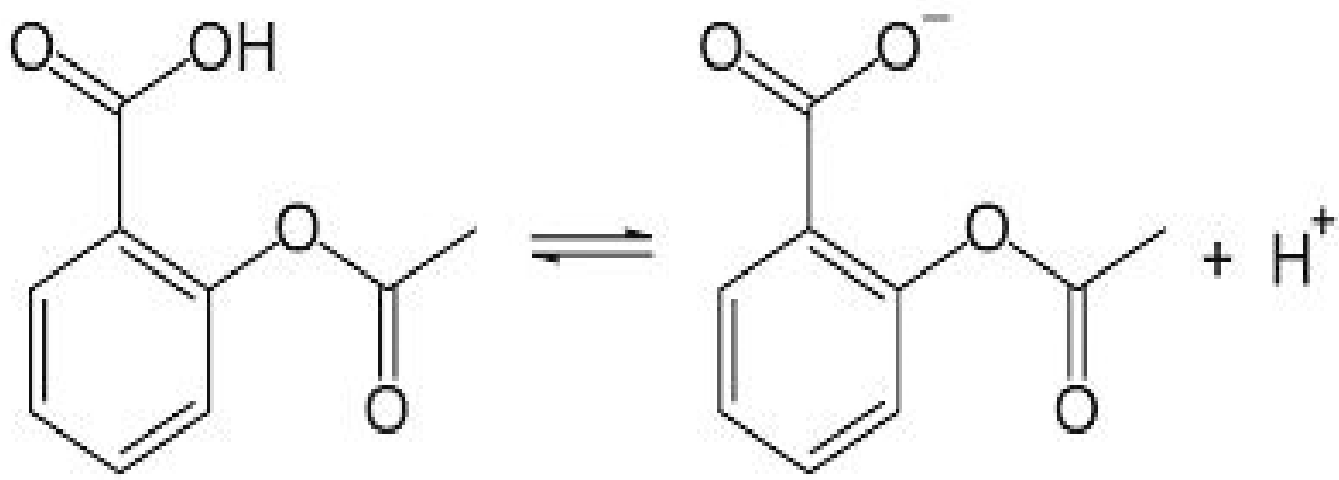


Figure 1.2: Released of proton (H+) from dissociation of aspirin

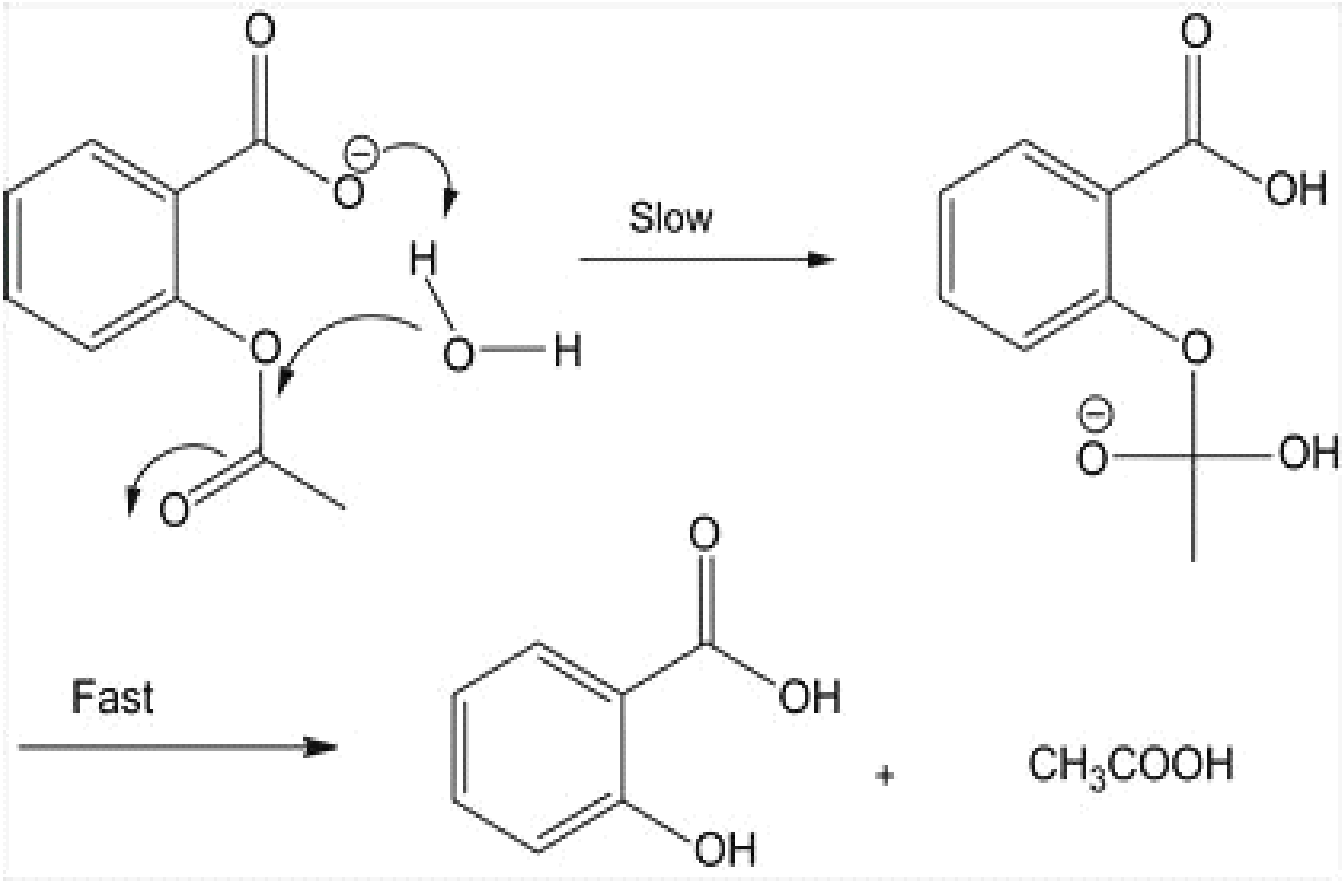


Figure 1.3: Mechanism of aspirin hydrolysis

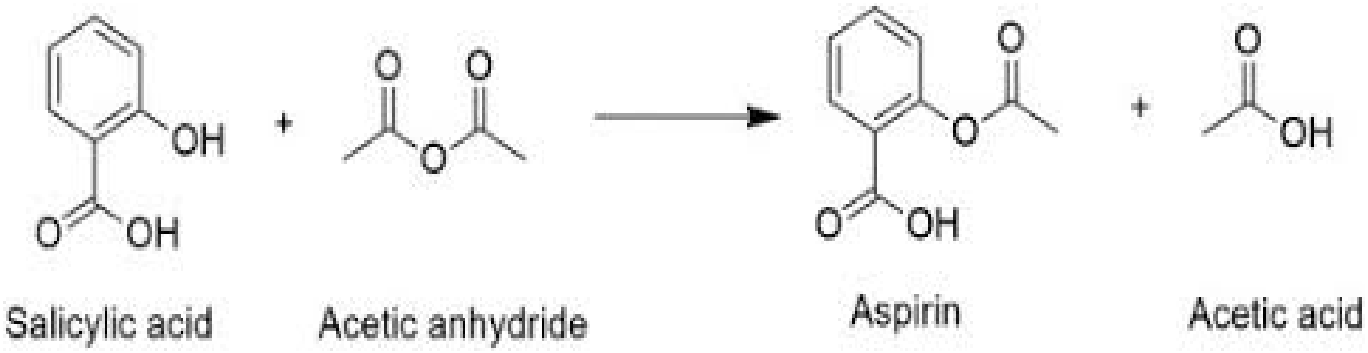


Figure 1.4: Hydrolysis of aspirin

Some drugs like aspirin hydrolysis in the human stomach allows part of the administrated volume of drug to be destroyed, which may exceed the full region of absorption in the small intestine. Researchers are also keen to keep aspirin absorbed steadily into the bloodstream using medicinally covered natural preservatives [41].

1.6.2 Acetaminophen (Paracetamol)

The structural formula and molecular weight of acetaminophen (paracetamol or N -acetyl-p-aminophenol) is $C_8H_9NO_2$ and 151.163 g/mol, respectively. It is maybe the most often available analgesic and antipyretic drug, and is found either on its own or in conjunction with other drugs in over 100 products. The medication is an appealing alternative to NSAID because it does not induce or interfere with platelet function or gastric discomfort. In fact, a daily dosage of 4000 mg was taken to revise the safety profile of acetaminophen [42]. The findings of a drug epidemiological analysis show that strong (defining 3,000 mg) of acetaminophen doses may be the same as conventional non-selective NSAIDs for the upper gastrointestinal complications. When given to humans, it decreases the levels of

prostaglandin metabolites in the urine but does not decrease the production of prostaglandins by blood platelets or stomach mucosa. Because acetaminophen is a weak inhibitor in vitro of both cyclooxygenase (COX)-1 and COX-2, the possibility exists that it inhibits a so far unidentified form of COX, perhaps COX-3. In animal studies, a COX enzyme in homogenates of different tissues vary in sensitivity to the inhibitory action of acetaminophen [43]. This may be evidence that there are >2 isoforms of the enzyme. A COX-2 form with elevated levels of anti-inflammatory nonsteroidal narcotics has recently been shown to be particularly vulnerable to inhibition. Acetaminophen (Paracetamol) is a p-aminophenol synthetic non-opioid analog and a basic bioactive molecule in several medication formulations for colds and flu [44].

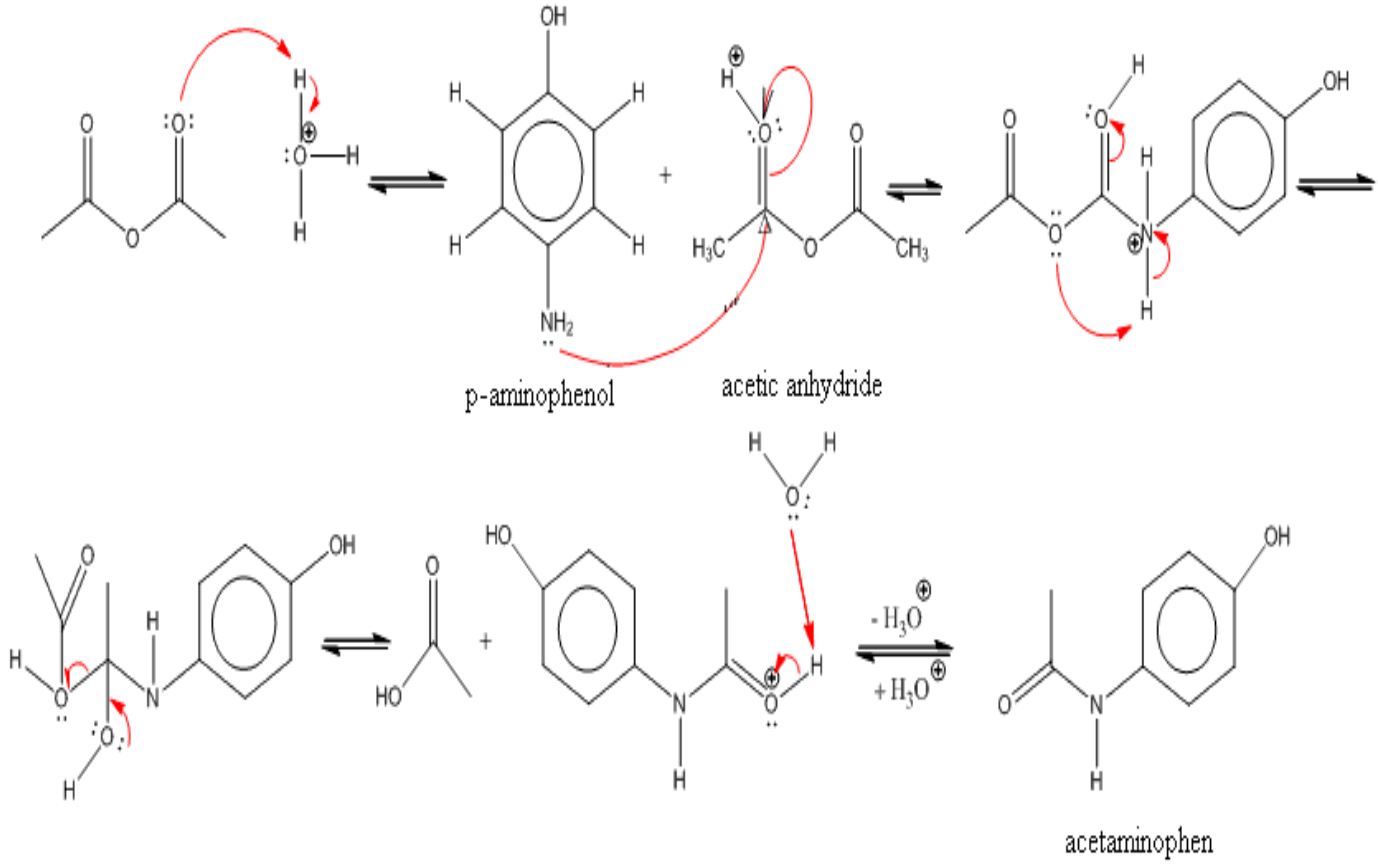


Figure 1.5: synthesis of acetaminophen.

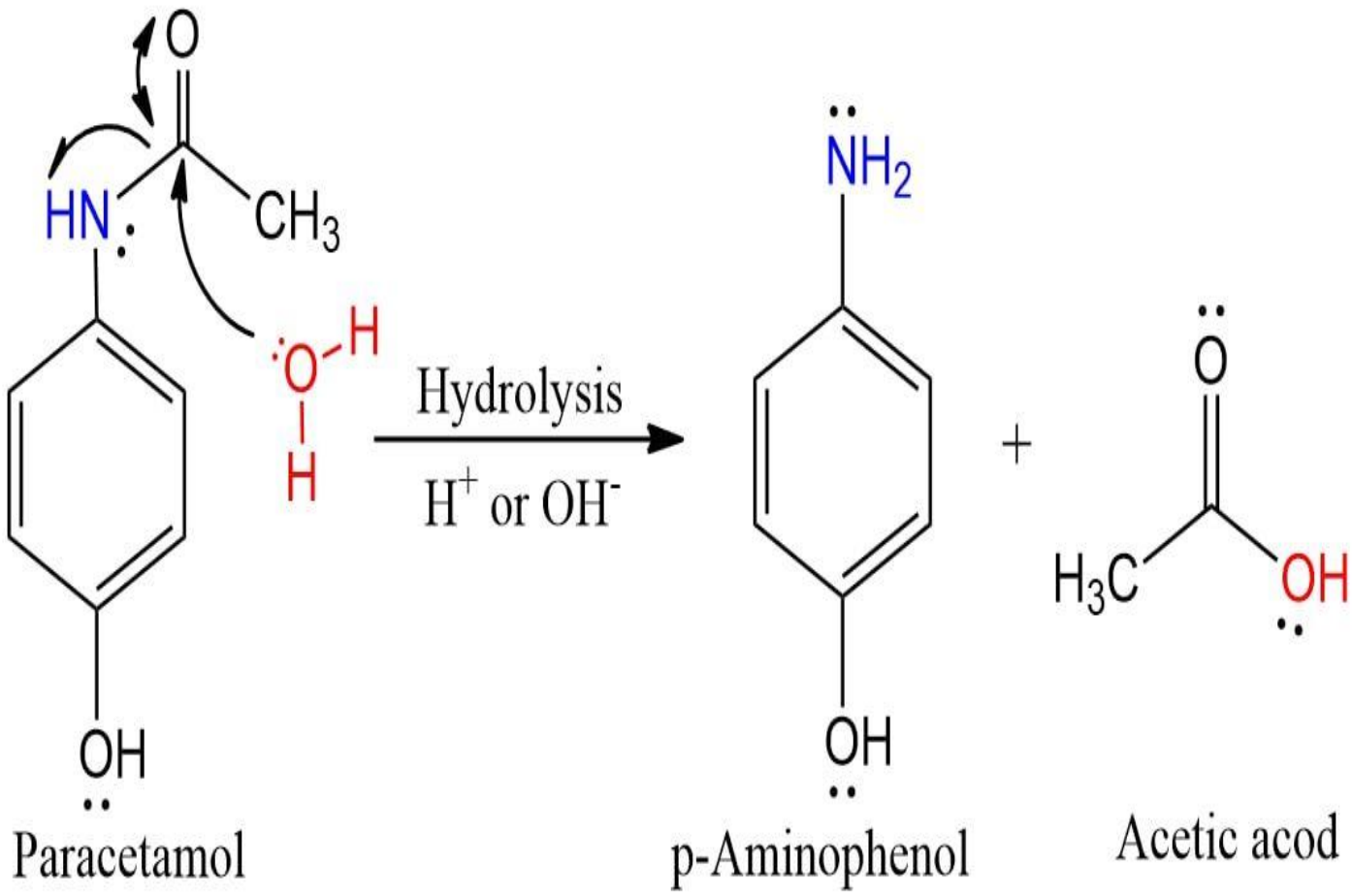


Figure 1.6: Hydrolysis of acetaminophen

1.6.3 Metronidazole (Flagyl)

The structure formula and molecular weight of metronidazole are $C_6H_9N_3O_3$ and 171.15 g/mol, respectively. Topical antibiotic in papulopustular rosacea is metronidazole. The cream, gel and lotion are available. Metronidazole also has antioxidant and anti-inflammatory properties in addition to its antimicrobial action [45]. To treat trichomonas vaginalis, metronidazole is the first drug of choice [46]. Metronidazole used for prevention and treatment of infections in oral and maxillofacial surgery is frequently prescribed three times daily [47]. Metronidazole is in the Mitroinidazole family. This function only happens when metronidazole is partly decreased and because this decline typically occurs only in anaerobic

bacteria and protozoans. It has extraordinarily little effect on human cells or aerobic bacteria. It also inhibits nuclear acid synthesizer by producing nitrous radicals, which disrupt DNA in microbic cells [48]. Methylimidazole (1) can be made with the imidazole synthesis Debus-Radziszewski or with acetic acid and ethylenediamine, supplemented by lime, and then nickel Raney. 2 - Methyl-methyl- 4(5)-nitroimidazole (2) is nitrated to create alkylated metronidazole in turn by ethylene oxides or 2-chloroethano [49-51]

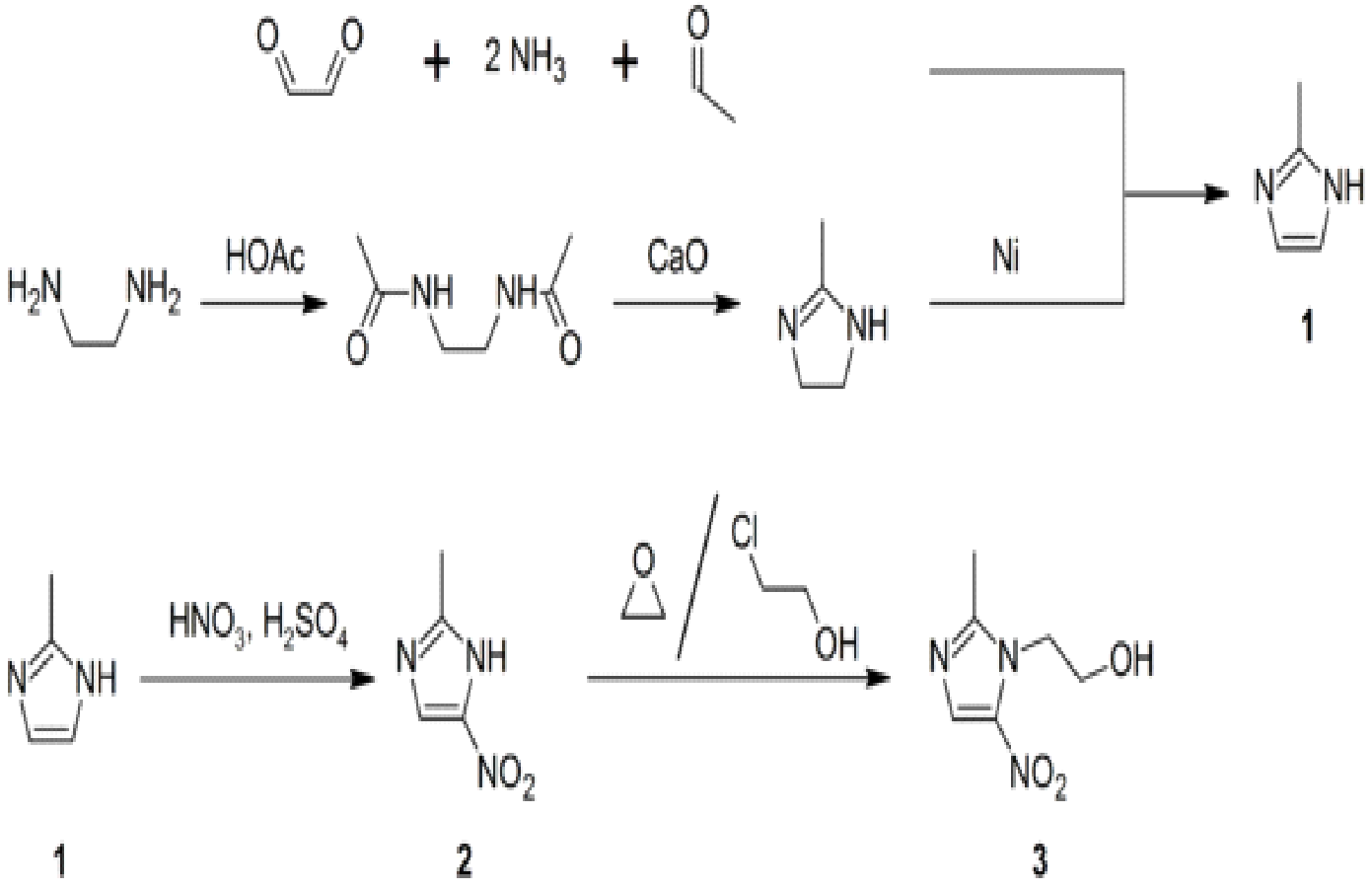


Figure 1.7: synthesis of Metronidazole

1.7 Literature Review

In the last few decades, green chemistry has widely been used as a good method to prepare the nanomaterials and use them for biomedical applications. There are **many similar studies have reported in the literature, as shown in Table 1.1.**

Table 1.1: The description of similar studies that are reported in the literature.

No.	Study Description	Sample type	Apllication	Name of used Method	Reference No.
1	This critical review provides a processing-structure-property perspective on recent advances in cellulose nanoparticles and composites produced from them. It summarizes cellulose nanoparticles in terms of particle morphology, crystal structure, and properties. Also described are the self-assembly and rheological properties of cellulose nanoparticle suspensions.	Wood,plant	Applications of cellulose nanoparticles. (a) Transparent paper for packaging, (b) luminescence of an organic light-emitting diode deposited onto a flexible, low-CTE and optically transparent wood–cellulose nanocomposite. Reprinted,	high-pressure homogenize Acid hydrolysis	27

No.	Study Description	Sample type	Application	Name of used Method	Reference No.
2	This review is aimed to discuss different extraction techniques along with their basic mechanism for extracting bioactive compounds from medicinal plants				32
3	brief account of delivery devices produced from green methods and describes site-specific drug delivery systems (including their pros and cons) and their relevance in the field of green Nano medicine	inorganic NPs,metallic NPs and quantum dots, and organic NPs, polymericNPs, mesoporous silica NPs	biomedicalapplications, disease diagnostics, and pharmaceuticals	. The approaches used for thesynthesis of metallic NPs mainly involves the following: (a)top-down approach (NPs are formed by size reduction from asuitable starting material) and (b) bottom-up approach (NPsare synthesized from the smaller things, and the nano-structured building blocks of NPs are formed at the initialstage that further leads to the formation offinal NPs)	33

		Sample type			
4	The retention ability of hydrogel has led to decrease the loss in aspirin due to its rapid release in the acidic medium of stomach and consequently increase absorbed aspirin in the small intestines. The hydrogel was made from natural products by using a green method.	potato	Drug delivery	Extraction	41
5	the use of Nano cellulose/NC in drug delivery studies and modification of NC with different antimicrobial agents. This review aims to outline the current state of research and the future development of NC in antimicrobial and drug delivery applications through selected examples. Most formulations of NC-based drugs can be used through various routes of administration and have	grape seed extract added chitosan and polycaprolact one	drug delivery and antimicrobial activity	chemical grafting	71

No	Study Description	Sample type	Application	Name of used Method	Reference No
	demonstrated controlled and, in many cases, also sustained drug release due to the addition of NC. Moreover, NC shows tremendous potential for further study and even more successful use in controlled drug delivery systems.				
6	In this context and underthe pressure of rapid development of this field, it is imperative to synthesize the successes and thenew requirements in a comprehensive review. The first part of this work provides a brief reviewof the characteristics of the NCs (cellulose nanocrystals—CNC, cellulose nanofibrils—CNF, andbacterial nanocellulose—BNC), as well as of the main functional materials based on NCs (hydrogels,nanogels, and nanocomposites).	Polymeric blends of chitosan (C) and gelatin	drug-delivery systems, materialsfor wound-healing applications, as well as tissue engineering	:	72

No	Study Description	Sample type	Application	Name of Used Method	References No
7	Nanocellulose, which can exist as either cellulose nanocrystals or cellulose nanofibrils, has been used as a biomaterial for drug delivery owing to its non-immunogenicity, biocompatibility, high specific area, good mechanical properties, and variability for chemical modification. Various water-soluble drugs can be bound to and released from nanocelluloses through electrostatic interactions. The high specific surface area of nanocellulose allows for high specific drug loading. Additionally, a broad spectrum of drugs can bind to nanocellulose after facile chemical modifications of its surface. Controlled release can be achieved for various pharmaceuticals when the Nano.	stimuli-responsive cubic phase, liposomal, and polymeric drug	stimuli-responsive drug carriers	Thermal method	

No	Study Description	Sample type	Application	Name of Used Method	References No
	cellulose surface is chemically modified or physically formulated in an adequate manner. This review summarizes the potential applications of nanocelluloses in drug delivery according to published studies on drug delivery systems.				

1.9 Aim and Objectives

1- The main aim of this study is to synthesis a Nano-cellulose from potato by using Green Synthesis of Nano Materials in this step no chemical has been used.

2- Using it as drug deliver. In addition, this process was carried out by using biomass in the simulated bowel and gut temperature and pH conditions, to verify its effect on the release rate of drugs(Aspirin, Acetaminophen , Metronidazole)

It was found that the FTIR spectra confirmed the presence of amorphous (Nano crystalline) cellulose's structure by detecting several functional groups such as (-OH) broad (3100-3600 cm-1), (C-H) (2800-3000 cm-1), (C-H) symmetric bending (1400 cm-1), and (C–O–C) stretching (856 cm-1).

AFM measurements and SPM analysis reports were proved the Nano scale of prepared cellulose particles by showing the average diameter was (23.44 nm) and

At applicable scale, different equivalent ratios of Nano cellulose were used with the medicines to find out the best quantity of nanoparticles that can be used for the purpose of encapsulating the medicine and keeping it from liberating and losing quantities of it in the acidity of the stomach, and then transferring it to the safest area of greatest absorption in the human body (small intestine, alkaline medium).

Chapter Two

Experimental Part

2.0 Introduction

This chapter describes the sampling, storage, and preparation methods that were carried out on the natural materials (Potato and lemon) and drugs (aspirin, acetaminophen, Metronidazole), as shown in.Table **2.1** The fundamental theory for each method, along with any development procedures used for the synthesis of cellulose are reported in Figure 2.1. The main technique used for the identification of Nano-cellulose was Fourier transform infrared spectroscopy (FTIR) and Scanning probe microscope (SPM), as outlined in **2.4.1 and 2.5**

2.1 Instrumentations

The following sub-sections describe the analytical instrumentation employed throughout this study, as shown in Table 2.1.

Table 2.1: Tools used during the entire work

No.	Instrument	Source & Model
1	Uv-vis double beam spectrophotometer with a quartz cell of 1 mL.	(Shimadzu uv spectrophotometer 1800 pc (Japan))
2	Scanning electron microscopy (SEM)	(JSM.6390A) (TOKYO JAPAN)
3	Sensitive balance ± 0.0001g.	Electronic balance ACS120-4 Kern& Sohn GmbH, Germany
4	Heating /string	(Germany)
5	Centrifuge	Germany)
6	Fourier-transform infrared Spectroscopy (FT- IR)	Shimadzu- 8000 (Japan)
7	Micropipette 1000µL	Dragon MED, china
8	Ultrasonic bath	(SONERX) (W. GERMANY)
9	Water bath	Memmert-854 Schwalbach, Germany
10	Hotplate with magnetic stirrer	Electrothermal, England

2.2 Reagents and Chemicals

There are several chemicals have been used in current study to prepare the samples and drugs as described in Table 2.2.

Table 2.2: List of chemicals

No.	Materials	M.wt	Purity	Suppliers
1	Methamphetamine	149.41	99.99	Sigma–Aldrich
2	Aspirin, (AS)	180.15	99.99	Sigma–Aldrich
3	Clopidogrel (**CLO**)	321.81	99.99	Sigma–Aldrich
4	Trimethylpropane trimethacrylate(TRIM)	338.40	99.99	Sigma–Aldrich
5	Methyl methacrylic acid (MAA)	100.12	99.99	Sigma–Aldrich
6	Styrene	104.15	99.99	Sigma–Aldrich
7	Acrylic acid (AA)	71.04	99.99	Sigma–Aldrich
8	Acrylamido-2-methyl propane Sulphonic acid (AMPS)	207.25	99.00	Sigma–Aldrich
9	ethylene glycol dimethyl acrylate (EGDMA)	198.22	99.99	Sigma–Aldrich
10	Benzoyl peroxide	242.23	99.99	Sigma–Aldrich
11	Chloroform	119.38	99.00	Merck
12	Methanol	32.04	99.90	Merck
13	Ethanol	46.07	99.90	Merck
14	Acetic acid	60.05	99.00	Merck
15	Acetonitrile	41.05	99.00	Fluka
16	Nitrogen gas	28.01	99.00	Arab gulf Factory Baghdad

2.3. Sample Collection and Preparation

In general, the material samples were either solid or liquid, and homogenous or heterogeneous in terms of physical and chemical composition. The accuracy of the analysis depends significantly on the conditions under which the sample is collected [52]. For example, heterogeneous samples require further care during sampling and will need special pre-analysis treatment before storage and analysis

[53]. However, certain precautions should be taken to prevent or minimize contamination, loss, decomposition, or matrix change.

2.3.1 Cellulose

In this procedure, the known weight (562.5 g) of the fresh potato sample was washed using enough volume of distilled deionized water. Acetone/distilled deionized water-washed knife was used to cut a sample into small pieces (~ 5 mm) to obtain a homogenous sample. This process was carried out to minimize contamination presented by the tools throughout sample collection and preparation [54]. Then the sample was squeezed mechanically for potato extract, then filtered using a piece of cloth. In addition, possible oxidation of sample by light or air was minimized by transferring the produced extract sample into a labelled dark container. After that, the extracted sample was heated at 50 °C. Several drops of citric acid (lemon juice) were added to the extracted sample. The extracted sample was centrifuged (10 minutes) at 6000 rpm, then and filtered through Whatman filter paper 42 (2.5 μm). The precipitate was washed by distilled deionized water, then dried at room temperature [55].

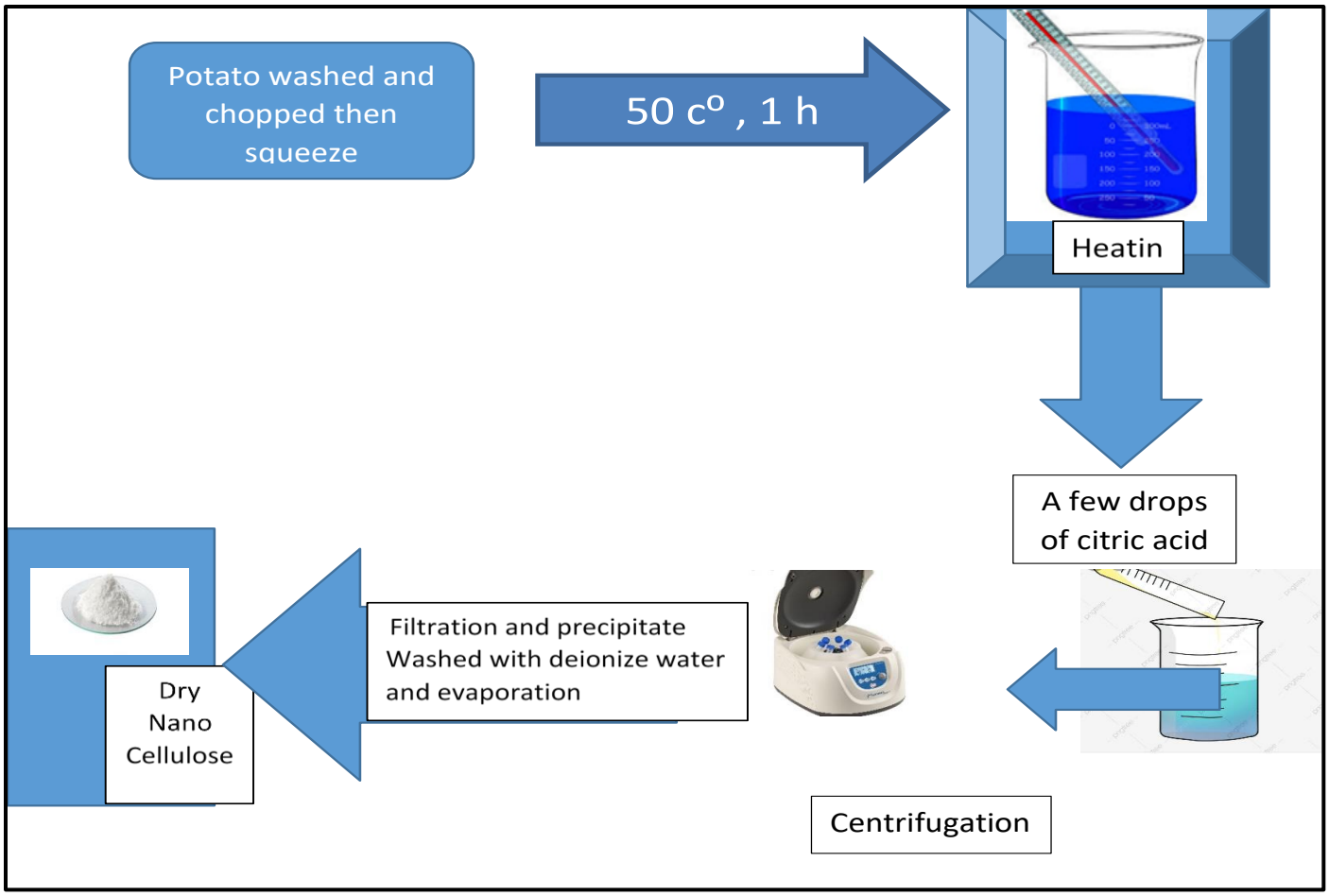


Figure 2.1: Scheme for preparation of cellulose particles.

2.3.2 Drugs

The three types of drugs, namely Paracetamol, Aspirin, and Metronidazole were selected in this study, as shown in Table 2.3. The purpose of this step was to investigate that the Nano cellulose particles providing spatiotemporal control of drug release contribute to decreasing toxicity and enhancing the therapeutic efficiency of a drug [56].

Table 2.3: Chemical properties of drugs

Trade name & (IUPAC ID)	Formula	Molecular weight (g/mol)	Melting point	Drug class
Paracetamol (N-(4-hydroxyphenyl)acetamide	$C_8H_9NO_2$	151.163	169 °C	Analgesics and antipyretics
Aspirin (2-Acetoxybenzoic acid)	$C_9H_8O_4$	180.187	135 °C	Antiplatelet Agents, Cardiovascular and Hematologic
Metronidazole (2-(2-Methyl-5-nitro-1H-imidazol-1-yl)ethanol)	$C_6H_9N_3O_3$	171.150	159 to 163 °C	Antibiotics

2.3.3 Applications

2.3.3.1 Standard solutions

Nano-Cellulose

In this work, stock solution (1000 mg/L) was prepared by dissolving 1g of Nano-cellulose in several milliliters of 1N sodium hydroxide, then the solution was transferred to a clean/dried and labeled 1L volumetric flask and diluted with de-ionized water. Several drops of 0.1N hydrochloric acid were added to this solution to fix the pH value on 7. Standard solutions (100, 200, 300, 400, and 500 mg/L) were prepared by serial dilution of standards from 1000 mg/L of cellulose.

Drugs

The stock solutions (1000 mg/L) of Aspirin, Paracetamol, and Metronidazole were prepared by dissolving 1g of each drug in several milliliters of 1N hydrochloric acid. then the solutions were transferred to a clean/dried and labeled 1L volumetric flask and diluted with de-ionized water. Several drops of 0.1N sodium hydroxide were added to this solution to fix the pH value on 7. Standard solutions (100, 200, 300, 400, and 500 mg/L) were prepared by serial dilution of standards from 1000 mg/L of a drug.

Standard solution of sodium hydroxide

Standard solution of 2000 mg/L of sodium hydroxide by dissolving 2g of NaOH in one litter of de-ionized water.

2.3.3.2 Titration procedure

Under the standard conditions, namely simulated conditions for the human body such as temperature (37.5°C), drinking water, and acidic function (pH=2), the titrations between sodium hydroxide and both of drug and mixture (drug and cellulose) were undertaken.

Aspirin

Titration of aspirin with NaOH

In this titration, three drops of phenolphthalein were added to 25 mL of 100 mg/L aspirin, then titrated with a standard solution of sodium hydroxide. The volume of NaOH was recorded to determine the concentration of aspirin in this solution.

Titration of mixture with NaOH

This titration aims to evaluate a controlled drug release system and whether nano-cellulose material can use as a pharmaceutical carrier for aspirin, the mixtures were prepared by using different ratios of aspirin and cellulose for five solutions (100, 200, 300, 400, 500 mg/L), as shown in Table 2.4. The concentration of aspirin for other solutions (200, 300, 400, 500 mg/L aspirin) was calculated

using the same manner as described above. The above procedure was repeated by using different values of pH (2, 4, 6, 8).

Table 2.4: The mixture ratios for aspirin and cellulose

PH	Mixture ratio (aspirin: Nano-cellulose)			
2	**1:1**	**1:2**	**1:3**	**1:4**
4	**1:1**	**1:2**	**1:3**	**1:4**
6	**1:1**	**1:2**	**1:3**	**1:4**
8	**1:1**	**1:2**	**1:3**	**1:4**

Paracetamol

Titration of paracetamol with NaOH

In this titration, three drops of phenolphthalein were added to 25 mL of 100 mg/L paracetamol, then titrated with a standard solution of sodium hydroxide. The volume of NaOH was recorded to determine the concentration of paracetamol in this solution.

Titration of mixture with NaOH

This titration aims to evaluate a controlled drug release system and whether nano-cellulose material can use as a pharmaceutical carrier for paracetamol, the mixtures were prepared by using different ratios of paracetamol and cellulose for five solutions (100, 200, 300, 400, 500 mg/l paracetamol), as shown in Table 2.5. The concentration of paracetamol for other solutions (200, 300, 400, 500 mg/l) was

calculated using the same manner as described above. The above procedure was repeated by using different values of pH (2, 4, 6, 8).

Table 2.5: The mixture ratios for paracetamol and cellulose

PH	Mixture ratio (paracetamol: nano-cellulose)			
2	**1:1**	**1:2**	**1:3**	**1:4**
4	**1:1**	**1:2**	**1:3**	**1:4**
6	**1:1**	**1:2**	**1:3**	**1:4**
8	**1:1**	**1:2**	**1:3**	**1:4**

Metronidazole

Titration of metronidazole with NaOH

In this titration, three drops of phenolphthalein were added to 25 cm3 of 100 mg/l metronidazole, then titrated with a standard solution of sodium hydroxide. The volume of NaOH was recorded to determine the concentration of metronidazole in this solution.

Titration of mixture with NaOH

This titration aims to evaluate a controlled drug release system and whether nano-cellulose material can use as a pharmaceutical carrier for metronidazole, the mixtures were prepared by using different ratios of metronidazole and cellulose for five solutions (100, 200, 300, 400, 500 mg/l), as shown in Table 2.6. The concentration of metronidazole for other solutions (200, 300, 400, 500 mg/l) was calculated using the same manner as described above. The above procedure was repeated by using different values of pH (2, 4, 6, 8).

Table 2.6: The mixture ratios for metronidazole and cellulose

PH	Mixture ratio (metronidazole: Nano-cellulose)			
2	**1:1**	**1:2**	**1:3**	**1:4**
4	**1:1**	**1:2**	**1:3**	**1:4**
6	**1:1**	**1:2**	**1:3**	**1:4**
8	**1:1**	**1:2**	**1:3**	**1:4**

2.4 Analytical Instrumentation

There is a wide range of analytical techniques that can use to evaluate the synthesis and characterization of Nano-cellulose along with its role to work as a pharmaceutical carrier for different drugs. For example, such as Fourier-transform infrared spectroscopy (FTIR) and atomic force microscopy (AFM) through scanning probe microscopy (SPM) technique. The following sub-sections describe in detail the analytical instrumentation utilized throughout this study [57].

2.4.1 Fourier-transform infrared spectroscopy (FTIR)

2.4.1.1 Introduction

The infrared region of the spectrum encompasses radiation with wavenumbers ranging from about 12,800 to 10 cm-1 or wavelengths from 0.78 to 1000 μm. The infrared spectrum is divided into near-, mid-, and far-infrared radiation, as shown in Table 2.7 [58].

Table 2.7: IR spectral regions.

Region	**Wavelengths (λ), μm**	**Wavenumbers (υ), cm^{-1}**	**Frequencies (υ), Hz**
Near	0.78 to 2.5	12800 to 4000	3.8×10^{14} to 1.2×10^{14}
Middle	2.5 to 50	4000 to 200	1.2×10^{14} to 6.0×10^{12}
Far	50 to 1000	200 to 10	6.0×10^{12} to 3.0×10^{11}
Most used	2.5 to 15	4000 to 670	1.2×10^{14} to 2.0×10^{13}

Based on IR absorption by molecules as undergo vibrational and rotational transitions. Absorption of radiation in this region by a typical organic molecule results in the excitation of vibrational, rotational, and blending modes, while the molecule itself remains in its electronic ground state, as shown in Figure 2.2.

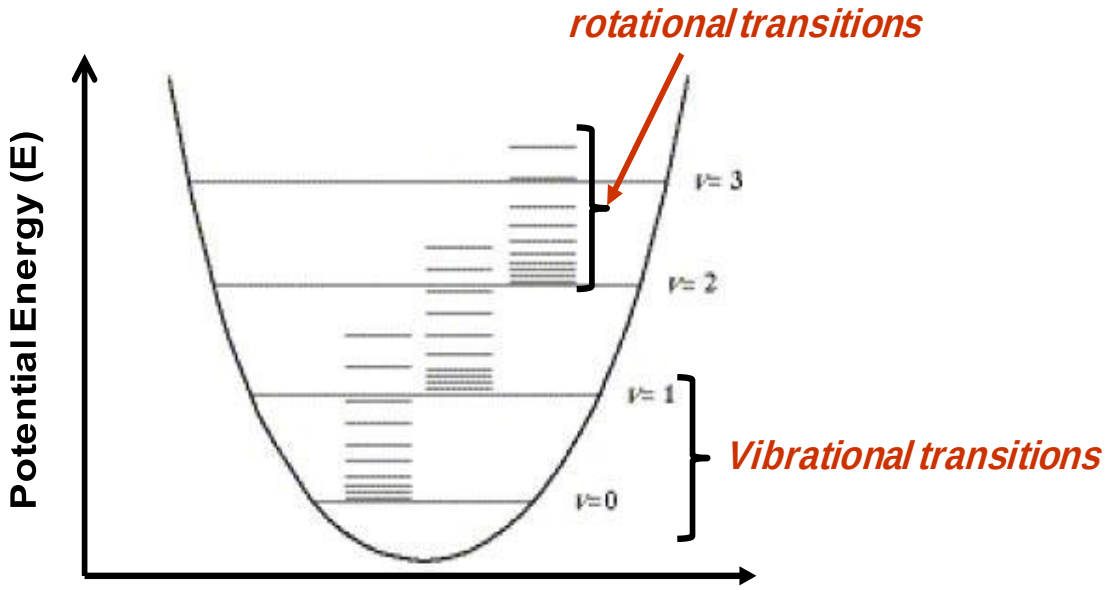


Figure 2.2. Potential energy resembles classic Harmonic Oscillator

2.4.1.1 Fundamental

In this technique, light from a source is split by a central mirror into two beams of equal intensity. Then beams go to two other mirrors, reflected by the central mirror, recombine and pass-through sample to the detector. There are two side mirrors, one fixed and the other movable. When the second mirror moves, light in two paths travels different distances before recombining. Constructive and destructive interference occurs as the mirror is moved, which leads to obtaining a change in signal [59], Light enters the spectrometer and is split by the beam splitter. Figure 2.3 shows what is referred to as the Michelson interferometer.

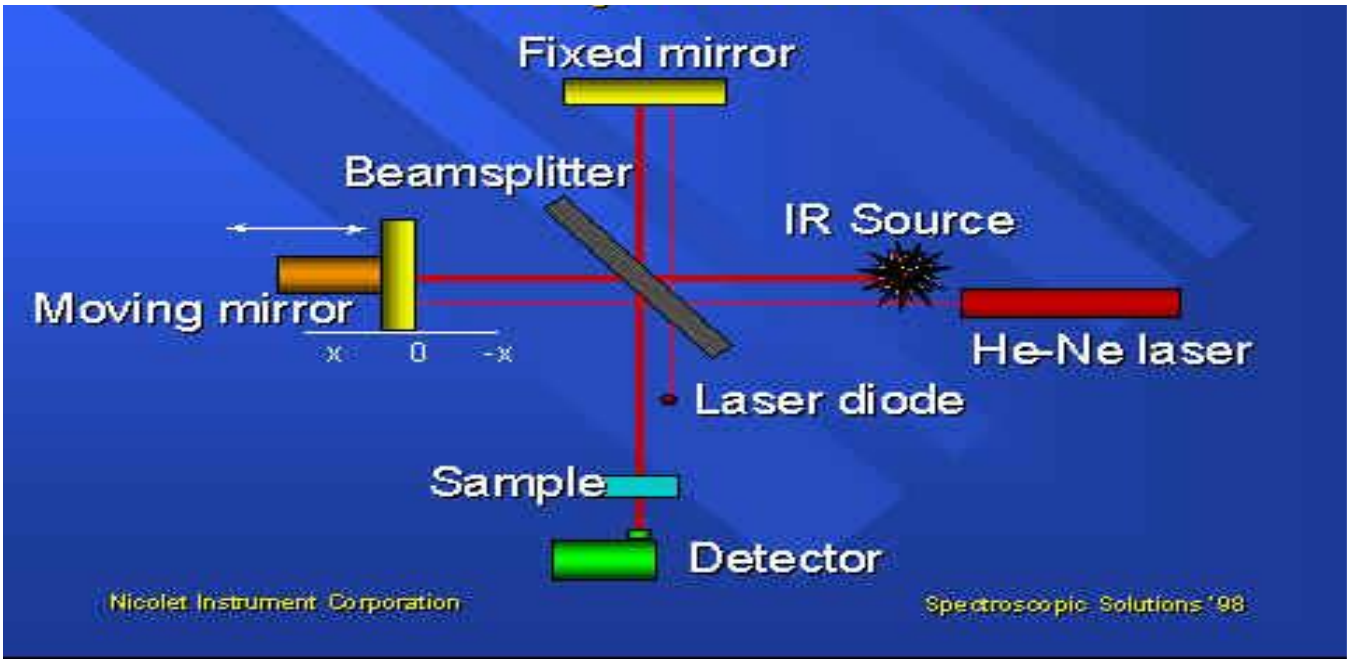


Figure 2.3: FT-IR spectrometer

Destructive Interference can be created when two waves from the same source travel different paths to get to a point. This may cause a difference in the phase between the two waves. If the paths differ by an integer multiple of a wavelength, the waves will also be in phase. While, if the waves differ by an odd multiple of half a wave, then the waves will be 180 degrees out of phase and cancel out. [60]

2.4.1.2 Advantages of FTIR

- Enhanced signal-to-noise
- Rapid scanning
- High resolution (<0.1 cm^{-1})
- Accurate and reproducible frequency determinations
- Larger energy throughput
- Free from problems of stray radiation[61]

2.4.1.3 Applications

Qualitative Analysis (Compound Identification)

The main use of FTIR with NMR and MS revolutionized organic chemistry due to it was decreased the time to confirm compound identification 10- 1000-fold. Figures 2.4 and 2.5 show the general Scheme which examines the functional groups are present by looking at group frequency region - 3600 cm^{-1} to 1200 cm^{-1}. The frequencies for organic groups are presented in Table 2.8.

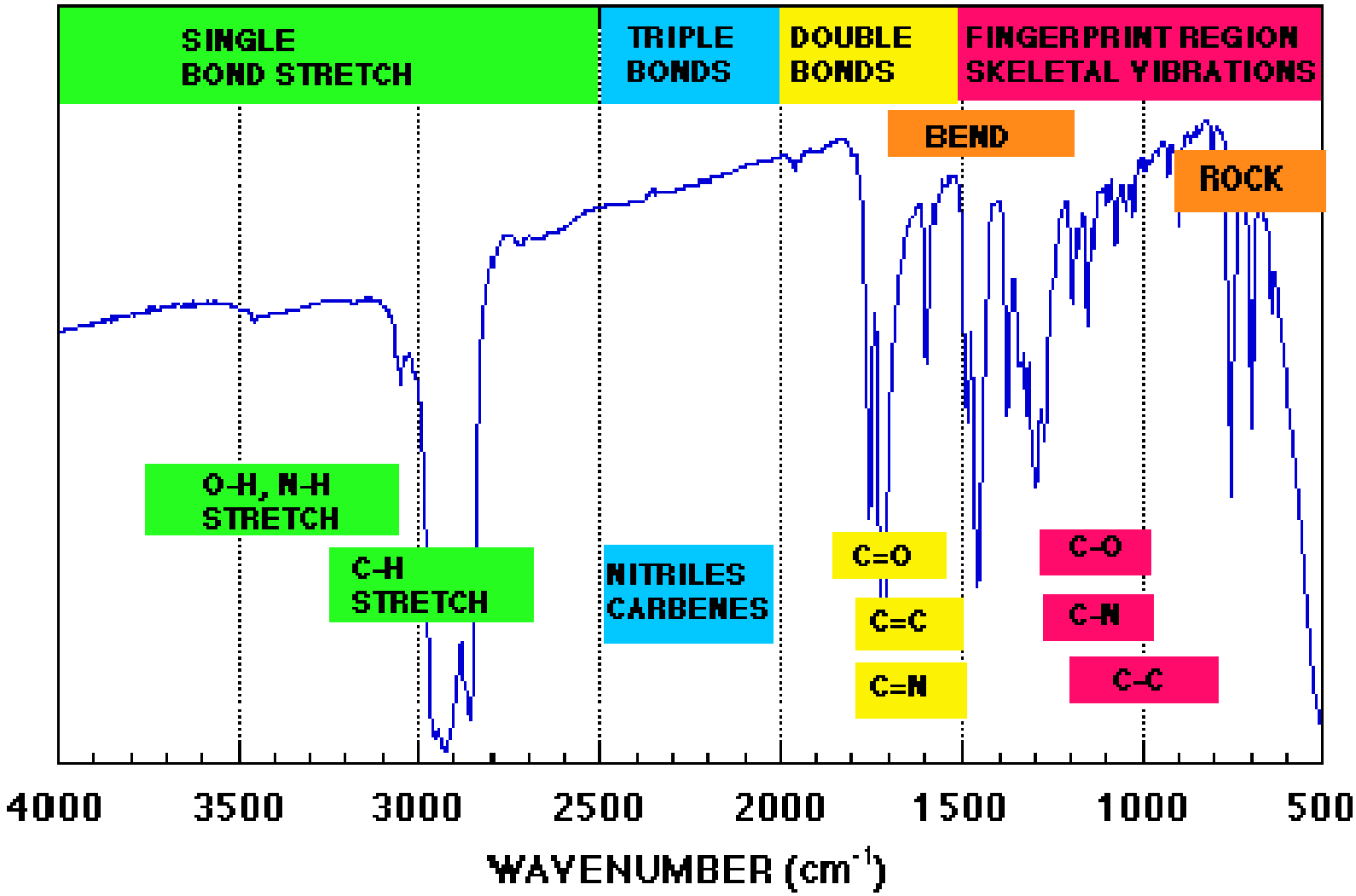


Figure 2.4: Functional groups are present at group frequency regions [62]

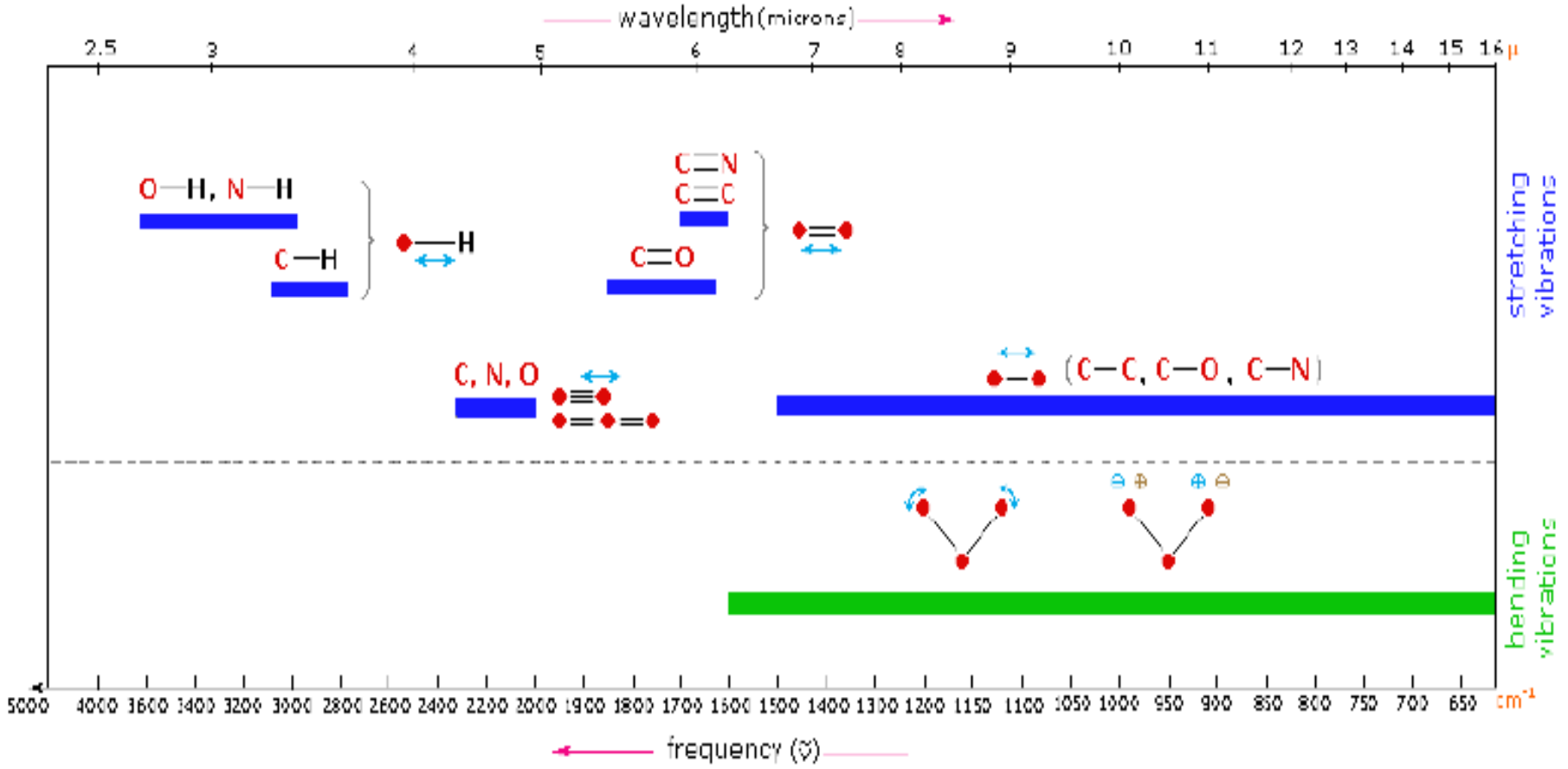
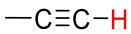


Figure 2.5: Group frequency regions at FT-IR chart [63]

Table 2.8: Frequencies for organic groups [64].

Bond	Type of Compound	Frequency Range , cm^{-1}	Intensity
C-H	Alkanes	2850-2970	Strong
C-H	Alkenes 	3010-3095 675-995	Medium Strong
C-H	Alkynes 	3300	Strong
C-H	Aromatic rings	3010-3100 690-900	Medium Strong
O-H	Monomeric alcohols, phenols Hydrogen- bonded alcohols ,phenols Monomeric carboxylic acids Hydrogen- bonded carboxylic acids	3590-3650 3200-3600 3500-3650 2500-2700	Variable Variable, sometimes broad Medium Broad
N-H	Amines , Amides	3300-3500	Medium
C=C	Alkenes	1610-1680	Variable
C=C	Aromatic rings	1500-1600	Variable
C≡C	Alkynes	2100-2260	Variable
C-N	Amines, Amides	1180-1360	Strong
C≡N	Nitriles	2210-2280	Strong
C-O	Alcohol ,ethers, carboxylic acids, esters	1050-1300	Strong
C=O	Aldehydes, ketones, carboxylic acids, esters	1690-1760	Strong
NO_2	Nitro compounds	1500-1570 1300-1370	Strong

2.4.2 Atomic Force Microscopy (AFM) - Scanning Probe Microscopy (SPM)

Scanning probe microscopes (SPMs) are a family of instruments used for studying surface properties of materials on the atomic level. A fine probe is scanned over a surface (or the surface is scanned under the probe). By using such a probe, researchers are no longer restrained by the wavelength of light or electrons. The resolution obtainable with this technique can resolve atoms, type. ~ 20 Å in x,y directions (ideal sample & instruments 1 Å), in z-direction 1 Å, where electron mic. ~ 50 Å. Unlike optical and electron microscopes SPMs details not only on the x, y-axis but also on the z-axis. In addition, true 3-D maps of surfaces are possible. Figure 2.6 shows the basic information of the scanned probe technique [65].

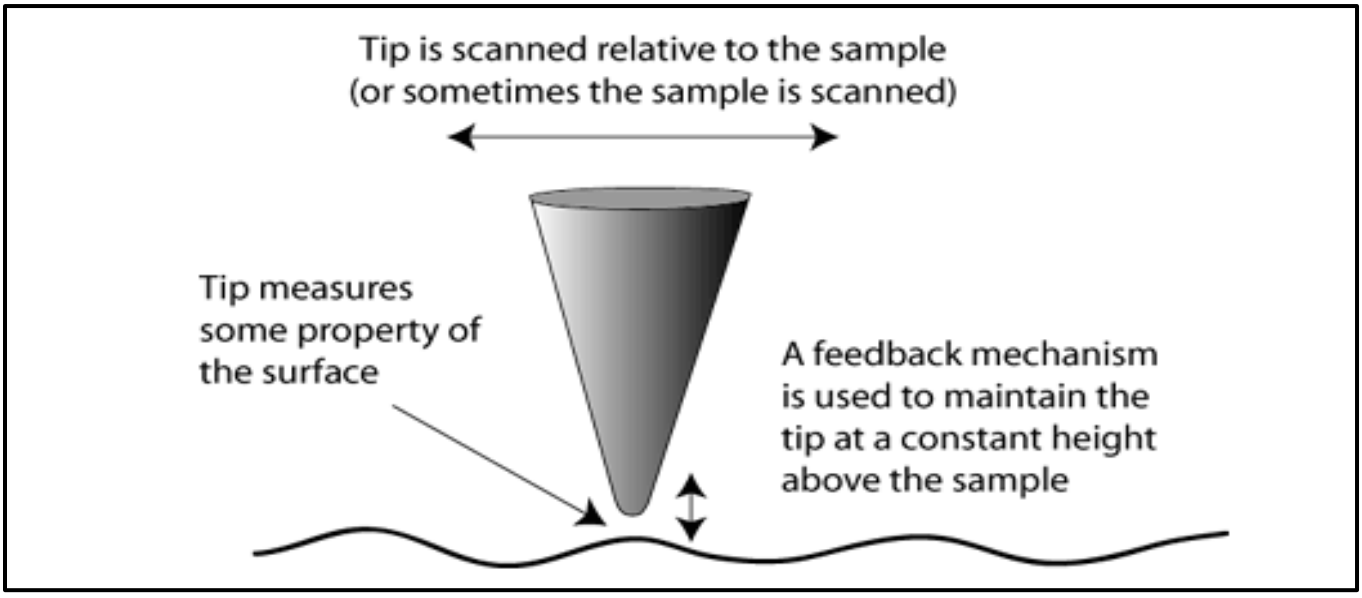


Figure 2.6: shows the basic idea of the scanned probe technique

There are three most common scanning probe techniques are described below [66]:

❖ Atomic Force Microscopy (AFM)

- ❖ measures the interaction force between the tip and surface. The tip may be dragged across the surface or may vibrate as it moves. The interaction force will depend on the nature of the sample, the probe tip, and the distance between them.
- ❖ Scanning Tunneling Microscopy (STM) measures a weak electrical current flowing between tip and sample as they are held a very distance apart.
- ❖ Near-Field Scanning Optical Microscopy (NSOM) scans a very small light source very close to the sample. Detection of this light energy forms the image. NSOM can provide resolution below that of the conventional light microscope.

AFMs can be used to study insulators and semiconductors as well as electrical conductors. Probes the surface of a sample with a sharp tip, a couple of microns long and often less than 100Å in diameter. (The tip is located at the free end of a cantilever that is 100 to 200μm long). Forces between the tip and the sample surface cause the cantilever to bend or deflect. A detector measures the cantilever deflection as the tip is scanned over the sample, or the sample is scanned under the tip. The measured cantilever deflections allow a computer to generate a map of surface topography, as shown in Figure 2.7. As in STM motion of the tip or sometimes the sample, is achieved with a piezoelectric tube. In this technique, 3-D Surface Topography and Force Measurements in pico-Newton - nano-Newton range can achieve [67].

Advantages and disadvantages

Advantages

- High scan speeds.
- Atomic resolution is possible.
- Easier scanning of rough samples with extreme changes in vertical topography.

Disadvantages

- Lateral forces can distort the image.
- Capillary forces from a fluid layer can cause large forces normal to the tip-sample interaction.
- The combination of these forces reduces spatial resolution and can cause damage to soft samples.

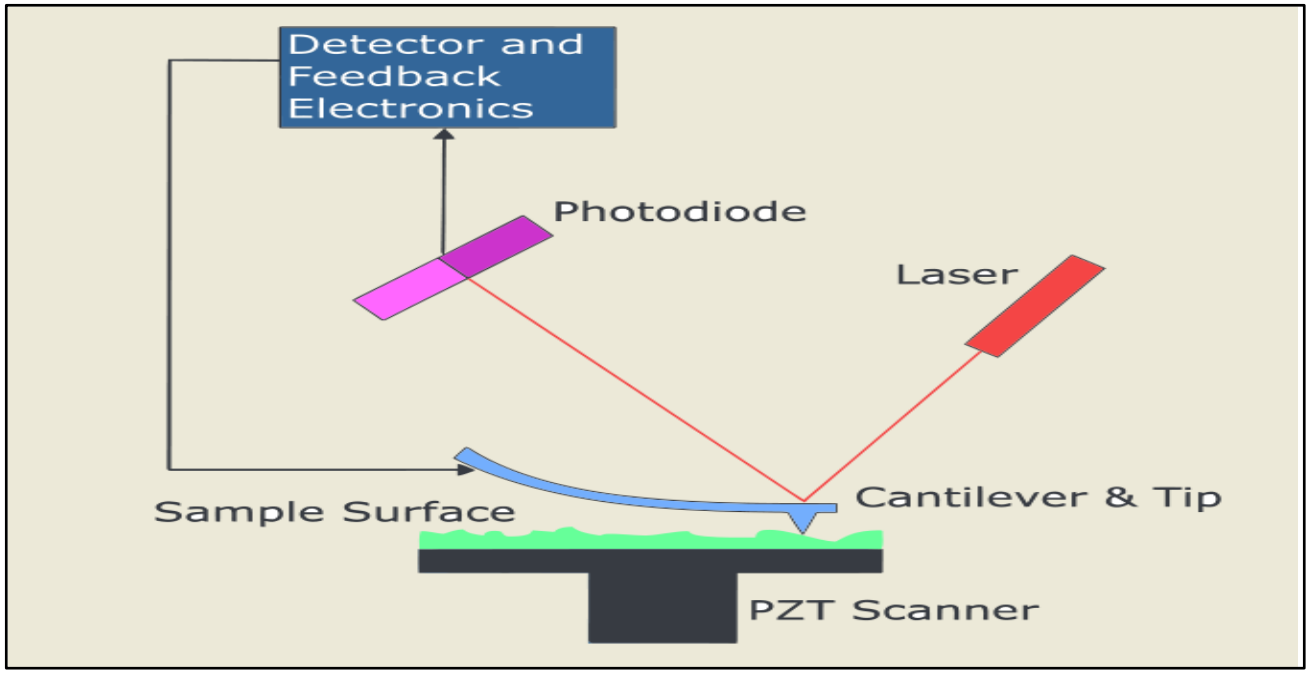


Figure 2.7: Schematic diagram of AFM machine

The developed methods and described techniques outlined in this chapter are now used for the analysis of prepared cellulose and drugs and the results are reported in Chapters 3.

Overview of the Study Area

This study was carried out in the Department of Chemistry, Faculty of Science, the University of Karbala in Karbala province. Karbala is a city in Iraq located about 60 miles south west of Baghdad at 32.61°N, 44.08°E with approximately one million inhabitants. This research is used to obtain the Degree of Master of Science in Chemistry.

Chapter Three

Results and Discussions

3. Results and Discussion

This chapter discussed the results of the preparation of Nano cellulose particles and their application as a system for medicines delivery. The prepared nanoparticles were characterized using FTIR to test the functional groups over their polymeric structure and to confirm their morphology of nanoparticles surface that was observed using Atomic Force Microscopy (AFM) through Scanning Probe Microscopy (SPM) technique.

FTIR spectra showed an absorption peak at the region of (3600-3100 cm^{-1}) was due to the stretching of the (-OH) group and peak appeared at (3000-2800 cm^{-1}) that belong to the stretching of (C-H) group. The band was observed at (1651 cm^{-1}) across from the bending (H-O-H) of the absorbed water. The symmetric bending for (C-H) group occurred at (1400 cm^{-1}).

The main characteristic peaks were detected at the fingerprint region of absorption band (856 cm-1), which assigned to the stretching of (C–O–C) group at β-(1→4)-glycosidic linkages, is designed as an “amorphous” absorption band. The IR spectra confirmed the presence of amorphous (Nano crystalline) cellulose’s structure, as in the following figures 1 and 2.

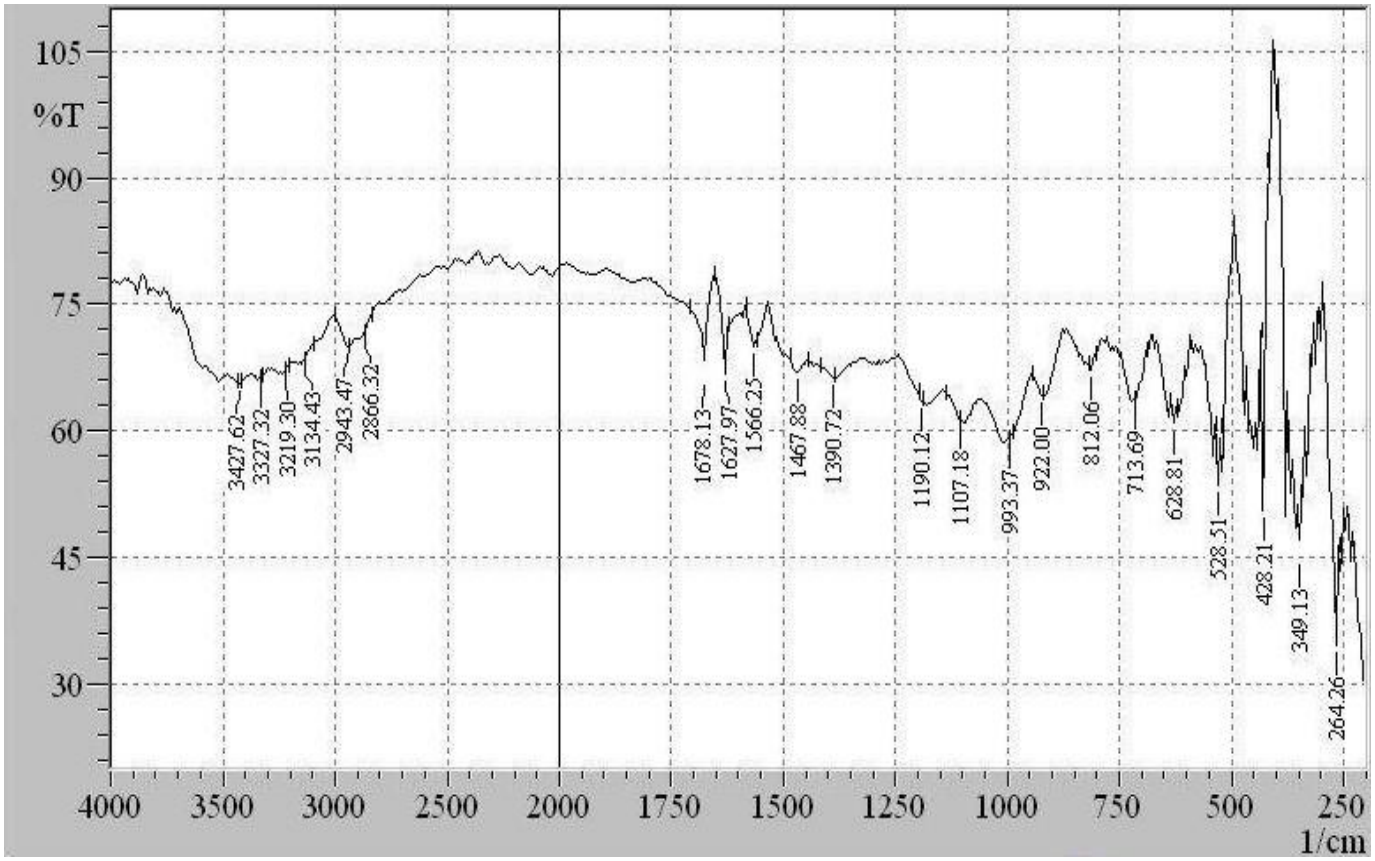


Figure 3.1 FTIR spectra for abstracted starch

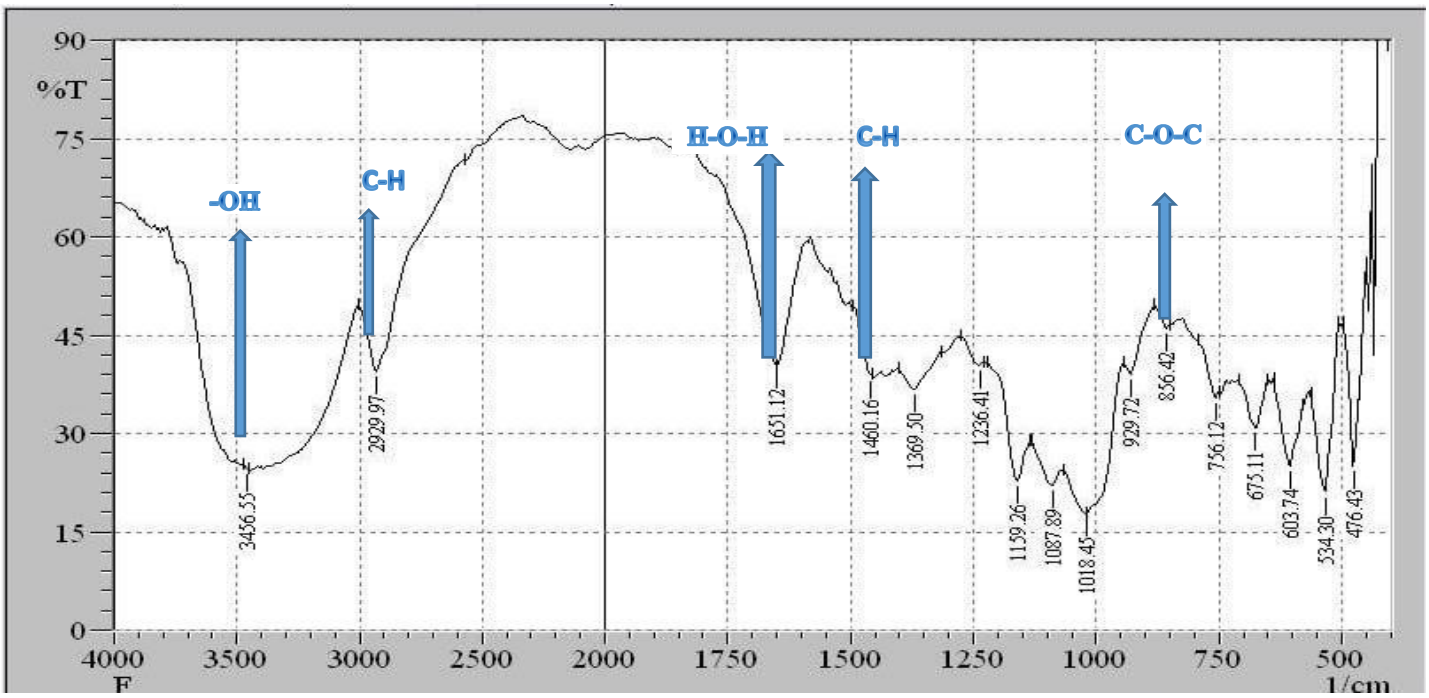


Figure 3.2 FTIR spectra for prepared Nano cellulose

AFM measurements and SPM analysis reports were proved the Nano scale of prepared cellulose particles by showing the average diameter was (23.44 nm) of Nano cellulose according to granularity cumulation distribution chart, while the average height was (12.714 nm) according to the height cumulation distribution chart, as in charts (3.1-3.2), respectively. Figures (3.3-3.5) shows the surface topology and roughness analysis and parameters as mentioned in Table (1).

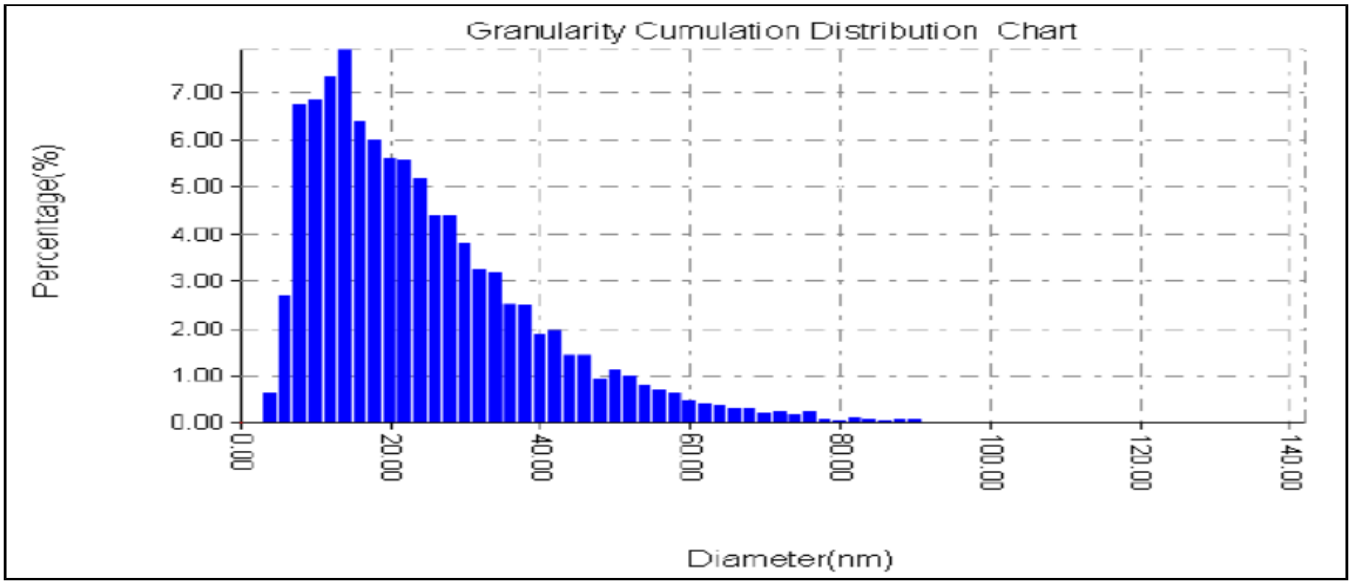


Chart 3.1 Granularity cumulation distribution of Nano cellulose particle

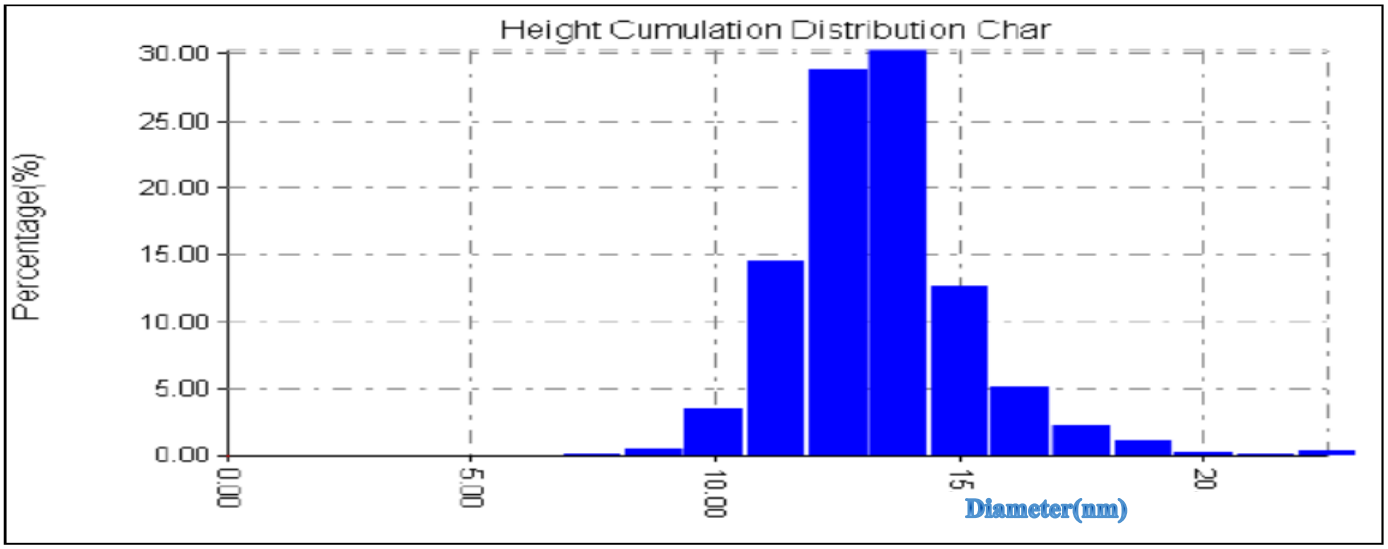


Chart 3.2 Height cumulation distribution of Nano cellulose particles

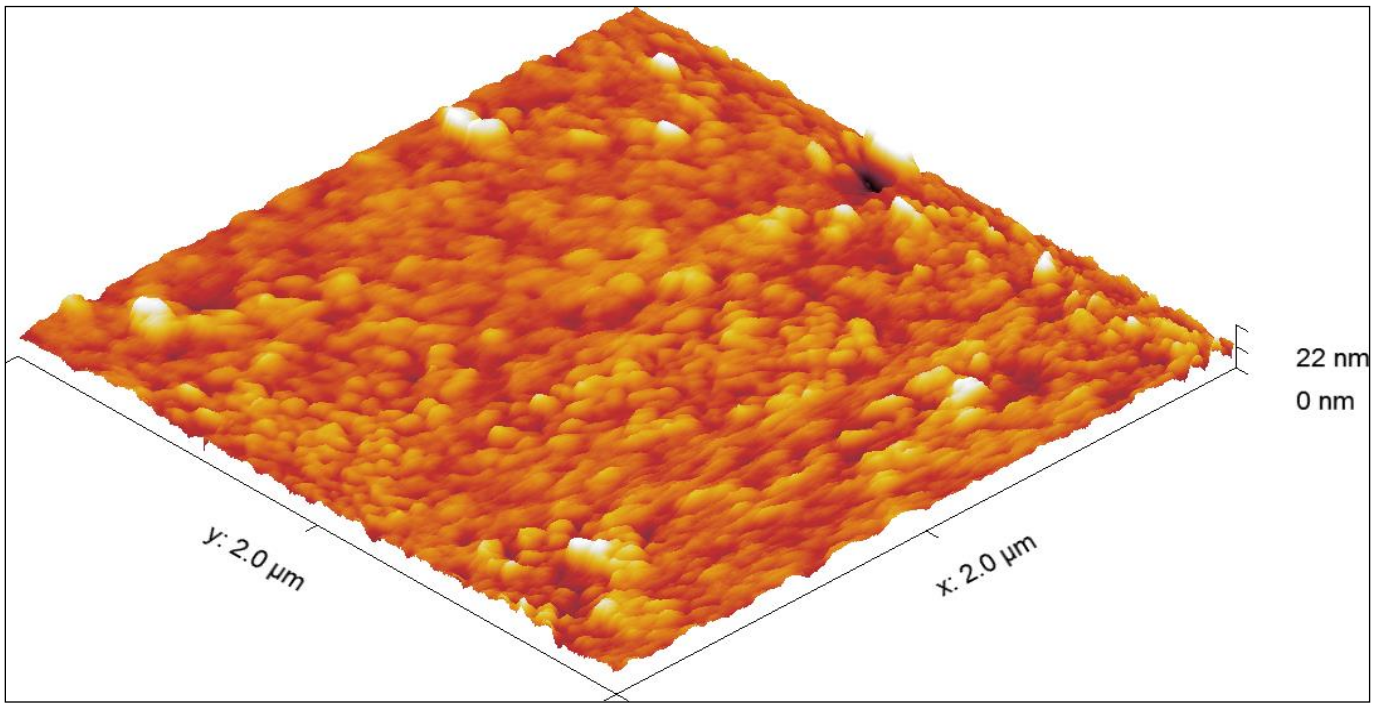


Figure 3.3 3D-Surface topology of Nano cellulose

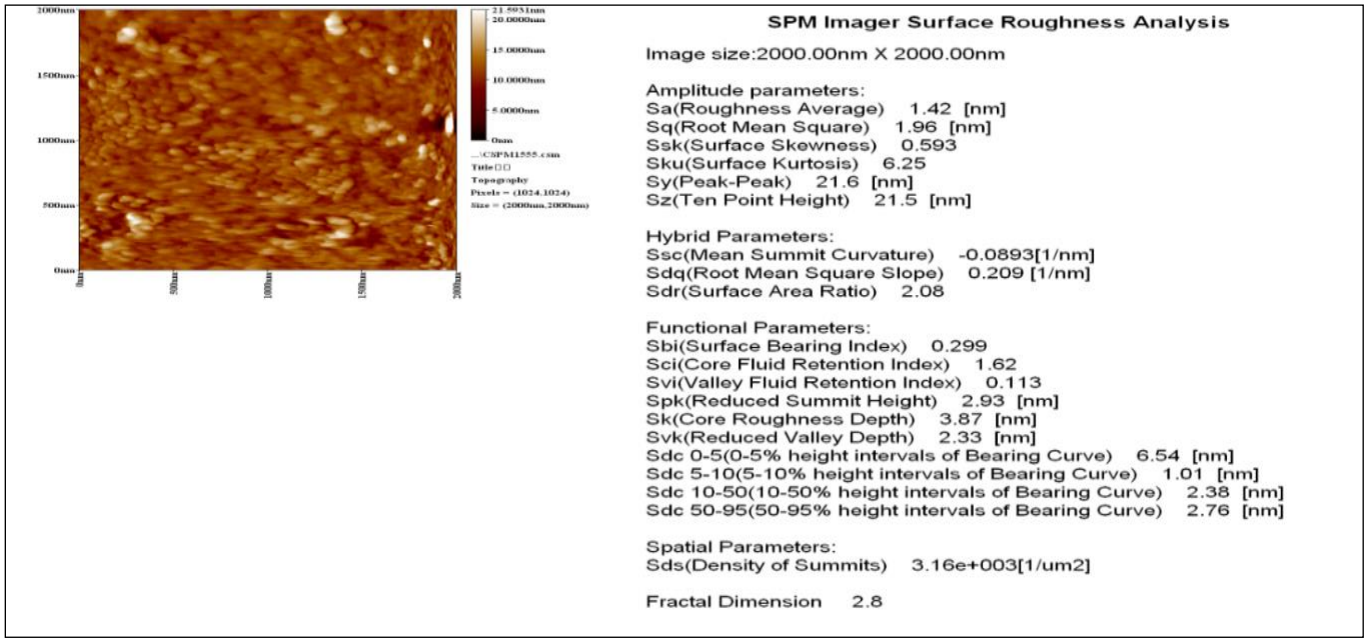


Figure 3. 4 SPM Imager surface roughness analysis

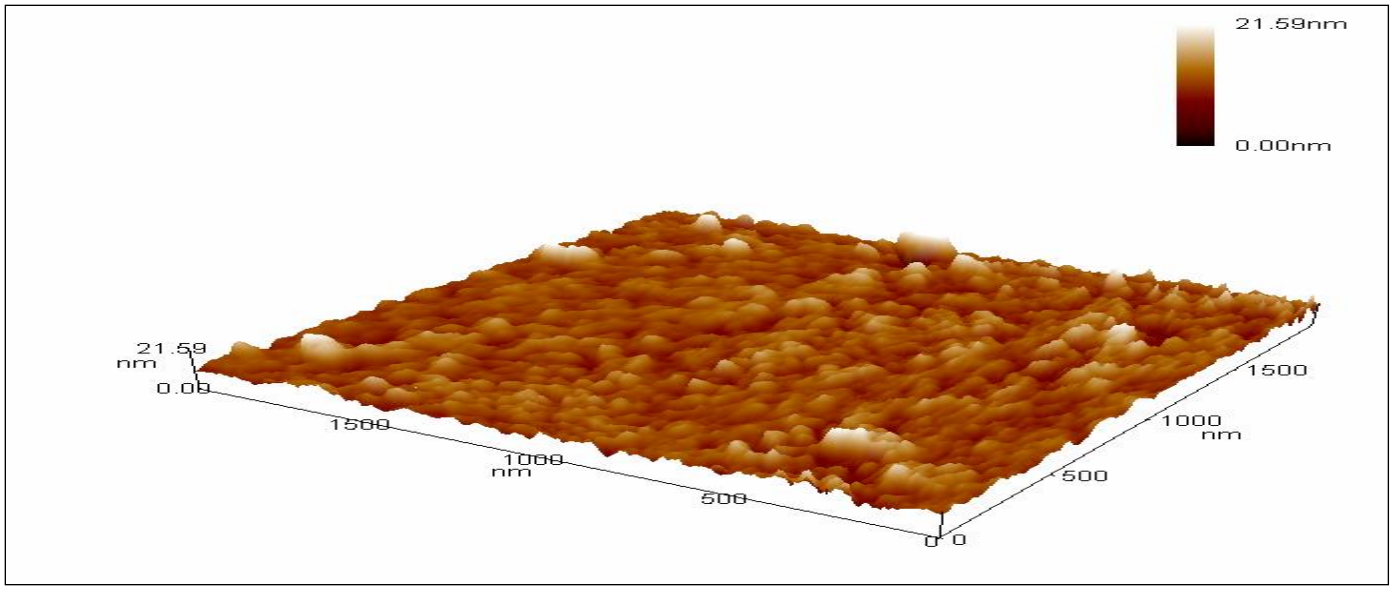


Figure 3.5 SPM 3D-nanocellulose surface

To gain some useful information regarding nanoparticle surface, the physical parameters such as core roughness depth (difference between the minimum and maximum heights of the surface), surface roughness average (mean deviation from the arithmetical mean surface plane), and surface area ratio (percentage additional area contributed by the texture compared to that of the arithmetical mean surface plane), and average diameter of granules (both average and median) as in table 1. More work would be required to characterize any chemical changes in the material after had been applied.

Table 3.1 Surface roughness analysis from AFM studies

Parameter	Nano cellulose
Core roughness depth (nm)	3.57
Roughness average (nm)	1.42
Surface area ratio	2.08
Average diameter of granules (nm)	23.44
Median diameter of granules (nm)	18.00

These reduced properties and parameters of the surface topology of the prepared tiny Nano cellulose particles that considered as the required useful low nanoscale at different vital aspects such in medicine and industrial applications**.** **(21-67)**

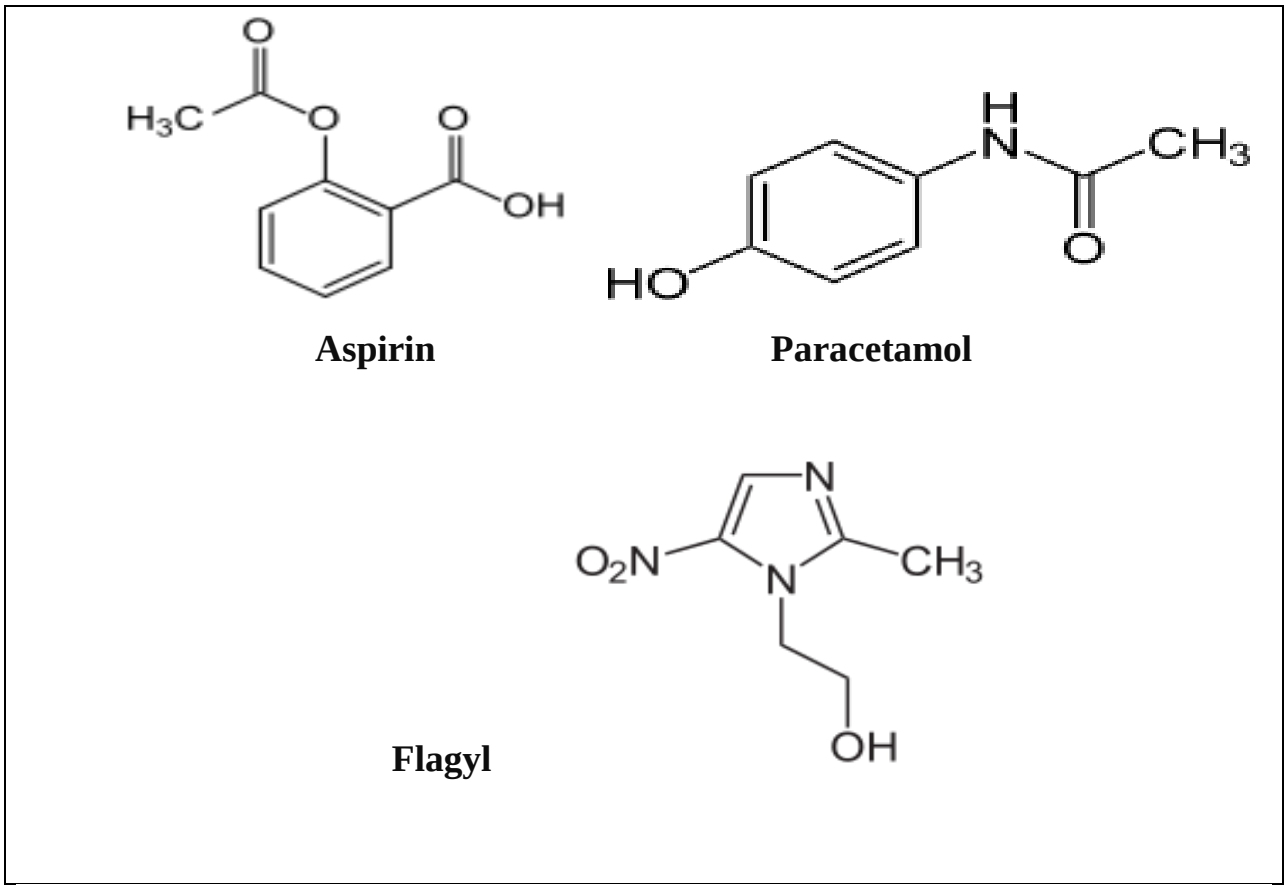
The nanoparticles prepared from cellulose with unique physicochemical properties as a sustainable green organic nanomaterial as drug transport systems according to their nature and chemical structure have been applied by mixing them with some common medicines taken by patients under mimicking the conditions of the human body.

This application aims to provide a safe treatment for health problems associated with the continuous intake of these medicines, such as gastric and duodenal ulcers, as well as preserving the dosage of medicines tablets from loss and release until reaching the required area of greatest absorption in the small intestine.

The correlation mechanism of such application among the commonly used medicines tablets, such as (Acetylsalicylic acid (Aspirin), Acetaminophen (Paracetamol), and Metronidazole (Flagyl)) with and without using transport systems of Nano organics such as Nano cellulose particles to observe the behavior and difference that occur and to know how much retained medicines by nanoparticles.

To use the prepared Nano cellulose for transportation of the selected medicines (Aspirin, Paracetamol, and Flagyl) according to their chemical structures as in (Figure 6). Many active functional groups like (-COOH, $-NO_2$, -OH, CH_3-COO-, -NH-CO-CH_3) that exist on their chemical rings of both benzene and imidazole, that provide a logical suggestion of chemical interactions by hydrogen bonding and connection with Nano cellulose through plenty of hydroxyl

groups (-OH) over their surface (Figure 7), at simulated conditions of a human body which includes temperature (37 °C), drinking water, and pH values from acidic as starting point into alkaline as terminating point which refers between the stomach and small intestine.



Aspirin **Paracetamol**

Flagyl

Figure 3.6 Chemical structure of the studied medicines

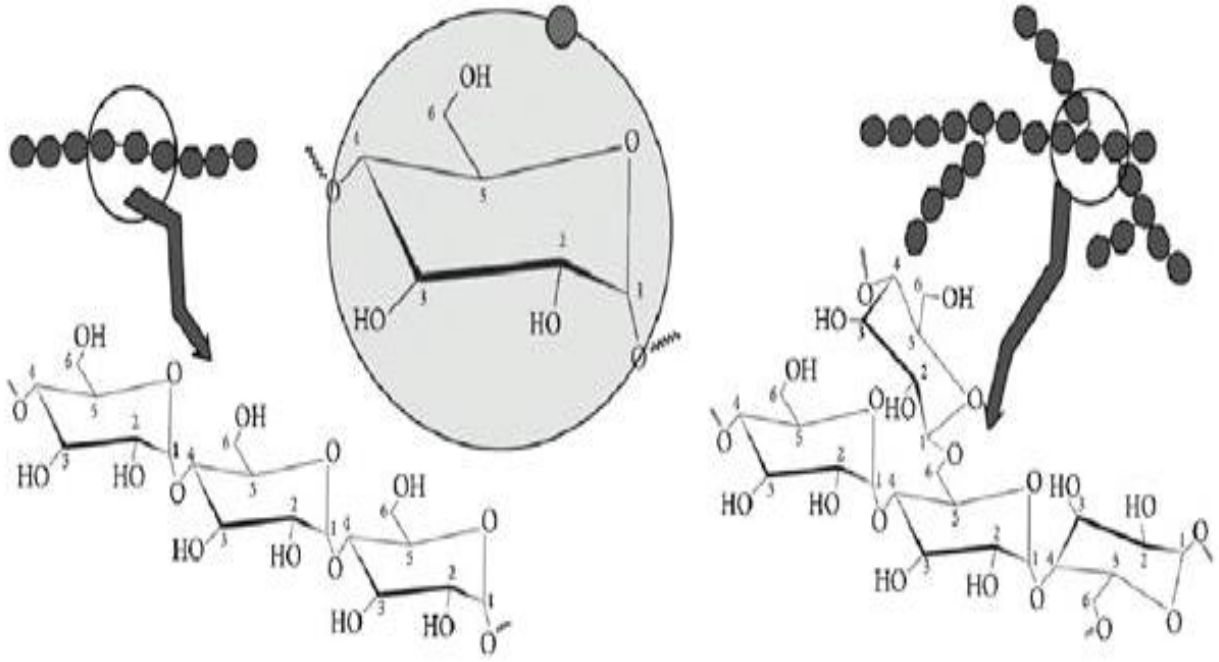


Figure 3.7 Chemical structure of the Nano cellulose

The efficacy of Nano cellulose in reducing (Aspirin, Paracetamol, Flagyl) dissociation has been conducted under the simulated stomach and intestinal conditions. Aspirin was dissolved in drinking water at pH 2 and 37 °C, which is the temperature of the human body.

The pH of titration (Aspirin, Paracetamol, Flagyl) solution ranged from 2-10. The correlation between pH and concentrations (ppm) of released three medicines without Nano cellulose is shown in figures (3.11,3.12,3.13.)

The released concentrations (ppm) from the reaction of medicines (Aspirin, Paracetamol, Flagyl) with and without Nano cellulose according to their addition ratios over pH functions, are recorded in tables (3.2-3.4).

Table 3.2 Released concentrations (ppm)* between Aspirin and Nano cellulose.

pH	Aspirin (ppm)*	1:1	1:2	1:3	1:4
2	320	133	120	100	95
4	120	80	53	48	40
6	40	20	13	12	10
8	0.0	0.0	0.0	0.0	0.0

*Data represents the average of triplicates.

Table 3.3 Released concentrations (ppm)* between Paracetamol and Nano cellulose

PH	Paracetamol (ppm)*	1:1	1:2	1:3	1:4
2	440	400	373	240	200
4	120	45	43	40	39
6	80	52	40	35	26
8	0.0	0.0	0.0	0.0	0.0

Table 3. 4 Released concentrations (ppm)* between Flagyl and Nano cellulose

PH	Flagyl (ppm)*	1:1	1:2	1:3	1:4
2	360	280	272	213	200
4	80	40	27	19	16
6	41	20	13	10	8
8	0.0	0.0	0.0	0.0	0.0

*Data represents the average of triplicates.

However, the ratio of reduction in the released aspirin was relatively small and gradual when the equivalents 2, 3, and 4 of Nano cellulose were used at pH=2, that corresponding to the concentrations of aspirin 120, 100, 95 ppm, respectively. The same trend has been shown when the same equivalents were used at pH 4 and 6, that corresponding to the concentrations 53, 48, 40 ppm and 13, 12, 10 ppm, respectively (Table3.2).

Generally, from the above tables, the effect of adding Nano cellulose to the medicine was observed through the gradual decrease in the liberated concentrations

The amounts of the medicines accompanying the increase in the addition ratios added of Nano cellulose released vary from one medicine to another depending on the chemical structure, their dissociation in water, type of functional groups of the medicine, the equivalents of Nano cellulose added, and the pH values.

To simplify the role of Nano cellulose in understanding how to preserve the medicine, the amount of retained medicine was calculated as in tables (3.5-3.7), for statistical analysis by determining the level of significant correlation between the data of pH values with the retained medicine concentrations at each addition ratio of (drug: Nano-cellulose), this correlation was performed by Pearson correlation by IBM SPSS 22.0 software (SPSS Inc., Chicago, IL, USA) (see appendix of data analysis).

The effect of 4 equivalents of Nano cellulose in reducing the concentration of released aspirin in acidic mediums was compared with the effects of 1, 2, and 3 equivalents. The correlation analysis between pH values and retained aspirin concentrations (ppm) at addition ratios of Nano cellulose was significant $P < 0.05$, where the concentration of retained aspirin increases as the amount of Nano cellulose increases steadily.

Table 3.5: Correlation analysis between pH and retained aspirin at 1:1 (Aspirin: Nano cellulose) Correlations

		pH	**RetainedAspirin1**
pH1	Pearson Correlation	1	-.882
	Sig. (1-tailed)		.059
	N	4	4
RetainedAspirin1	Pearson Correlation	-.882	1
	Sig. (1-tailed)	.059	
	N	4	4

The maximum retention ability of aspirin by Nano cellulose was graded (62-68-70%) of the released (lost) aspirin, which was achieved by using 2, 3, 4 equivalents of Nano cellulose, while the ability decreased if 1 equivalent was used (Table 3.5), at pH equal 2.

This was reflected in data analysis, where the correlation is significant at the 0.05 level at addition ratios 1:2, 1:3, and 1:4 of (aspirin: Nano cellulose).

Table 3.6: Correlation analysis between pH and retained aspirin at 1:2 (Aspirin: Nano cellulose) Correlations

		PH	RetainedAspirin2
PH2	Pearson Correlation	1	-.931*
	Sig. (1-tailed)		.034
	N	4	4
RetainedAspirin2	Pearson Correlation	-.931*	1
	Sig. (1-tailed)	.034	
	N	4	4

***. Correlation is significant at the 0.05 level (1-tailed).**

Table 3.7: Correlation analysis between pH and retained aspirin at 1:3 (Aspirin: Nano cellulose) Correlations

		PH	RetainedAspirin3
PH3	Pearson Correlation	1	-.928*
	Sig. (1-tailed)		.036
	N	4	4
RetainedAspirin 3	Pearson Correlation	-.928*	1
	Sig. (1-tailed)	.036	
	N	4	4

***. Correlation is significant at the 0.05 level (1-tailed).**

Table 3.8: Correlation analysis between pH and retained aspirin at 1:4 (Aspirin: Nano cellulose) Correlations

		PH	RetainedAspirin4
PH4	Pearson Correlation	1	-.938*
	Sig. (1-tailed)		.031
	N	4	4
RetainedAspirin4	Pearson Correlation	-.938*	1
	Sig. (1-tailed)	.031	
	N	4	4

***.** Correlation is significant at the 0.05 level (1-tailed).

However, when medicine changed and paracetamol used instead of aspirin, the maximum retention ability of paracetamol by Nano cellulose was ranged (45-54 %) of the released (lost) paracetamol, which was achieved by using 3 and 4 equivalents of Nano cellulose, respectively, while 1 and 2 equivalents give a very low retention ability that ranged (9-15 %), at pH equal 2 (Table 3. 6).

This is completely involved with the correlation that was significant at the 0.05 level, only at addition ratios 1:3 and 1:4, while it is not significant at addition ratios 1:1 and 1:2 of (paracetamol: Nano cellulose).

Table 3.9: Correlation analysis between pH and retained Paracetamol at 1:1 (Paracetamol: Nano cellulose) Correlations

		PH	**RetainedParacetamol1**
PH1	Pearson Correlation	1	-.694
	Sig. (1-tailed)		.153
	N	4	4
RetainedParacetamol 1	Pearson Correlation	-.694	1
	Sig. (1-tailed)	.153	
	N	4	4

Table 3.10: Correlation analysis between pH and retained Paracetamol at 1:2 (Paracetamol: Nano cellulose) Correlations

		PH2	RetainedParacetamol2
PH2	Pearson Correlation	1	-.893
	Sig. (1-tailed)		.054
	N	4	4
RetainedParacetamol 2	Pearson Correlation	-.893	1
	Sig. (1-tailed)	.054	
	N	4	4

Table 3.11: Correlation analysis between pH and retained Paracetamol at 1:3 (Paracetamol: Nano cellulose) Correlations

		PH3	RetainedParacetamol3
PH3	Pearson Correlation	1	-.957*
	Sig. (1-tailed)		.022
	N	4	4
RetainedParacetamol 3	Pearson Correlation	-.957*	1
	Sig. (1-tailed)	.022	
	N	4	4

***.** Correlation is significant at the 0.05 level (1-tailed).

Table 3.12: Correlation analysis between pH and retained Paracetamol at 1:4 (Paracetamol: Nanocellulose) Correlations

		PH4	RetainedParacetamol4
PH4	Pearson Correlation	1	-.935*
	Sig. (1-tailed)		.033
	N	4	4
RetainedParacetamol4	Pearson Correlation	-.935*	1
	Sig. (1-tailed)	.033	
	N	4	4

***.** Correlation is significant at the 0.05 level (1-tailed).

In contrast, when the Flagyl used, the maximum retention ability was ranged between (40-44 %) of the released (lost) Flagyl concentration, which was achieved by 3 and 4 equivalents used of Nano cellulose, respectively, while 1 and 2 equivalents give half retention ability of paracetamol (22-24 %) at pH equal 2 (Table 3.7).

This behavior gives a correlation that was significant at 0.05 level at addition ratios 1:3 and 1:4, while was less significant at 0.01 level at ratios 1:2 and 1:1 of (Flagyl: Nano cellulose)

Table 3.13: Correlation analysis between pH and retained Flagyl at 1:1 (Flagyl: Nano cellulose) Correlations

		PH1	RetainedFlagyl1
PH1	Pearson Correlation	1	-.983**
	Sig. (1-tailed)		.008
	N	4	4
RetainedFlagyl 1	Pearson Correlation	-.983**	1
	Sig. (1-tailed)	.008	
	N	4	4

****.** Correlation is significant at the 0.01 level (1-tailed).

Table 3.14: Correlation analysis between pH and retained Flagyl at 1:2 (Flagyl: Nano cellulose) Correlations

		PH	RetainedFlagyl2
PH	Pearson Correlation	1	-.998**
	Sig. (1-tailed)		.001
	N	4	4
RetainedFlagyl 2	Pearson Correlation	-.998**	1
	Sig. (1-tailed)	.001	
	N	4	4

****.** Correlation is significant at the 0.01 level (1-tailed).

Table 3.15: Correlation analysis between pH and retained Flagyl at 1:3 (Flagyl: Nano cellulose) Correlations

		PH	RetainedFlagyl3
PH	Pearson Correlation	1	-.961*
	Sig. (1-tailed)		.020
	N	4	4
RetainedFlagyl 3	Pearson Correlation	-.961*	1
	Sig. (1-tailed)	.020	
	N	4	4

***.** Correlation is significant at the 0.05 level (1-tailed).

Table 3.16: Correlation analysis between pH and retained Flagyl at 1:4 (Flagyl: Nano cellulose) Correlations

		PH	RetainedFlagyl4
PH	Pearson Correlation	1	-.973*
	Sig. (1-tailed)		.014
	N	4	4
RetainedFlagyl4	Pearson Correlation	-.973*	1
	Sig. (1-tailed)	.014	
	N	4	4

***.** Correlation is significant at the 0.0 5 level (1-tailed).

From the tables (3.2-3.4), the retention ability of Nano cellulose towards medicines at pH of stomach acidity follows the following arrangement:

Aspirin > Paracetamol > Flagyl

It may be caused by the chemical structure of each studied medicine (Figure 6) and their dissociation equations in water and the effect of varied pH values on the behavior of Nano cellulose between high retention ability at acidic medium and low retention ability at alkaline medium.

From published literature, the hydrolysis of aspirin (acetylsalicylic acid) gives salicylic acid and acetic acid, thus the released aspirin can be easy to estimate (Figure 3. 8).

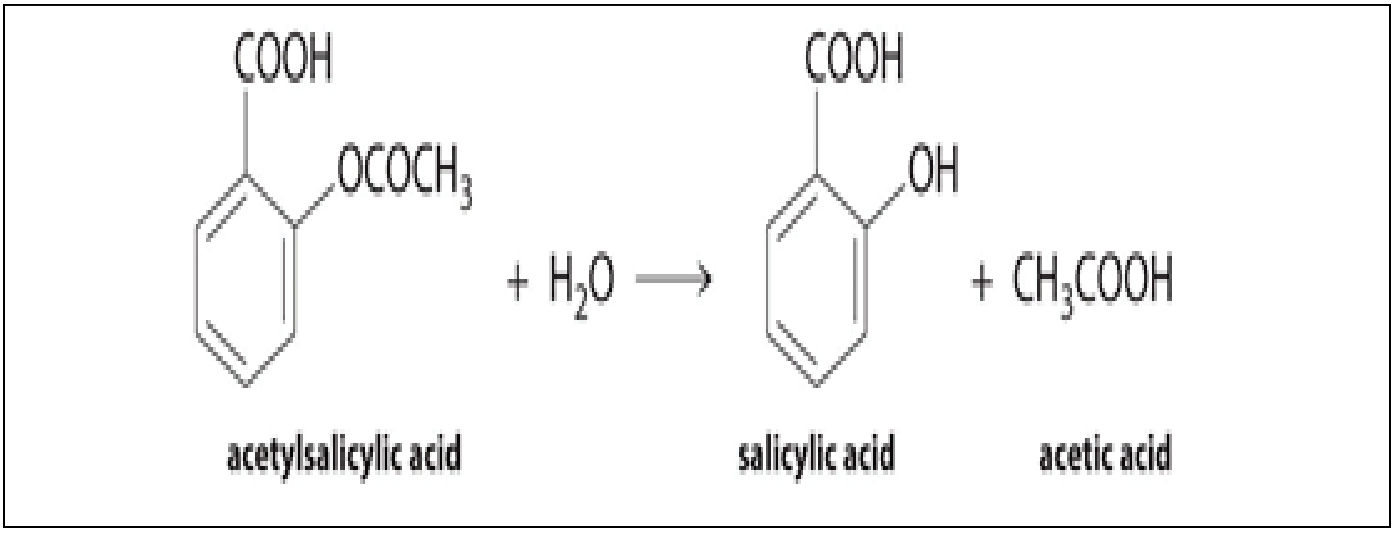


Figure 3.8 Hydrolysis of aspirin.

In case paracetamol molecule has many resonance structures by free electron pair of the nitrogen atom (Figure 9) that makes the carbonyl group within large functional amide group (para-position in a molecule) ready to a nucleophilic addition reaction, thus, the retaining process might be struggling due to steric effect as a result.(68)

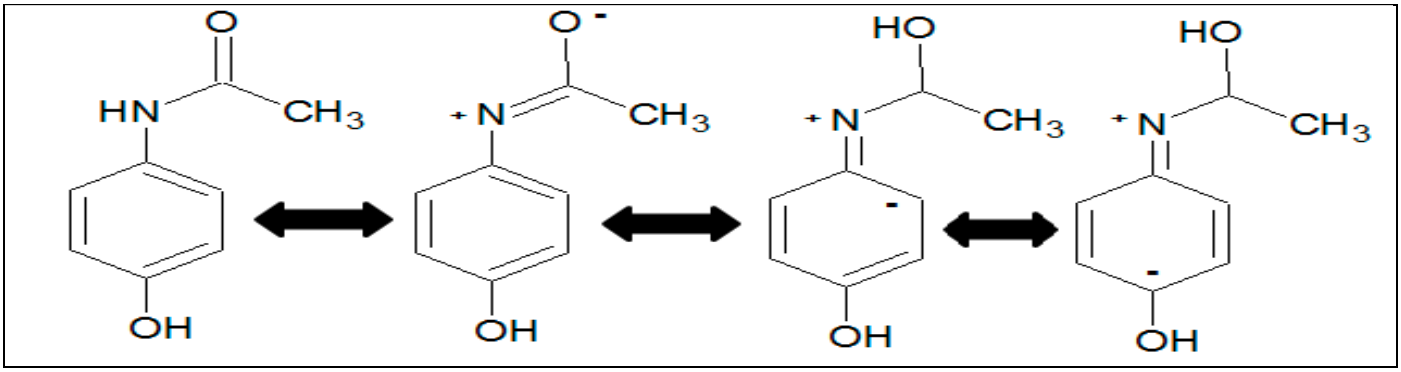


Figure 3.9 Resonance structures in a paracetamol molecule.

In chemical structure of Flagyl molecule as a derivative of metronidazole having nitro group can be either reduced into nitroso group or by electron transfer into nitro radical anion to causes generation of reactive oxygen species (oxidative damage), in addition to the presence of imidazole ring with free electron pairs of the two nitrogen atoms (Figure 10).

This probably made the Flagyl more reactive towards other components such as Nano cellulose at acidic or alkaline medium.(69)

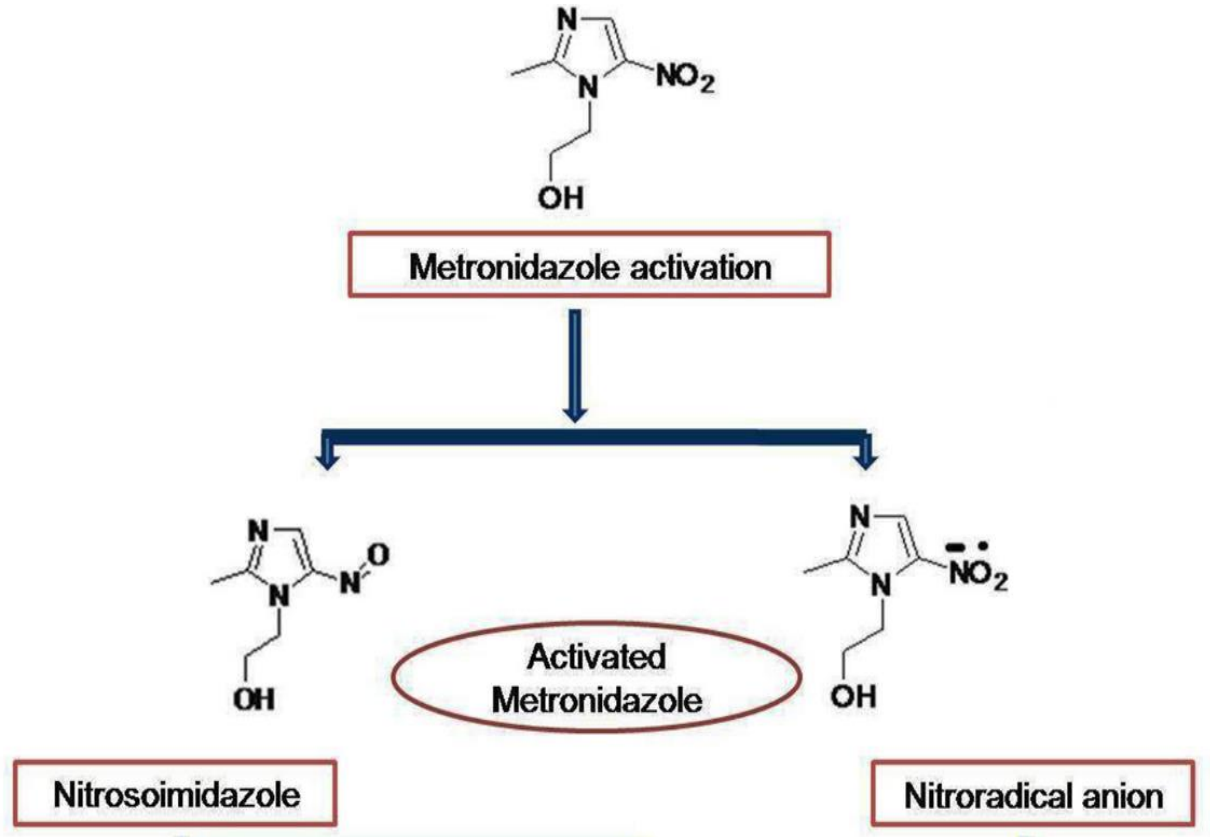


Figure 3.10 Flagyl activation according to their pharmaceutical pathways

In the basic environment, when pH = 8, the medicines do not decompose, meaning that the concentration of the dissolving medicine is equal to zero, while in the acidic environment, the medicine dissolves rapidly and since the stomach is acidic, the medicine decomposes quickly, meaning that its concentration in it is greater.(70)

At pH equal 2, the concentrations of the released medicine without Nano cellulose were (320,440,360) ppm, and at pH equal 4, the released concentrations decrease to (120,120,80) ppm, while at pH equal 6, the concentration of released medicine (Aspirin, Paracetamol, Flagyl) decrease to (40,80,41) then it was a sharp drop at pH 6 and 8, as in figures (3.11-3.13).

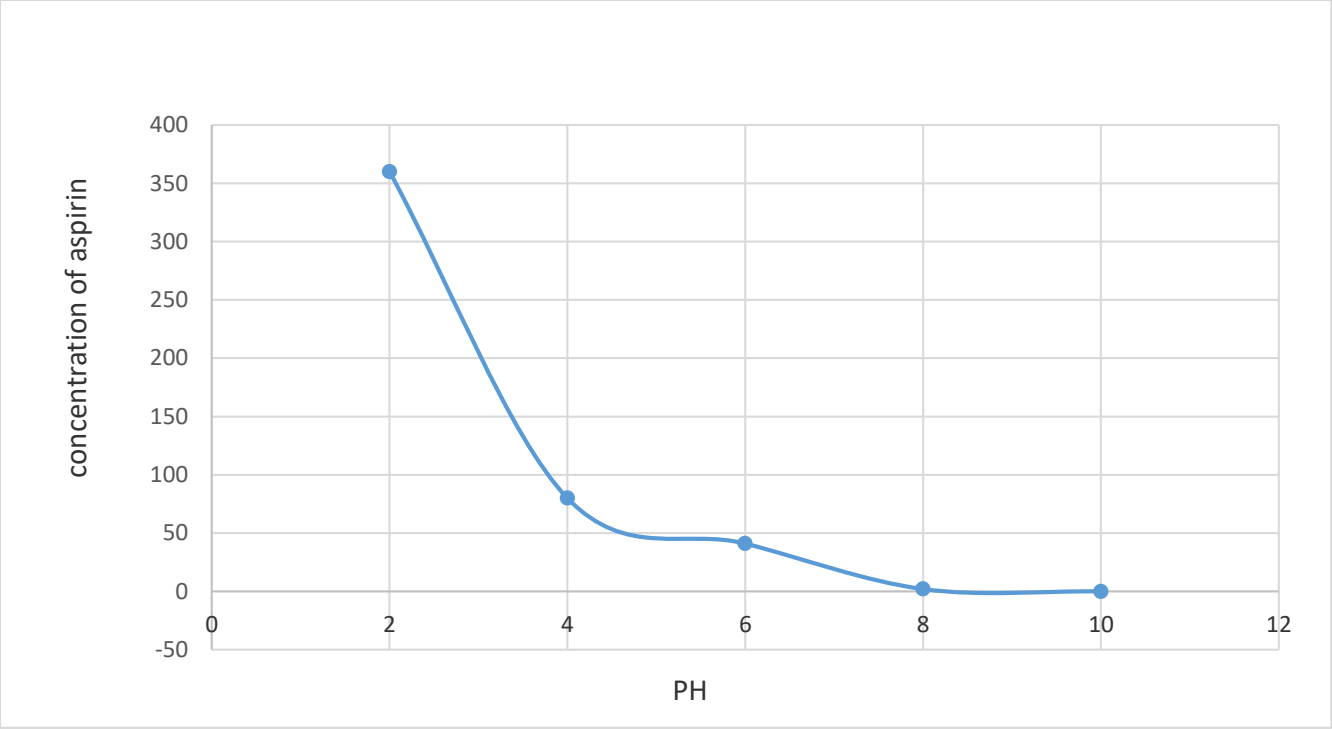


Figure 3.11 Correlation between pH and released aspirin without Nano cellulose.

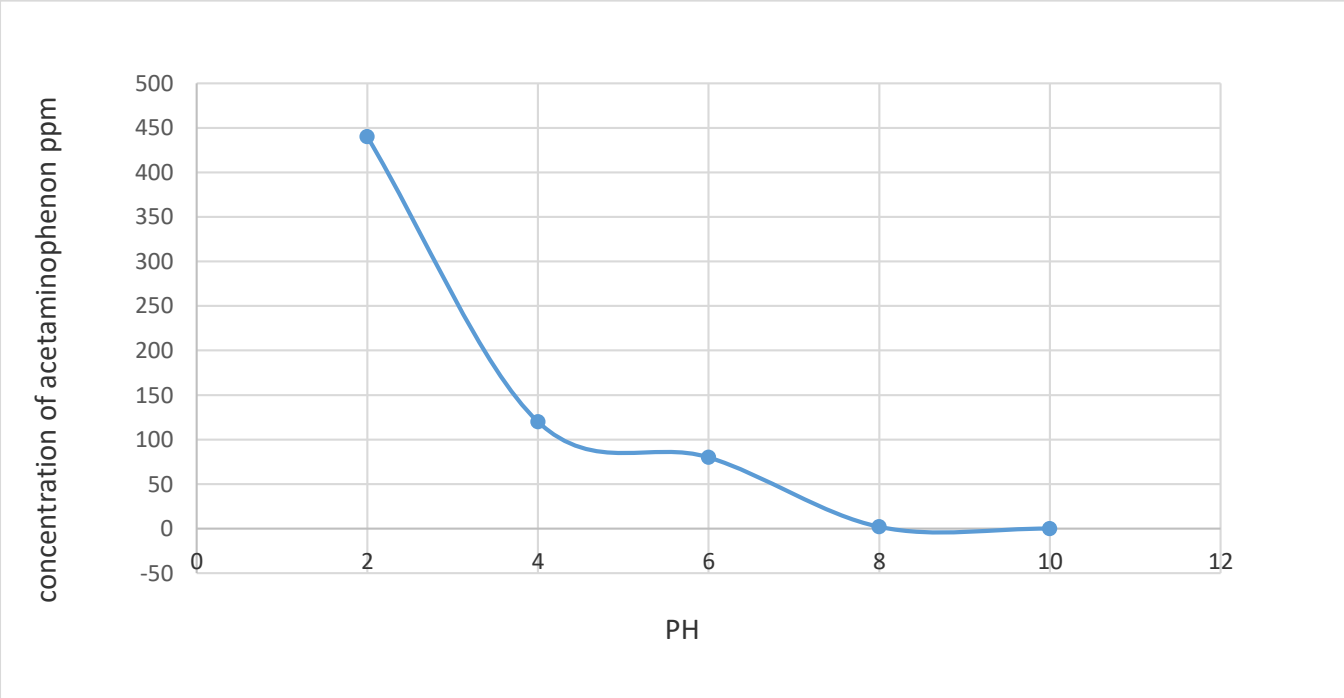


Figure 3.12 Correlation between pH and released paracetamol without Nano cellulose.

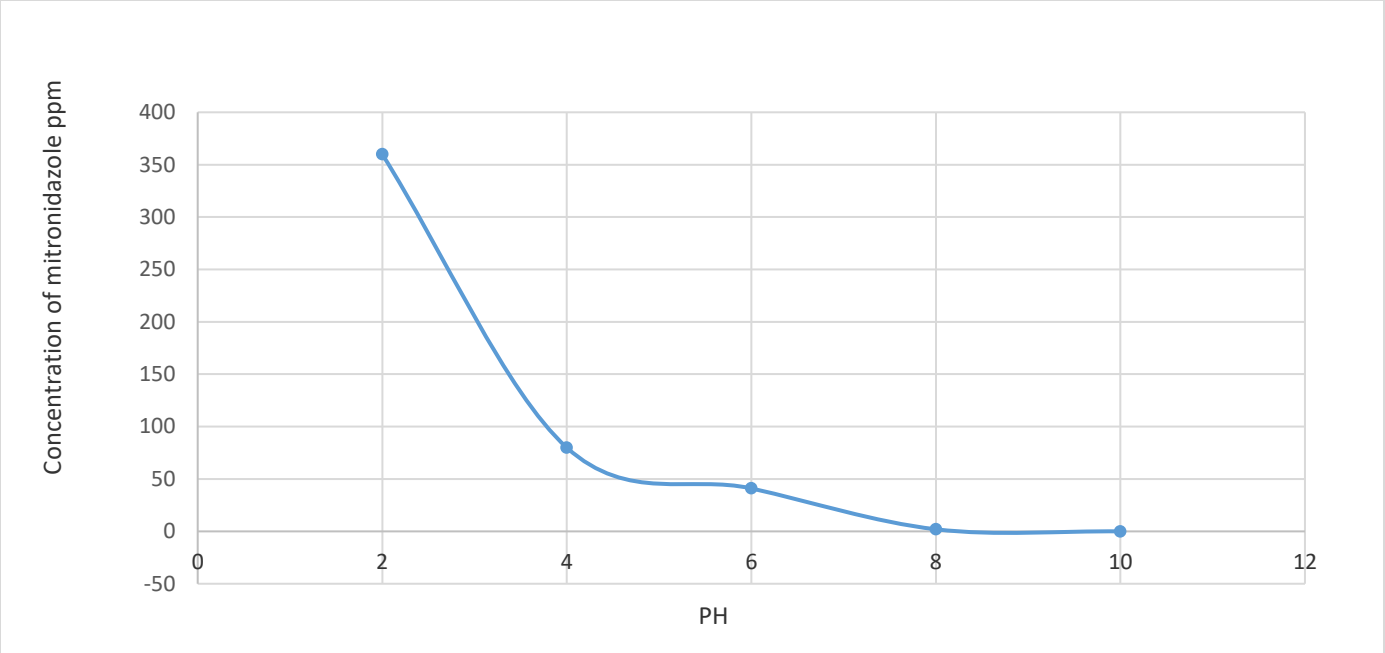


Figure 3.13 Correlation between pH and released Flagyl without Nano cellulose.

When each of the following medicines (Aspirin, Paracetamol, Flagyl) was mixed with the same equivalent of Nano cellulose (w/w) the released concentration of medicines was decreased from (320,440,360) ppm to (133,400,280) ppm at pH equal 2, where the biggest decreasing was happened at aspirin due to presence of hydroxyl group available on the chemical surface of Nano cellulose, the chemical structure of aspirin and high dispersion of nanoscale advantage. [5]

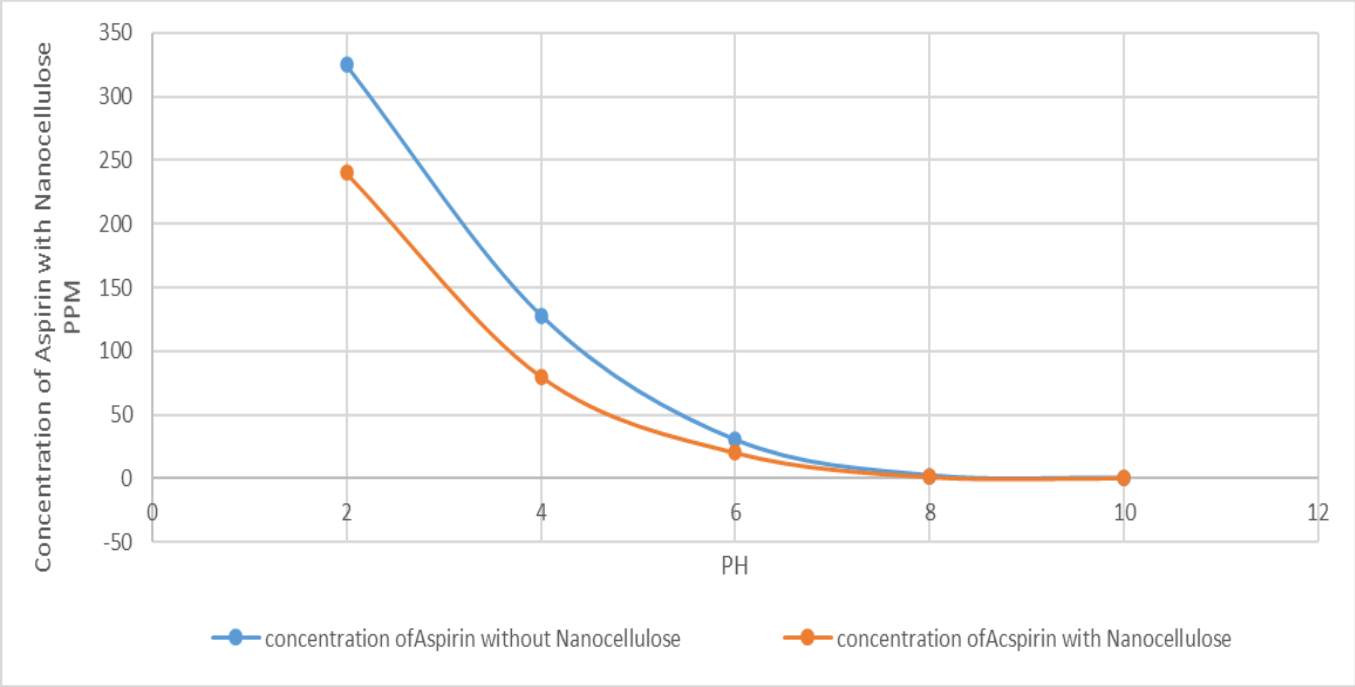


Figure 3.14 Correlation between pH and released aspirin without and with addition ratio of Nano cellulose (1:1).

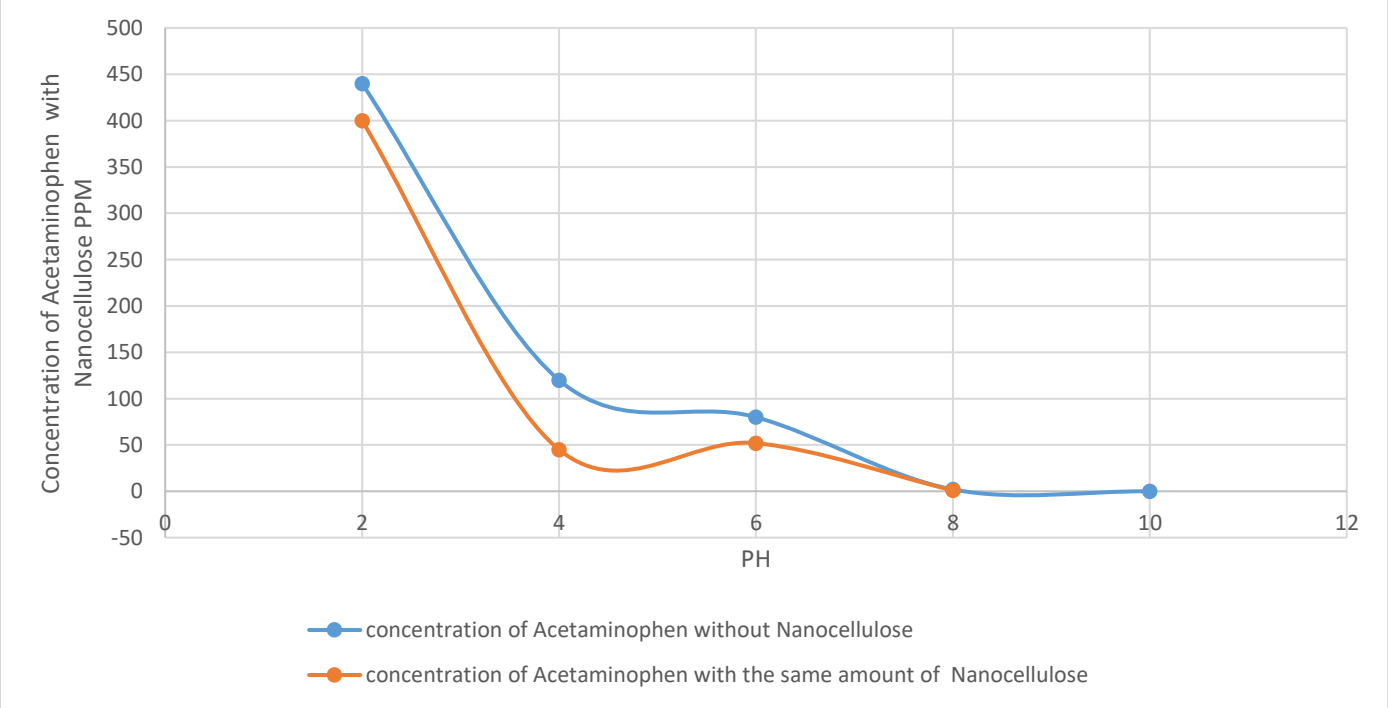


Figure 3.15 Correlation between pH and released paracetamol without and with addition ratio of Nano cellulose (1:1).

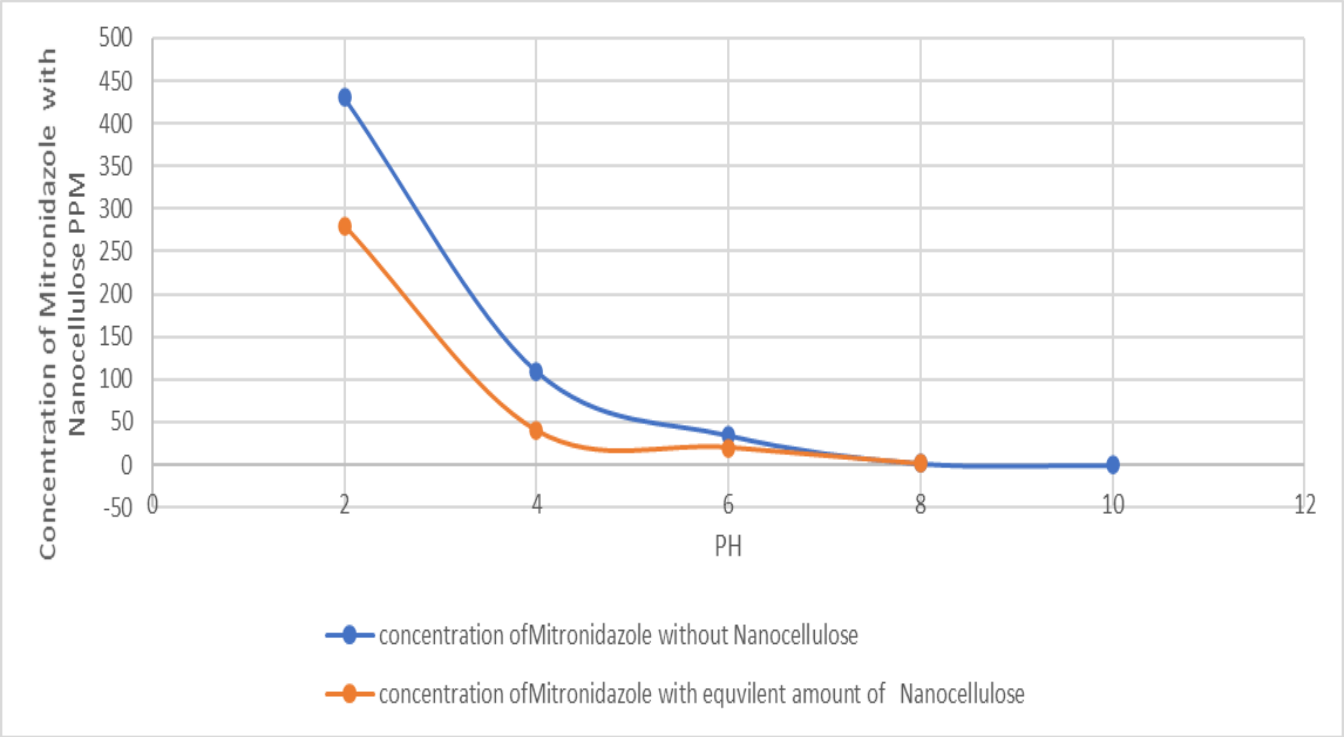


Figure3. 16 Correlation between pH and released Flagyl without and with addition ratio of Nano cellulose (1:1).

When the addition ratio of Nano cellulose becomes doubled, the concentration of the released medicines in the stomach was reduced in comparison due to the presence of the hydroxyl group on the surface of the tiny Nano cellulose, as shown in the following figures (3.17-3.19).

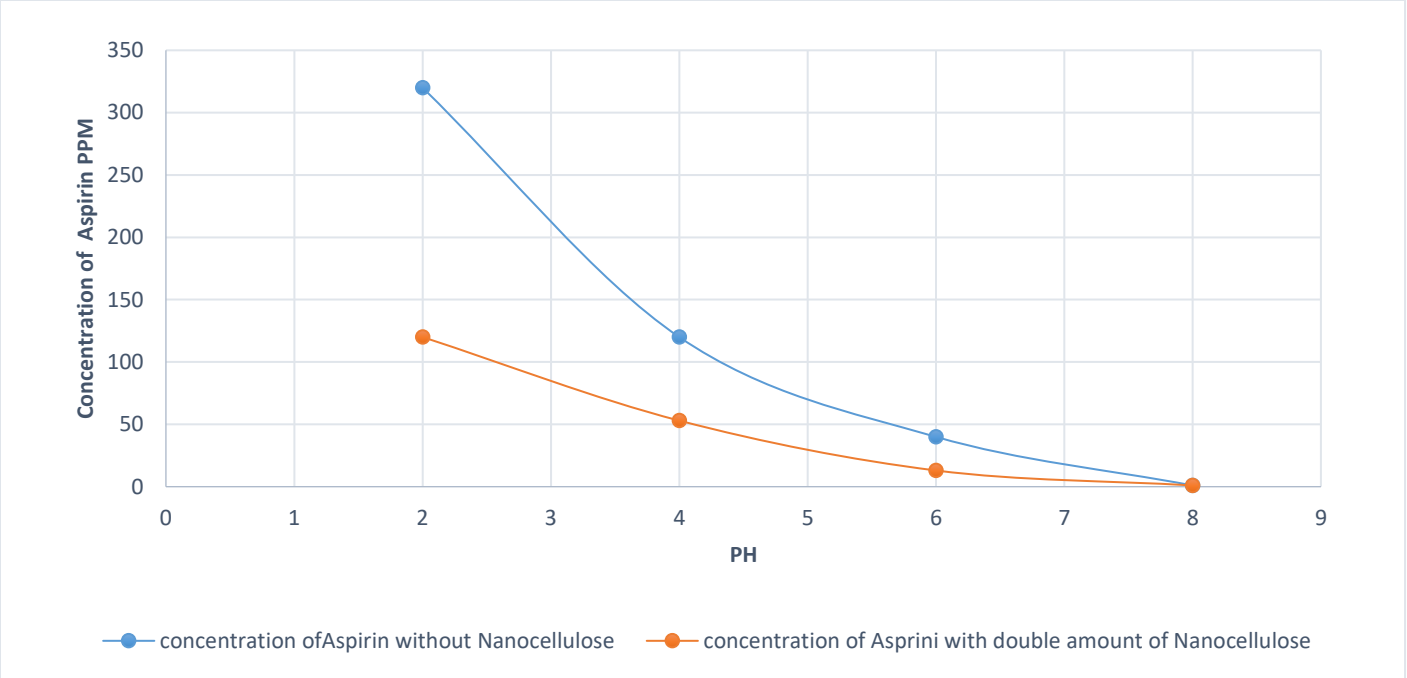


Figure 3.17 Correlation between pH and released aspirin without and with addition ratio of Nano cellulose (1:2)

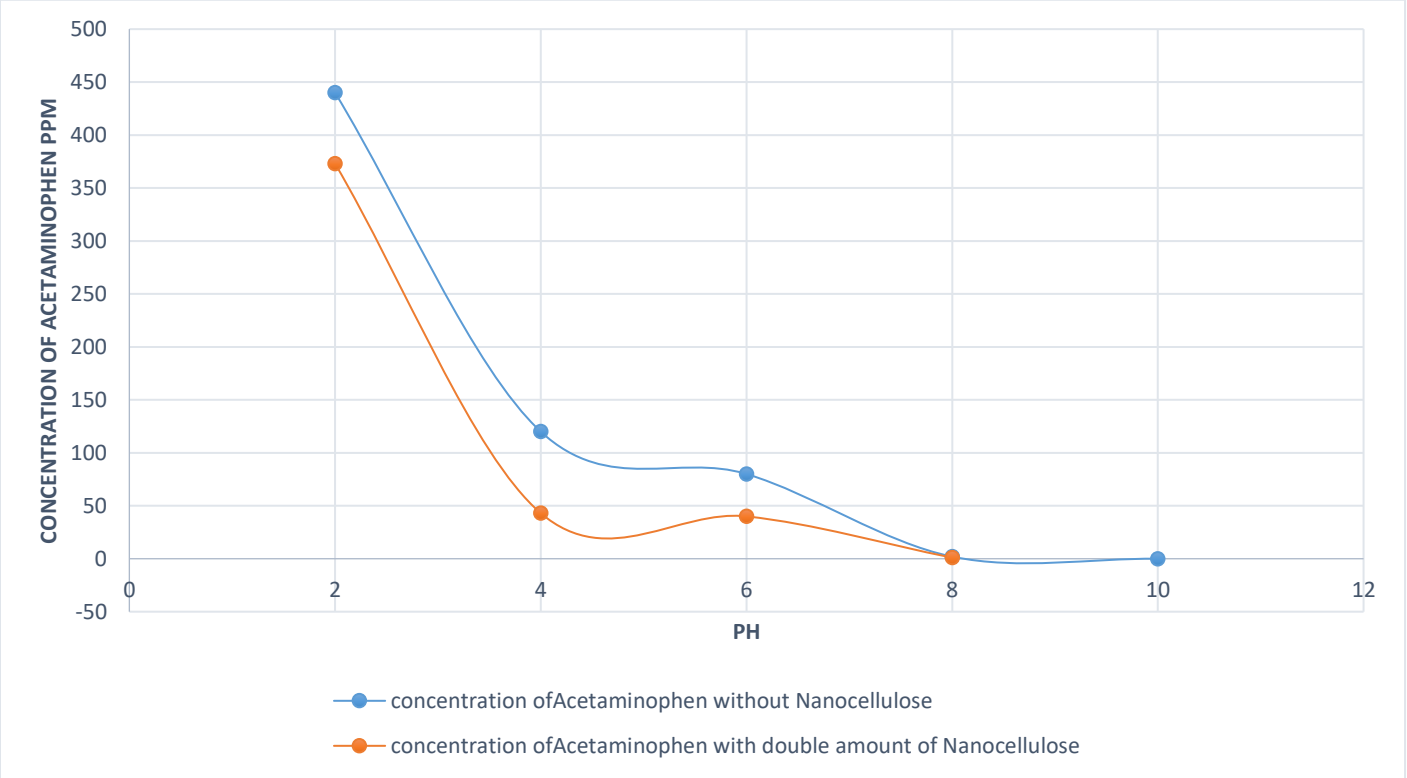


Figure 3.18 Correlation between pH and released paracetamol without and with addition ratio of Nano cellulose (1:2)

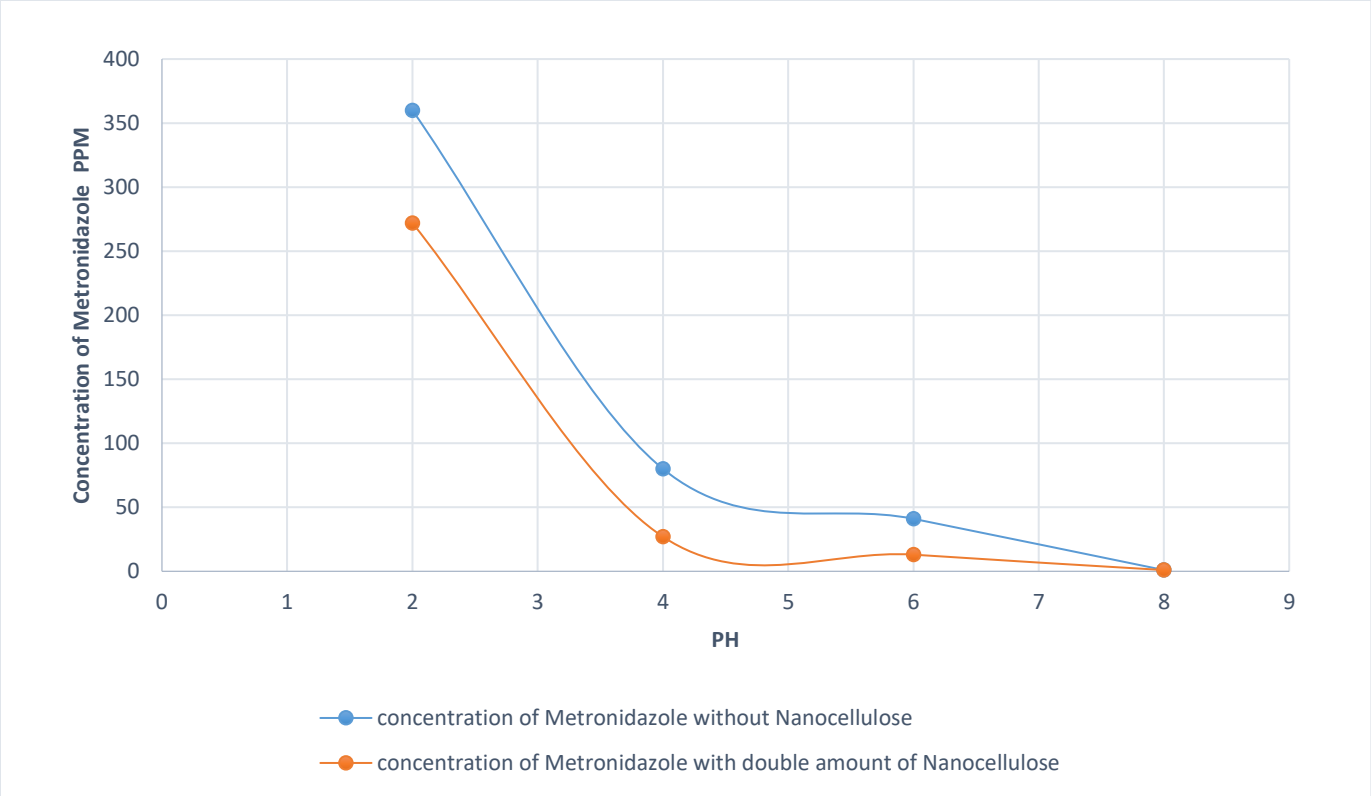


Figure3. 19 Correlation between pH and released Flagyl without and with addition ratio of Nano cellulose (1:2)

When the addition ratio of Nano cellulose becomes tripled, the concentration of the released medicines in the stomach was reduced greatly (correlation is significant at 0.05 level at all of them) due to the presence of the hydroxyl group on the surface of the tiny Nano cellulose, as shown in figures (3.20-3.22).

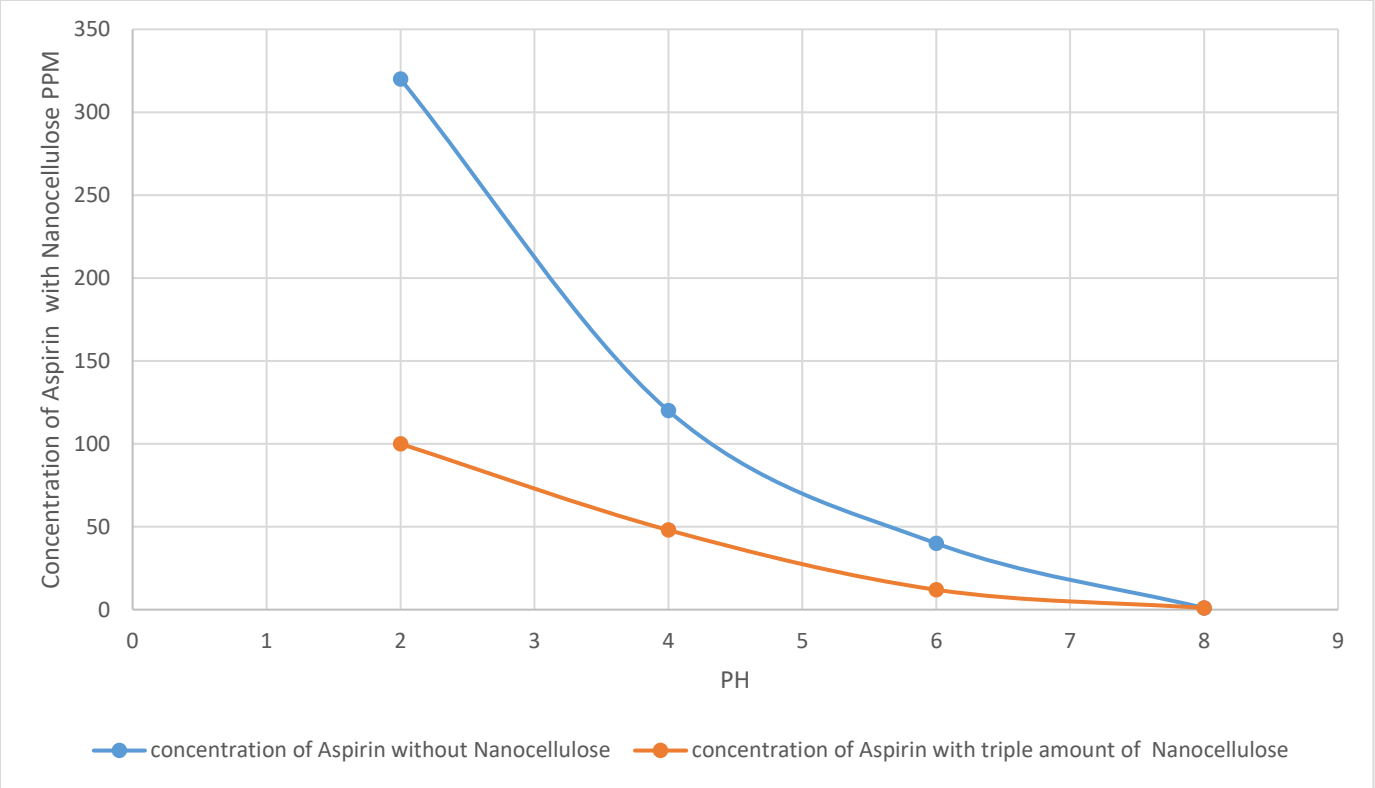


Figure 3.20 Correlation between pH and released aspirin without and with addition ratio of Nano cellulose (1:3)

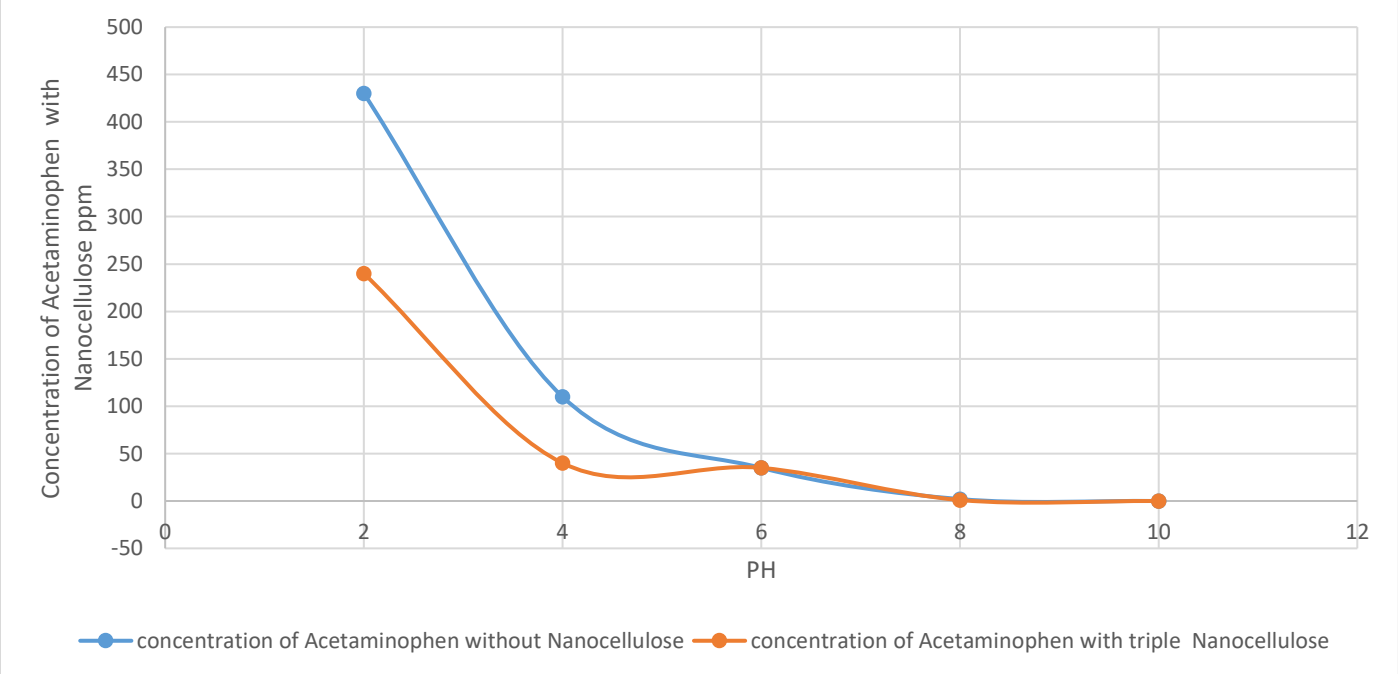


Figure 3.21 Correlation between pH and released paracetamol without and with addition ratio of Nano cellulose (1:3).

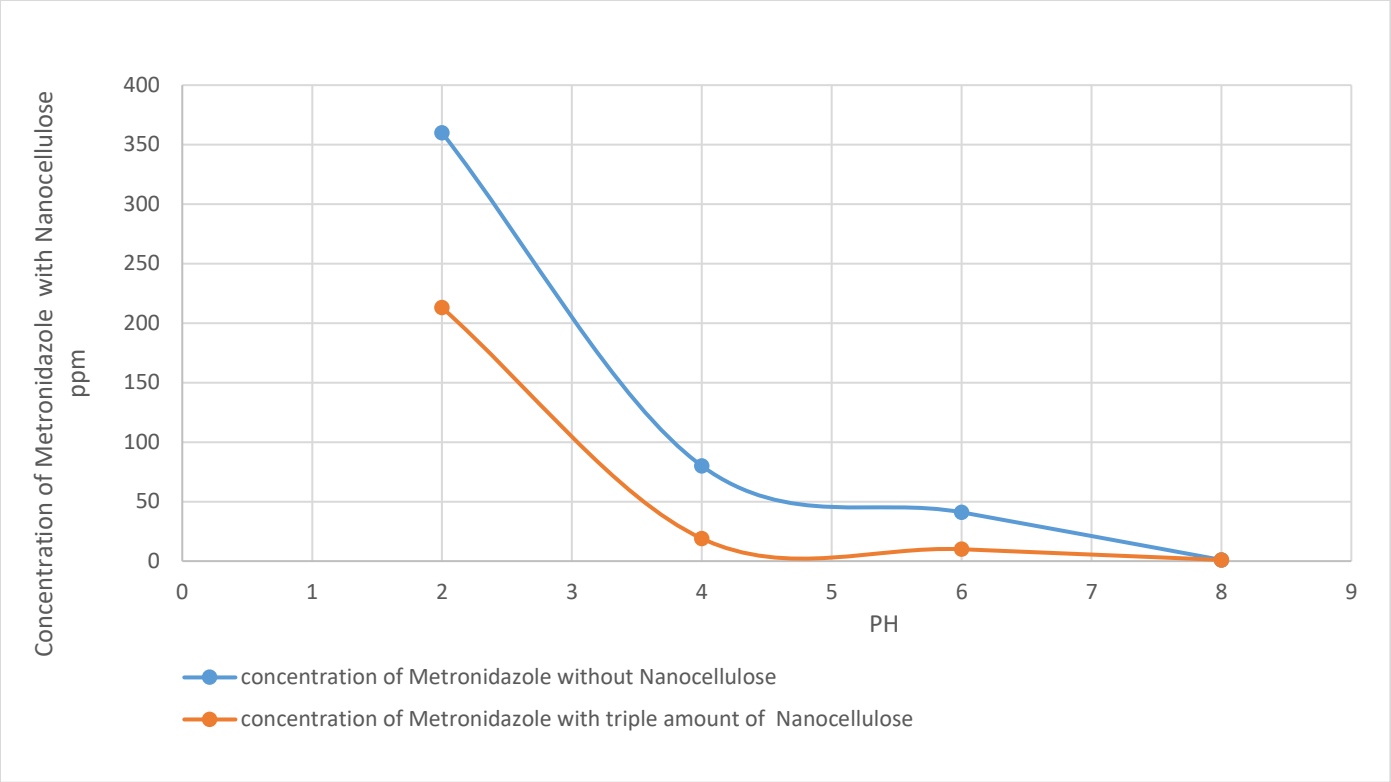


Figure 3.22 Correlation between pH and released Flagyl without and with addition ratio of Nano cellulose (1:3)

When the addition ratio has become quadruple of Nano cellulose, the concentration of the released medicines in the stomach was reduced greatly (correlation is significant at 0.05 level at all of them) due to the presence of the hydroxyl group on the surface of the tiny Nano cellulose with high equivalents, as shown in figures (3.23-3.25).

For example, from figure (23) the retention ability reaches up to (70 %) for aspirin; from figure (3.24) the retention ability reaches up to (54 %) for paracetamol; from Figure (3.25) the retention ability reaches up to (44) for Flagyl by using 4 equivalents of Nano cellulose.

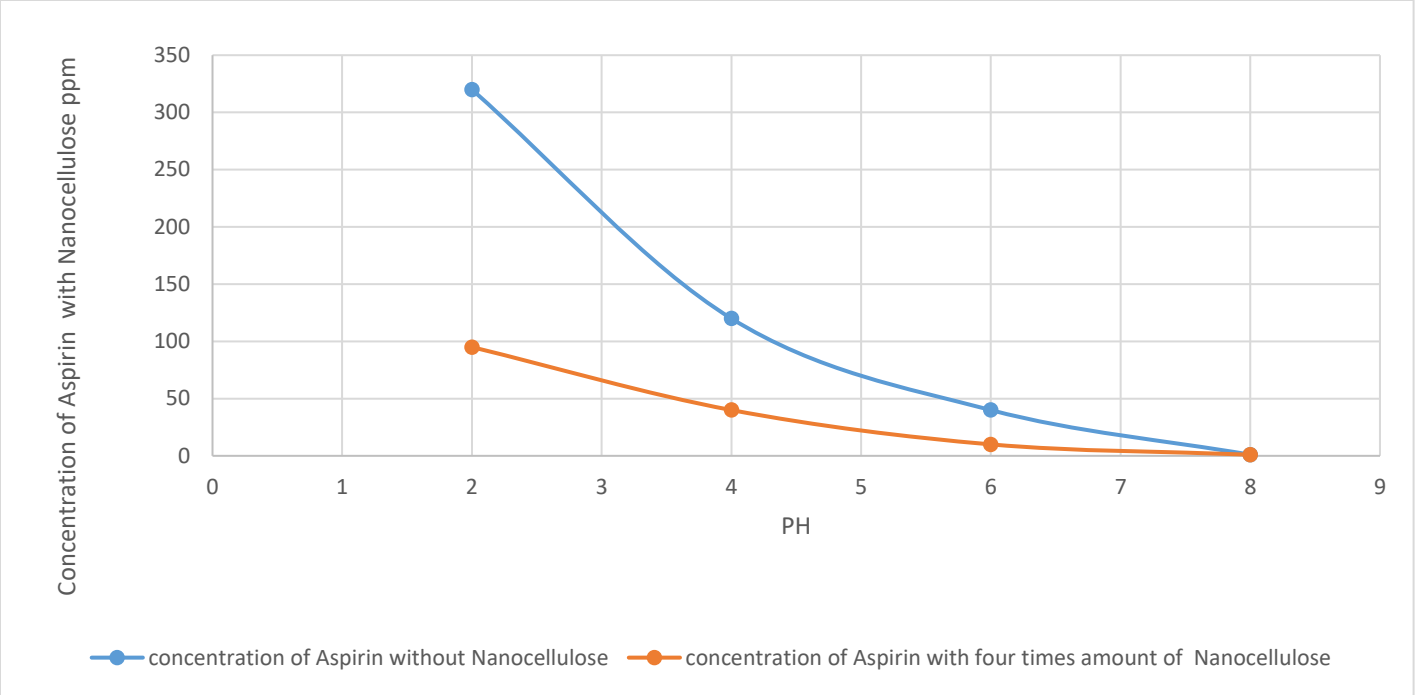


Figure 3.23 Correlation between pH and released aspirin without and with addition ratio of Nano cellulose (1:4)

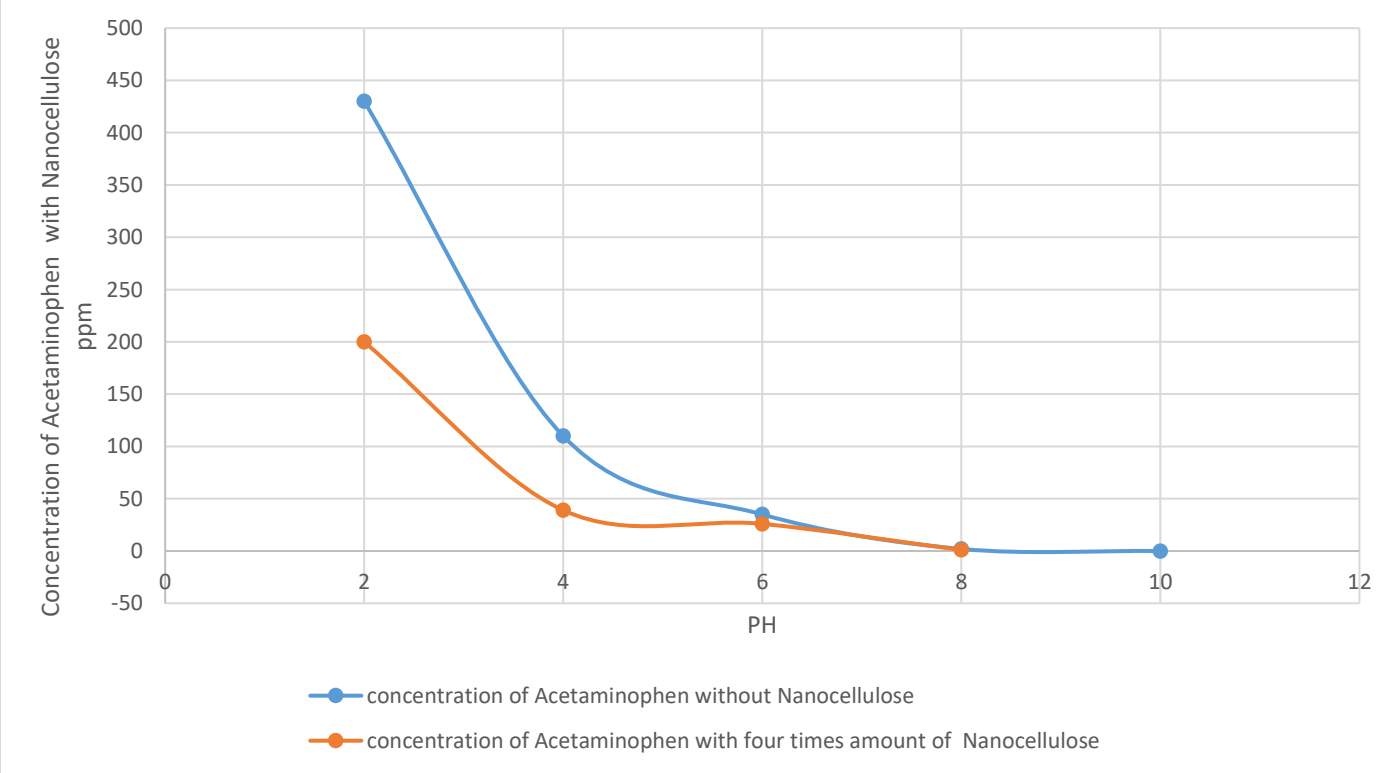


Figure 3.24 Correlation between pH and released paracetamol without and with addition ratio of Nano cellulose (1:4).

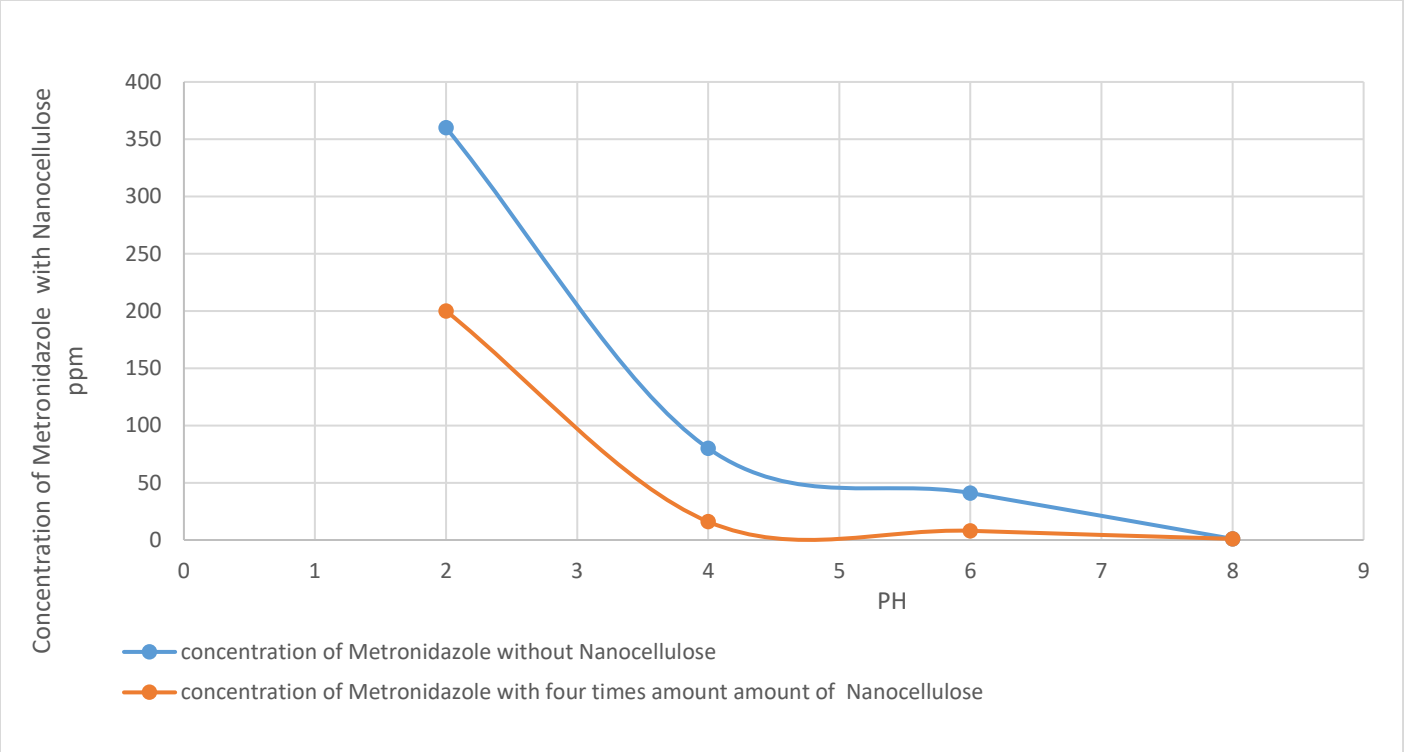


Figure 3. 25 Correlation between pH and released Flagyl without and with addition ratio of Nano cellulose (1:4)

From the Figures (3.26-3.28), where plot all released concentrations of medicines by using addition ratios of (medicines: Nano cellulose) against pH values. From figure (3.26) of the released aspirin, it is shifting was happened among without or with Nano cellulose was used over various addition ratio

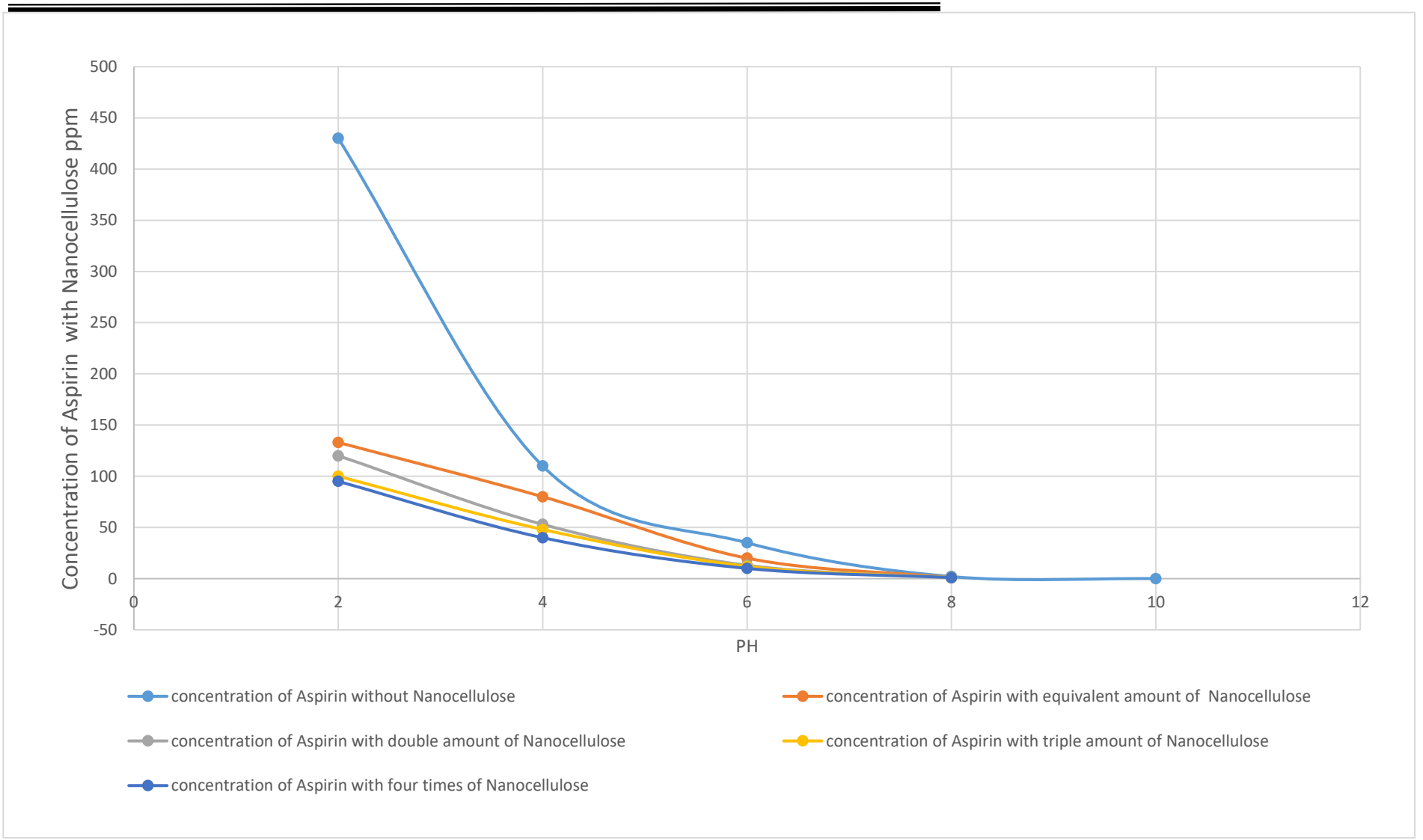


Figure 3.26 Correlation between pH and released aspirin without and with addition ratios of Nano cellulose.

Different amounts of Nano cellulose were used with the medicines to find out the best amount of nanoparticles that can be used to encapsulate and surround the drug and keep it from liberating and losing quantities of it in the acidity of the stomach, and then transferring it to the safest area of greatest absorption in the human body (small intestine, alkaline medium).

From Figure (3.26), the effect of the presence of Nano cellulose is clear in reducing the amount of aspirin liberated, starting in the acidity of the stomach, down in the acidic function, all the way to the small intestine.

The optimum amount of nanoparticles at the addition ratio was at (1:4), the same result was for the rest of the medicines, as noted in the figures (3.27) and (3.28) but was agreed with data analysis explanation.

The reason for obtaining the best percentage of addition when using nanoparticles by four equivalents of medicine amount can be attributed to reaching the greatest ability of Nano cellulose to bind with the largest possible medicine molecules and adsorb them on its surface and between its folds with polar electrostatic physical bonds in addition to forming ionic and hydrogen bonds

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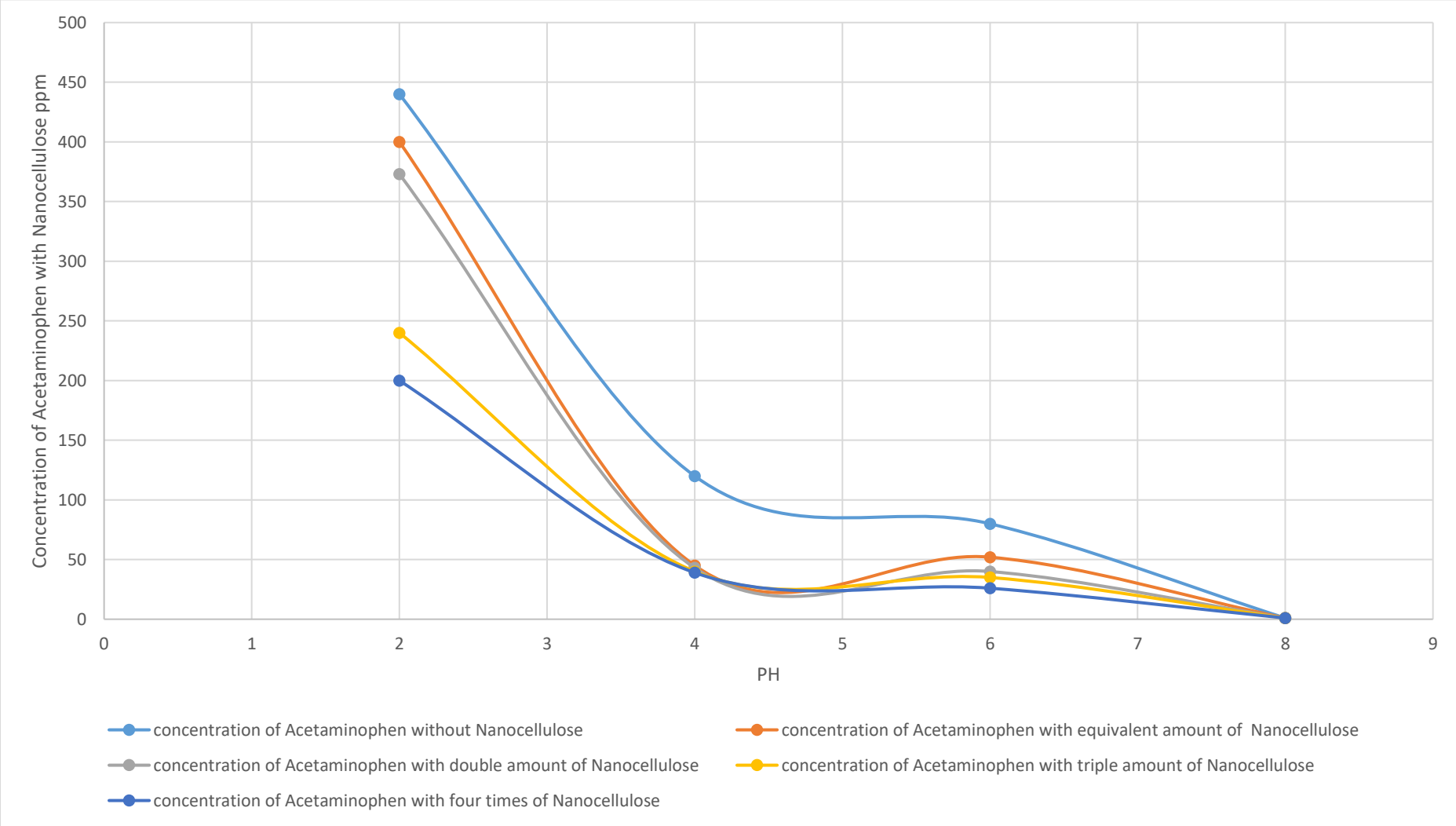

Figure 3.27 Correlation between pH and released paracetamol without and with various addition ratios of Nano cellulose

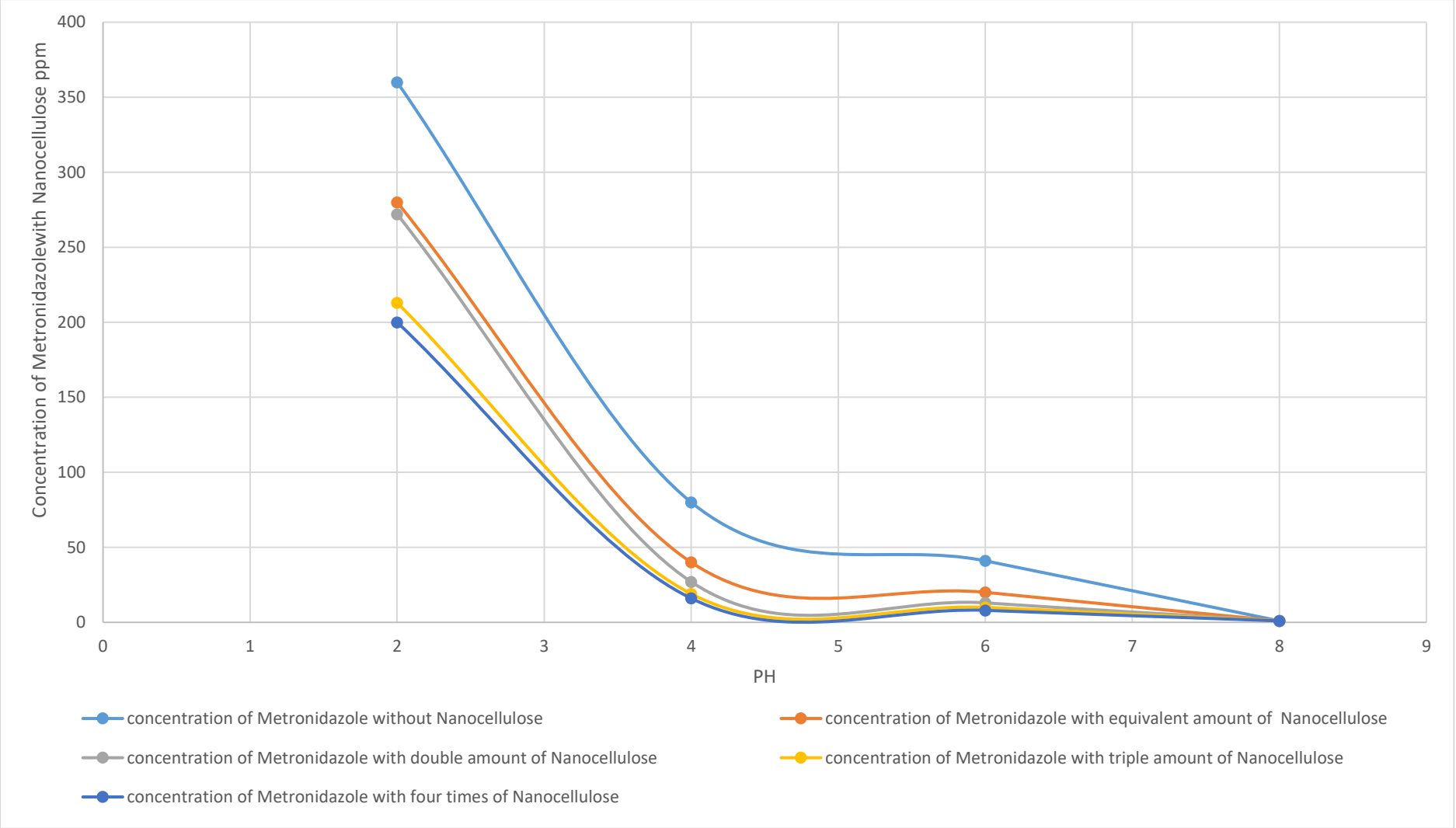

Figure 3. 28 Correlation between pH and released Flagyl without and with various addition ratios of Nano cellulose.

Finally, the prepared Nano cellulose was used by mixing with three types of medicines, namely (Aspirin, Paracetamol, and Flagyl), thus reducing their dissociation in the acidic environment that mimics the human stomach due to the availability of groups hydroxylate on the surface of Nano cellulose, which is linked by hydrogen bonds with groups (-COOH), (-OH), ($-NO_2$), and (-NH-CO-), and thus maintains a higher concentration of medicines until it reaches the small intestine region at the human body where it is absorbed, and the best mixing ratio is the ratio (1 medicine: 4 Nano cellulose).

From the figures (3.25,3.26, and 3. 27), the order of medicine response to the controlled Nano carrier system (Nano cellulose) statistically was in the following order:

Aspirin > Flagyl > Paracetamol

Because of the high number of active functional groups in the chemical structure of medicine, in addition to the steric effect of their sites and position on benzene (more stable) and imidazole ring of medicine

Chapter Four

Conclusion and Future Works

4-1 Conclusion

Green analytical methods were used in the research to extract Nano cellulose from potatoes and mix it with drugs to improve its performance without using chemicals and in a way that was not used previously in any research. The structure and nanoparticles of Nano cellulose were identified using a Fourier-Transform Infrared Spectroscopy (FTIR) and Scanning Probe Microscope (SPM) Combined with Atomic Force Microscope (AFM). The results confirm nanoparticles shape with diameter of granules (23.44 nm) and median diameter of granules (18 nm).

Three types of medicines were used with Nano cellulose by mixing them together in different proportions, where the amount of Nano cellulose added to the drugs was quadrupled, and this led to a decrease in the concentration of the drug released in the stomach and an increase in the concentration released in the intestine, where the drug is absorbed and the best ratio of mixing is 1:3

Using Nano cellulose prepared by encapsulating the three drugs used in the research, the risks resulting from the rapid decomposition of drugs in the stomach, which leads to stomach ulcers and bleeding, will be reduced, in addition to reducing the concentration of drugs released in the acidic medium of the stomach until it reaches the intestine, where it will be absorbed more and thus a number of Less pills than medicine.

4-3 **Recommendation**

1- Establishing a technological information network for the latest information on green nanotechnology in environment.
2- Increasing communication between universities, ministries and relevant departments and exchanging information regarding the latest developments related to green nanotechnology and its use in the field of drug transportation
3- Increasing interest in nanotechnology and green chemistry, teaching it and adding it as an independent subject at the university to familiarize students with its importance.
4- Holding monthly seminars and periodic conferences for research and the latest progress made by green nanotechnology
5- The use of different types of medicines instead of the medicines used in this research in order to take advantage of the advantages of Nano cellulose by increasing the body's absorption of the medicine used, thus consuming fewer tablets than medicines.
6- Use the latest types of Nano cellulose to prevent leukocytes using the green nanoparticles technology

4-4 **Future work**

In addition to its drug-transporting properties, Nano cellulose should be distinguished by its low toxicity and three dimensions in the Nano fiber network, as well as its natural source. A good drug carrier must have several advantages, including low toxicity, biocompatibility, biodegradability, improved drug solubility, a large surface area to carry a large amount of drug, and so on.

More drugs should be tried by mixing it with Nano cellulose because of its effectiveness in transporting drugs and increasing its concentration in the intestinal absorption area, in addition to its experience in other medical or nutritional fields such as food packaging.

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الخلاصة

الهدف من العمل المذكور في هذه الأطروحة هو تطوير طرق مناسبة للطريقة التحليلية التخليقية الخضراء للمواد القيمة من المواد العضوية النانوية بشكل نظيف وفعال. زاد استخدام الجسيمات النانوية العضوية المشتقة من الكتلة الحيوية في الدراسات الطبية والصيدلانية من حيث الدراسات البحثية المنشورة. كان الهدف الرئيسي من هذه الدراسة هو التحقق من صحة استخدام البطاطس الطازجة الصالحة للأكل لتخليق النانو السليلوز. في هذا الإجراء ، لم يتم استخدام أي مواد كيميائية في أي خطوة. تم تنفيذ هذه الطريقة لتحضير الجزيئات النانوية المستخرجة من البطاطس من خلال الاستخلاص الطبيعي والخطوات الفنية الفيزيائية.

وجد أن أطياف FTIR أكدت وجود هيكل السليلوز غير المتبلور (بلوري النانو) من خلال الكشف عن عدة مجموعات وظيفية مثل (OH) واسع (3100-3600 سم -1) ، (-2800) (CH 3000 سم -1) ، (CH) الانحناء المتماثل (1400 سم -1) ، وتمتد (856) (C – O – C سم - 1).

تم إثبات قياسات AFM وتقارير تحليل SPM مقياس النانو لجزيئات السليلوز المحضرة من خلال إظهار متوسط القطر (23.44 نانومتر) والقطر الوسيط (18 نانومتر) من النانو سليلوز وفقًا لمخطط التوزيع التراكمي الحبيبي ، بينما كان متوسط الارتفاع (12.714) نانومتر) وفقًا لمخطط توزيع تراكم الارتفاع. تمت مناقشة طوبولوجيا السطح وتحليل الخشونة والمعلمات.

في النطاق القابل للتطبيق ، تم استخدام نسب مكافئة مختلفة من السليلوز النانوي مع الأدوية لمعرفة أفضل كمية من الجسيمات النانوية التي يمكن استخدامها لغرض تغليف الدواء وحمايته من التحرر وفقدان كميات منه في حموضة المعدة. ، ومن ثم نقله إلى المنطقة الأكثر أمانًا ذات الامتصاص الأكبر في جسم الإنسان (الأمعاء الدقيقة ، الوسط القلوي).

قدرة استبقاء تصل إلى (70٪) للأسبرين. قدرة الاحتفاظ تصل إلى (54٪) للباراسيتامول. قدرة الاستبقاء تصل إلى (44٪) لـ فلاجيل باستخدام 4 مكافئات من النانو سيليلوز.

كان ترتيب استجابة الدواء لنظام ناقل النانو (Nano cellulose) إحصائيًا بالترتيب التالي:

الأسبرين >باراسيتامول >فلاجيل

جمهورية العراق
وزارة التعليم العالي والبحث العلمي
جامعة كربلاء/كلية العلوم
قسم الكيمياء

تخليق مركبات عضوية نانوية خضراء بطرق تحليلية ودراسة فعاليتها البيولوجية

رسالة مقدمة الى

مجلس كلية العلوم- جامعة كربلاء

كجزء من متطلبات نيل درجة الماجستيرفي الكيمياء من قبل

زينة محمد عبد الكاظم الكناني

بكالوريوس علوم كيمياء – جامعة كربلاء(2006)

بأشراف

أ.م.د . باقر عبد الزهرة جودة **أ.د.علاء هاشم ال خلف**

1443هـ **2022م**