COMPARATIVE EVALUATION OF THE PHYSICOCHEMICAL AND RHEOLOGICAL PROPERTIES OF SELECTED SEMI-SYNTHETIC AND SYNTHETIC SUSPENDING AGENTS IN PHARMACEUTICAL SUSPENSIONS

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A PROJECT SUBMITTED TO THE DEPARTMENT OF PHARMACEUTICS AND PHARMACEUTICAL TECHNOLOGY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DOCTOR OF PHARMACY(PHARM.D) DEGREE OF THE UNIVERSITY OF BENIN, BENIN CITY, EDOSTATE , NIGERIA.

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CERTIFICATION

This is to certify that this work was done by **OSARODE DANIEL NOSA-ODIA**, in the Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, University of Benin, Benin City, Nigeria, in partial fulfillment for the award of the Pharm. D degree from the University.

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DEDICATION

This work is sincerely dedicated to God Almighty, whose grace, wisdom, and divine guidance have been my greatest source of strength.

To my wonderful parents, Dr. Nosakhare Odia and Mrs. Osaro Dorothy Odia, for their endless love, sacrifices, and encouragement that have shaped every part of my journey.

In loving memory of my grandmother, Mrs. Mary Igbinosa, whose prayers, encouragement, and kindness was a constant source strength, whose prayers and nurturing spirit continue to live on and to everyone striving to advance the field of Pharmacy and contribute to the growth of scientific knowledge, this work stands as a humble contribution to that shared pursuit.

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Finally, in all honour and love, I dedicate this achievement to my family my siblings Emmanuel, Aisosa, and Osamudiamen**,** my strong and constant support system, and to my wonderful parents, Dr. Nosakhare Odia and Mrs. Osaro Dorothy Odia, whose love, prayers, and sacrifices remain the foundation of all my accomplishments.

TABLE OF CONTENTS

CHAPTER ONE: INTRODUCTION

CHAPTER TWO: MATERIALS AND METHOD

CHAPTER THREE: RESULT AND DISCUSSION

CHAPTER FOUR:

LIST OF TABLES

ABSTRACT

Background: The stability of pharmaceutical suspensions depends on their rheological properties, which are influenced by the type and concentration of suspending agents. This study evaluated and compared the rheological properties and performance of various suspending agents in ibuprofen suspension formulations.

Methodology: Ten suspending agents Chitosan, Sodium Alginate, NaCMC, HPMC, HEC, Carbopol, CMEC, MC, Eudragit L-100, and PVP, were prepared using appropriate solvents. Eudragit L-100 was dissolved in ethanol, HEC**,** HPMC, and Carbopol in hot water, Chitosan in 1% H_2SO_4, while others were dispersed in distilled water. Each was evaluated for pH, density, and viscosity. Six agents (NaCMC, CMEC, Sodium Alginate, MC, HPMC, and Carbopol**)** were selected to formulate ibuprofen suspensions, assessed for pH**,** viscosity**,** and sedimentation rate at ambient temperature.

Results: All suspending agents produced formulations with acceptable pH (4.1–5.9). Viscosity increased with polymer concentration; Carbopol and NaCMC at 1.0% formed gel-like systems, while 0.5% gave smooth, pourable suspensions. Sedimentation tests showed the control settled rapidly, whereas Carbopol and NaCMC formulations exhibited the highest stability with uniform sedimentation over seven days.

Conclusion:

All agents improved suspension stability, though performance varied with concentration. Carbopol and NaCMC at 0.5% provided the best balance between viscosity and pourability, making them most suitable for ibuprofen suspensions.

CHAPTER ONE

INTRODUCTION

1.1. Background of the Study

Suspensions are heterogeneous liquid dosage forms in which finely divided insoluble drug particles are dispersed throughout a liquid medium. They are widely used in Pharmaceutics because they offer flexibility in administering poorly soluble drugs, improve stability of certain drug substances, and enhance patient compliance in paediatric and geriatric populations (Aulton & Taylor, 2018).

A major challenge in formulating Pharmaceutical suspensions is ensuring Physical stability. Particles tend to settle due to gravity, which may lead to caking, poor redispersibility, and dosage inaccuracy (Allen & Ansel, 2020). To overcome these challenges, suspending agents are incorporated. Suspending agents are substances that increase the viscosity of the dispersion medium, thereby reducing sedimentation rate and improving the uniform distribution of particles (kumar *et al.,* 2019).

The importance of suspending agents lies not only in retarding sedimentation but also in enhancing the pour ability and redispersibility of suspensions, which directly influences patient compliance and dose uniformity. An ideal suspending agent should impart adequate viscosity, be inert and non-toxic, remain stable under varying pH and temperature conditions, and not interfere with the therapeutic activity of the drug (Martin & Bustamante, 2011).

Closely linked to this is the role of rheological properties, which determine the flow behaviour of suspensions. Rheology is crucial in ensuring that a suspension is not excessively viscous to pour yet viscous enough to keep particles suspended. Properties such as pseudoplastic flow allow suspensions to become less viscous when shaken or poured but regain viscosity when at rest, preventing sedimentation. Thixotropy ensures ease of redispersion, while yield stress prevents rapid settling during storage (Martin & Bustamante, 2011).

Therefore, the evaluation and ranking of suspending agents based on their rheological characteristics is critical for guiding Pharmaceutical formulation. This ensures stability, patient acceptability, and therapeutic reliability.

1.2. Problem Statement

Although many natural, semi-synthetic, and synthetic suspending agents are available, their performance in Pharmaceutical suspensions varies significantly. The formulation of stable Pharmaceutical suspensions is challenging due to the tendency of insoluble particles to settle, leading to non-uniform dosing and reduced therapeutic efficacy (Kulshreshtha *et al.,* 2010). Inappropriate selection often results in unstable products with rapid sedimentation, poor redispersibility, and non-uniform dosing (Kumar *et al.,* 2019). While various suspending agents are available, their performance varies significantly depending on their rheological properties, such as viscosity and thixotropy, which influence sedimentation rates and redispersibility (Tadros, 2010). Moreover, while Pharmacopeia's provide recommended concentration ranges, they do not directly compare the rheological performance of different agents under standardized conditions. This gap in knowledge creates challenges for formulation scientists who must balance viscosity, stability, and patient acceptability. Without clear guidance on selecting the most effective suspending agent, formulators may face difficulties in achieving stable, user-friendly suspensions, potentially compromising patient safety and compliance. This study addresses this gap by evaluating and ranking suspending agents based on their rheological performance to provide evidence-based recommendations for Pharmaceutical formulations.

1.3 Scope and Limitations of the study:

This study is limited to the evaluation of selected suspending agents commonly used in Pharmaceutical formulations, such as sodium carboxymethylcellulose (NaCMC), carbopol, hydroxypropyl methylcellulose (HPMC), sodium alginate, and polyvinylpyrrolidone (pvp). The evaluation will focus primarily on their rheological properties under controlled laboratory conditions. Other factors such as taste masking, toxicity, or cost-effectiveness will not be addressed in detail.

1.4 Literature Review

1.4.1. Overview of suspending Agents:

Suspensions are heterogeneous systems widely utilized in pharmaceutical formulations for the oral, parenteral, and topical delivery of poorly soluble drugs. These biphasic systems consist of finely divided insoluble solid particles dispersed in a liquid vehicle (Aulton & Taylor, 2018). While offering benefits like improved drug stability and enhanced patient compliance, suspensions are inherently unstable due to particle movement driven by gravity, leading to sedimentation, aggregation, and, ultimately, irreversible caking.

To counteract these physical stability problems and ensure dose uniformity, suspending agents are incorporated. These agents are typically high molecular weight polymers—ranging in origin from natural to semi-synthetic and synthetic—that primarily modify the viscosity and flow behavior of the continuous phase.

The mechanism by which suspending agents function is mathematically described by Stokes' Law, which posits that the sedimentation velocity (v) of a spherical particle is inversely proportional to the viscosity (n) of the medium:

$$V= d^2(p-m)g / 18n$$

where d is the particle diameter, p is the particle density, m is the medium density, and g is the acceleration due to gravity (Kulshreshtha *et al.,* 2010). By significantly increasing the viscosity (n), the suspending agent minimizes the sedimentation velocity, thus retarding the settling rate of the dispersed particles.

The selection of an ideal suspending agent is critically dependent on its rheological properties, which govern the flow behavior of the suspension. An ideal pharmaceutical suspension must exhibit non-Newtonian flow (specifically, pseudoplasticity), which is defined by a decrease in viscosity when subjected to increased shear stress (shaking or pouring), allowing for easy administration (Aulton & Taylor, 2018).

Pseudoplasticity: Ensures the suspension flows easily from the bottle or through a needle.

Thixotropy: A time-dependent decrease in viscosity when shear is applied, followed by a gradual recovery of viscosity when the shear is removed. This ensures the dispersed particles remain stable during storage but can be easily redispersed upon agitation.

Yield Stress: The minimum shear stress required to initiate flow. Suspending agents that impart a measurable yield stress help prevent particle settling while the formulation is at rest, providing stability against sedimentation during storage (Martin & Bustamante, 2011).

Therefore, the function of these excipients extends beyond simple thickening; they are indispensable in establishing a formulation that balances physical stability (high viscosity at rest) with patient acceptability and ease of administration (low viscosity during shear). The comparative evaluation of suspending agents based on these critical rheological and physicochemical parameters is essential for guiding rational pharmaceutical formulation design.

The selection of suspending agents is influenced by factors such as compatibility with the Api, Ph stability, and rheological requirements. For instance, in formulations involving poorly soluble drugs like paracetamol or ciprofloxacin, suspending agents help mitigate issues like caking and aggregation, which can lead to inconsistent bioavailability. Recent advancements in suspension technology have emphasized the use of polymers that impart non-Newtonian flow properties, allowing high viscosity at rest for stability and low viscosity under shear for pourability (aulton and taylor, 2018). Moreover, suspending agents contribute to the overall sensory attributes of the formulation, such as texture and mouthfeel in oral preparations, and can influence drug release profiles in controlled-release systems.

1.4..2. Historical Background of Suspending Agents

1. Early Beginnings (Ancient and Pre-Modern Pharmacy)

The concept of suspension formulations dates back to ancient apothecaries, where healers mixed insoluble powdered drugs in water, honey, or wine to make them easier to swallow. However, these early mixtures were physically unstable, with particles rapidly settling at the bottom, leading to inconsistent dosing. To reduce sedimentation, pharmacists began adding natural plant gums and mucilages, such as acacia gum (gum arabic) and tragacanth, which were among the earliest known suspending agents. These natural polymers increased viscosity and helped the insoluble particles remain dispersed longer.

2. The 19th Century – Birth of Scientific Formulation

During the 19th century, pharmacy evolved from a craft to a science. The idea of colloidal dispersion and rheology began to take shape. Pharmacists realized that adding viscous agents could stabilize suspensions by reducing sedimentation rate (as explained later by *Stokes' Law*). Natural gums like acacia, tragacanth, and xanthan gum were used extensively, often sourced from plants or microbial fermentation. Formulators also experimented with gelatin, starch, and pectin as thickening and suspending agents.

3. The 20th Century – Industrial and Syntgetic Era

The pharmaceutical industry's expansion in the early 20th century led to the search for more stable, reproducible, and purified suspending agents. Cellulose derivatives (like carboxymethyl cellulose (CMC)**,** methylcellulose (MC)**,** and hydroxypropyl methylcellulose (HPMC)**)** were developed and quickly became standards. These agents were chemically modified to achieve controlled viscosity, better solubility, and improved stability over natural gums. Around this time, researchers began formally studying suspension stability, zeta potential, and particle interaction mechanisms, leading to the introduction of synthetic polymers such as carbopol (carbomers) and polyvinylpyrrolidone (PVP).

4. Modern Development (Late 20th-21st century

With advances in polymer chemistry and biotechnology, newer agents were designed for controlled rheology, pH stability, and biocompatibility. Sodium alginate, derived from seaweed, and chitosan, derived from chitin, gained popularity as natural but modifiable biopolymers. Focus shifted toward environmental sustainability and biodegradability, leading to renewed interest in natural gums (guar gum, xanthan gum, locust bean gum) and hybrid systems combining natural and synthetic agents. Current pharmaceutical suspensions are carefully engineered using polymeric blends and nanostructured stabilizers to achieve optimal flow, redispersibility, and shelf stability.

5. Scientific significance

The historical development of suspending agents mirrors the progress of pharmaceutical formulation science itself, moving from empirical mixtures to precision-engineered delivery systems.

Each generation of agents improved upon the weaknesses of the last, from natural gums (unstable, microbial growth) to cellulose derivatives (more consistent) to modern carbomers and alginates (highly stable and versatile).

1.4.3. Classification of Suspending Agents

Suspending agents are categorized by origin: natural, semi-synthetic, and synthetic, each with unique advantages in biocompatibility, cost, and rheological tunability. Natural agents offer eco-friendliness but vary in batch quality; semi-synthetics provide consistency through modification; synthetics enable precise engineering for specific applications (rowe *et al.,* 2009).

- **i.** **Natural suspending agents:** Derived from plant or microbial sources, examples include acacia, tragacanth, and xanthan gum. They are biodegradable, biocompatible, and cost-effective but may exhibit variability in quality, susceptibility to microbial contamination, and batch-to-batch inconsistency (nair *et al.,* 2020).
- ii. **Semi-synthetic suspending agents**: These are chemically modified natural polymers (primarily cellulose derivatives) that offer improved stability and controlled viscosity. Examples include polysaccharides like sodium alginate and chitosan. Sodium alginate, derived from brown algae. Chitosan, from crustacean shells, methylcellulose (MC), hydroxypropylmethylcellulose (HPMC), sodium carboxymethylcellulose (NaCMC), and hydroxyethylcellulose (HEC). They are widely used due to reproducibility, safety, and regulatory acceptance (Rowe *et al.,* 2012). These agents offer versatility but may cause coagulation in certain Apis.
- **iii.** **Synthetic suspending agents:** These are completely man-made polymers (lab-designed polymer) with controlled structure and functionality, such as carbopol, polyethylene oxide (PEO), and eudragit derivatives. They provide excellent rheological control, stability across wide Ph ranges, and multifunctional properties, including mucoadhesion and drug release modification (Sheskey *et al.,* 2020).

1.4.4 Mechanisms of Suspension Stabilization:

Suspension stabilization by polymers primarily involves steric and electrostatic mechanisms, often working in tandem to prevent particle aggregation and sedimentation. Various mechanisms have been found through which suspending agents stabilize Pharmaceutical suspensions, some of these mechanisms include:

1. **Viscosity enhancement:** According to stokes' law, the rate of sedimentation is inversely proportional to the viscosity of the dispersion medium. By increasing viscosity, suspending agents reduce the sedimentation velocity of particles (lachman *et al.,* 2021).
2. **Electrostatic stabilization**: Electrostatic Stabilization, Relies On Charged Polymers (Such As Sodium Carboxymethylcellulose (NaCMC) Or Carbopol) Which Impart Surface Charges Leading To Coulombic Repulsion That Prevent Flocculation And Caking, For Example, Carbopol, An Acrylic Acid Polymer, Swells And Ionizes At Neutral Ph, Forming A Negatively Charged Network That Repels Anionic Particles.
3. **Steric stabilization**: Steric stabilization occurs when polymer chains adsorb onto particle surfaces, creating a steric barrier (Repulsive barrier) that prevents close approach and aggregation between particles due to osmotic and elastic effects. This is particularly effective with non-ionic polymers like hydroxypropylmethyl cellulose (HPMC), which form extended layers in the solvent (Tadros, 2010).
4. **Network formation:** Some suspending agents form structured, three-dimensional networks within the dispersion medium that trap particles and resist settling, as seen with carbopol and xanthan gum (Allen & Ansel, 2014).
5. Flocculation; a controlled form of aggregation, is another mechanism where polymers bridge particles to form loose flocs that settle slowly but redisperse easily, as seen with chitosan in acidic environments. In addition to these, depletion stabilization can occur with non-adsorbing polymers, where osmotic pressure differences create a depletion zone around particles.

The efficacy of these mechanisms depends on polymer concentration, molecular weight, and environmental factors like ionic strength. In low-density gastroretentive systems, polymers like sodium alginate and chitosan combine mucoadhesion with stabilization to prolong gastric residence time (Sinko, 2017). Recent studies highlight hybrid mechanisms, such as in Eudragit L-100, where Ph-dependent ionization enhances electrostatic effects in enteric formulations.

1.4.5 Role of Suspending Agents in Formulations:

The inclusion of suspending agents plays multiple roles in pharmaceutical dosage forms:

- Stability: preventing sedimentation and caking ensures uniform dosing.
- Palatability and appearance: agents improve texture and mouthfeel, especially in paediatric suspensions.
- Drug release control: certain suspending agents (e.g., carbopol, chitosan) also function as release modifiers, prolonging drug release from suspensions.
- Topical utility: in dermatological suspensions, they improve spreadability, residence time, and skin adherence.

Suspending agents play multifaceted roles in pharmaceutical formulations, extending beyond mere stabilization to influence drug release, bioavailability, and patient acceptability. In oral suspensions, agents like nacmc and hpmc provide controlled viscosity to ensure uniform dosing while improving palatability by masking bitter tastes. For gastro-retentive formulations, pvp and sodium alginate facilitate floating or bioadhesive properties, enhancing drug absorption in the upper gastrointestinal tract. Chitosan, with its mucoadhesive nature, is used in nasal or ocular suspensions to prolong contact time and improve permeation.

In parenteral suspensions, biocompatibility is key; carbopol and hydroxyethyl cellulose (hec) are favored for their sterility and low immunogenicity. Synthetic agents like eudragit l-100 enable ph-triggered release in colonic delivery systems. Combinations, such as nacmc with carbopol, yield synergistic effects, enhancing thixotropy for better injectability. Overall, suspending agents optimize formulation performance by modulating rheological properties, ensuring stability during manufacturing, storage, and use (Rowe *et al.,* 2009).

1.4.6 Current Methods for Evaluating Suspending agents:

Evaluation of suspending agents involves a suite of Physicochemical and rheological tests to assess stability and performance.

- Sedimentation volume and redispersibility tests; measure how well a suspension maintains particle distribution during storage and after agitation. Sedimentation volume ratio (f = vu/vo, where vu is ultimate settled volume and vo is original volume) measures resistance to settling, with values closer to 1 indicating better stability. Redispersibility is evaluated by shake tests, counting inversions needed for uniform resuspension.
- Viscosity and rheological profiling ; are performed using viscometers or rheometers to determine flow curves and assess behaviour under different shear rates (Barnes, 1997). Rheological assessments use viscometers (e.g., brookfield) for viscosity, rotational rheometers for flow curves, and oscillatory rheometry for viscoelastic moduli (g' and g").
- Ph and specific gravity; are measured to assess compatibility with active ingredients and vehicle stability. Ph and specific gravity tests check environmental compatibility.
- Environmental stress testing under varied temperature, humidity, and light conditions helps determine robustness.
- Modern evaluation emphasizes rheology, including thixotropy, yield stress, and shear-thinning behaviour, because these directly affect patient use (pourability, syringeability) and storage stability (Mezger, 2017).
- Electrokinetic methods, like zeta potential measurement, gauge electrostatic stability, with values > ±30 mv indicating good repulsion. Particle size analysis via laser diffraction ensures uniform distribution.
- For model Apis like metronidazole or paracetamol, accelerated stability studies under temperature cycling simulate real-world conditions. Advanced techniques include atomic

force microscopy for surface interactions and fourier-transform infrared spectroscopy for polymer-Api compatibility (Adeoye and Alebiowu, 2014).

1.4.7. Rheological properties of suspending agents

Rheological properties govern the flow and deformation of suspensions, essential for stability and application. These include viscosity, thixotropy, yield stress, and shear dependencies, measured via rheometers to predict behaviour under stress (Tadros, 2010). The rheological behaviour of suspending agents determines suspension stability, pourability, syringeability, and patient compliance.

1. **Viscosity and flow behaviour:** Viscosity is the resistance of a fluid to flow, with higher values at low shear preventing settling. Higher viscosity slows sedimentation but must remain within acceptable limits for pourability. Flow can be Newtonian (constant viscosity) or non-Newtonian; suspensions often display non-Newtonian flow due to the polymeric nature of suspending agents (barnes, 1997). Pharmaceutical agents typically exhibit non-Newtonian behaviour for optimal stability. For example, carbopol suspensions show increasing viscosity with concentration, following power-law models ($\eta = k\gamma^{n-1}$, where $n<1$ for shear-thinning).
2. **Thixotropy**: Thixotropy is the reversible decrease in viscosity under shear, followed by recovery when shear is removed. Thixotropy involves reversible, time-dependent viscosity decrease under shear, recovering at rest. It is desirable in suspensions because it facilitates easy pouring/shaking while maintaining stability at rest (Mezger, 2017). Agents like NaCMC and carbopol exhibit this, ensuring storage stability and easy dispensing. Hysteresis loops in rheograms quantify thixotropy, with larger areas indicating stronger effects.
3. **Yield stress and sedimentation resistance**: Yield stress (τ_y) is the minimum stress required for flow initiation, calculated via models like bingham ($\tau = \tau_y + \eta_p \gamma$). High

τ_y in carbopol or sodium alginate networks resists sedimentation. Sedimentation resistance is assessed by volume ratios, with yield stress correlating inversely with settling rates. A suspension with an adequate yield stress resists sedimentation during storage but allows redispersion upon shaking (martin *et al.,* 2020).

4. **Temperature and ph effects:** Temperature and ph strongly affect polymer viscosity and solubility. Temperature typically decreases viscosity via reduced molecular interactions; e.g., hpmc gels at >50°c. Ph affects ionization: carbopol exhibits maximum viscosity at neutral ph but loses viscosity under acidic conditions, chitosan dissolves below 6.5. These factors must be optimized for formulation stability.
5. **Shear rate dependency:** Shear rate influences non-newtonian viscosity.
    i. **Shear-thinning (pseudoplastic) behavior:** Most pharmaceutical suspensions exhibit shear-thinning behaviour, where viscosity decreases with increasing shear rate. This ensures easy pouring and mixing while providing stability at rest (barnes, 1997). Most agents like hpmc and sodium alginate follow this, aligning polymer chains under stress.
    ii. **Shear thickening (dilatant) fluid:** Less common in pharmaceuticals but seen in high-solid suspensions, potentially causing processing issues. Dilatant behaviour occurs when viscosity increases with shear rate. This can create processing difficulties and is generally undesirable (Mezger, 2017).

1.4.8. Factors affecting rheological behavior

The rheology of suspending agents is influenced by:

- Polymer concentration: higher concentrations increase viscosity exponentially and yield stress.
- Particle size and shape: smaller particles interact more with polymers, enhancing viscosity.
- Ph: affects ionization of polymers.

- Ionic strength: electrolytes can reduce viscosity of ionic polymers by shielding charges.
- Drug–excipient interactions: some drugs may bind or interact with polymers, altering rheology (Allen & Ansel, 2014).
- Temperature: reduces viscosity
- Molecular weight (longer chains enhance entanglement),
- Electrolytes; screen charges in ionic polymers and api interactions.

For nacmc, salts induce flocculation; in carbopol, concentration and ph dictate gel strength. Particle size and distribution also play roles, with smaller particles increasing viscosity via hydrodynamic effects (Kulshreshtha *et al.,* 2010).

1.5 Overview of Selected Active Pharmaceutical Ingredient (api): Ibuprofen

Ibuprofen is a widely used non-steroidal anti-inflammatory drug (nsaid) belonging to the propionic acid derivatives class. Chemically, It is a synthetic compound derived from propionic acid, originally developed in the 1960s by Boots Group (now part of Reckitt Benckiser) as a safer alternative to aspirin. it is known as **(±)**-2-(4-isobutylphenyl) propionic acid with the molecular formula $C_{13}H_{18}O_2$ and molecular weight 206.28 g/mol**.**

It is included in the World Health Organization (WHO) Model List of Essential Medicines and is available in various dosage forms such as tablets, capsules, oral suspensions, and topical gels.

It is available over-the-counter (OTC) in lower doses (e.g., 200 mg) and by prescription in higher doses (e.g., 400–800 mg) under brand names like Advil, or Nurofen.

2. Type / pharmacological class

- Therapeutic class**:** Analgesic, antipyretic, and anti-inflammatory agent.
- Pharmacological class: Non-steroidal anti-inflammatory drug (NSAID).
- Chemical class: Derivative of arylpropionic acid**.**

3. Mechanism of Action

Ibuprofen exerts its pharmacological effects primarily by inhibiting the cyclooxygenase (COX) enzymes; both COX-1 and COX-2. This inhibition reduces the synthesis of prostaglandins, which are mediators responsible for pain, inflammation, and fever.

As a result, ibuprofen provides pain relief (analgesia), reduces inflammation, and lowers elevated body temperature (antipyresis).

4. Physicochemical characteristics of ibuprofen

Property	Description
Chemical Name	(±)-2-(4-Isobutylphenyl) propionic acid
Molecular Formula	$C_{13}H_{18}O_2$
Molecular Weight	206.28 g/mol
Appearance	White or almost white crystalline powder
Odor	Odorless or slightly characteristic odor
Taste	Slightly bitter taste
Solubility	Practically insoluble in water; freely soluble in ethanol, acetone, chloroform, and ether
Melting Point	75 – 78°C
pKa (acid dissociation constant)	4.4 – 4.9
Partition Coefficient (log P)	3.5 (lipophilic)
Stability	Stable under ordinary conditions; may degrade in strong light or high temperature
Density	~1.1 g/cm³

5. Biopharmaceutical properties

- BCS Classification: Class II (Low solubility, high permeability).
    - This means ibuprofen has good absorption through biological membranes but limited solubility in aqueous systems, which is why **suspensions** are useful dosage forms for it.
- Absorption: Rapidly absorbed from the gastrointestinal tract.
- Bioavailability: 80–100%.
- Protein binding: High (~99%).
- Elimination half-life: 1.5 – 2 hours.

6. Pharmaceutical significance

- Ideal for suspension formulation: Because ibuprofen is poorly soluble in water, it is frequently formulated as an oral suspension for pediatric and geriatric use.
- Model API in research: It is often selected as a model hydrophobic drug in formulation studies (like yours) to test the efficiency of different suspending agents or solubilizers.
- Ease of characterization: Its physicochemical parameters (pH, solubility, particle size, etc.) are well documented, making it suitable for comparative rheological and stability studies.

7. Storage

Ibuprofen should be stored in a well-closed container, protected from light, and at a temperature not exceeding 30°C to maintain stability.

8. Rational for selecting ibuprofen as the Model Drug

Ibuprofen was selected as the model active pharmaceutical ingredient (API) for this study because it represents a typical poorly water-soluble drug, which makes it an ideal candidate for suspension formulation. Its low aqueous solubility (approximately 21 mg/L at 25 °C) poses a challenge in maintaining uniform drug dispersion and ensuring dose uniformity.

Evaluating different suspending agents using ibuprofen therefore provides valuable insight into how effectively each polymer can enhance physical stability, sedimentation control, and redispersibility in suspensions. Moreover, ibuprofen is safe, widely available, and well characterized, making it a suitable reference compound for comparative rheological and stability studies.

1.6 Overview of Selected Suspending Agents

The successful formulation of a pharmaceutical suspension relies critically on the selection of an appropriate suspending agent. These excipients are typically hydrophilic polymers that, when dissolved in the aqueous phase, increase the viscosity and impart a favorable non-Newtonian (pseudoplastic) flow (thixotropy) to the vehicle. This action effectively retards the sedimentation rate of the dispersed phase particles, while still allowing for easy pouring and redispersion upon shaking (Aulton, 2018).

The project will comparatively evaluate the rheological and physicochemical properties of a diverse group of Ten agents, spanning from two main sources: semi-synthetic and purely synthetic compounds.

1. Carbopol (Carbomers)

Category: Synthetic

Source: Produced entirely from chemical synthesis. It is a high-molecular-weight polymer of acrylic acid cross-linked with polyalkenyl ethers or divinyl glycol (Rao *et al.,* 2010).

Relevant Properties: It is an anionic polymer known for its excellent ability to form clear gels at low concentrations when neutralized, resulting in high viscosity and notable pseudoplastic and bioadhesive properties (Rao *et al.,* 2010). Its viscosity is highly pH-dependent.

2. Eudragit-L100

Category: Synthetic

Source: A family of functional synthetic polymers based on methacrylic acid and methyl methacrylate copolymers (Evonik, 2024). Eudragit-L100 is specifically a copolymer with an anionic nature.

Relevant Properties: While primarily used as an enteric coating agent due to its solubility above pH 6.0, its polymer structure and ability to dissolve/swell under specific conditions make it a suitable candidate for evaluating its impact on suspension rheology in different media (Ahuja & Shah, 2024).

3. Polyvinylpyrrolidone (PVP)

Category: Synthetic

Source: A linear polymer derived from the monomer N-vinylpyrrolidone (Popescu *et al.,* 2020). The process involves the synthesis of the monomer, which is then polymerized.

Relevant Properties: PVP is a non-ionic, water-soluble polymer with excellent chemical and thermal stability. Its function in suspensions is primarily as a protective colloid or wetting agent, though its high capacity for forming inter-polymer complexes and stabilizing effects make it a relevant viscosity modifier (Popescu *et al.,* 2020).

1. **Chitosan**

Category: Semi-Synthetic (often obtained via chemical deacetylation)

Source: Derived from the natural polymer chitin, which is extracted primarily from the shells of crustaceans (e.g., shrimp, crabs), but also from insects or fungi (Hamid *et al.,* 2023). Chitin is partially deacetylated using an alkaline solution to produce chitosan.

Relevant Properties: Chitosan is a unique cationic polysaccharide due to the presence of free amino groups, making it soluble in dilute acids where these groups are protonated (Hamid *et al.,* 2023). Its positive charge makes it an excellent mucoadhesive agent, and its polycationic nature makes its rheology sensitive to anionic APIs or excipients.

5. Sodium Alginate

Category: Semi-Synthetic

Source: A naturally occurring linear polysaccharide extracted from the cell walls of various species of brown algae (Phaeophyceae) (Rusu *et al.,* 2022). It is the sodium salt of alginic acid.

Relevant Properties: A strong polyanionic polymer that is readily soluble in water. Its most defining characteristic is its ability to undergo ionotropic gelation—forming stable gels instantly in the presence of divalent cations like \text{Ca}^{2+} (Rusu *et al.,* 2022). This property is crucial for its use in suspensions, particularly in systems where gelation is desired in situ or for matrix formation.

Cellulose Derivatives (Semi-Synthetic)

These agents are modified natural polymers, chemically derived from cellulose, which is extracted from plants (e.g., wood pulp, cotton). The chemical modification (etherification) imparts water solubility and viscosity-modifying properties.

6. Hydroxyethyl Cellulose (HEC)

Category: Semi-Synthetic

Source: Derived from cellulose through the reaction of alkali cellulose with ethylene oxide (etherification) (Fartak Lotus, 2023).

Relevant Properties: A non-ionic polymer that is soluble in both hot and cold water. It is known to be effective across a broad pH range, offering good heat stability and acting as a protective colloid and stabilizer in addition to a thickener.

7. Hydroxypropyl Methylcellulose (HPMC or Hypromellose)

Category: Semi-Synthetic

Source: Derived from cellulose where hydroxyl groups are partly substituted by ether-linked methoxy and hydroxypropyl side groups (Hypromellose Ph. Eur., 2025).

Relevant Properties: A widely used non-ionic agent that is cold-water soluble. Its physicochemical properties, particularly viscosity, are largely governed by its degree of substitution and molecular weight, making it a versatile thickener, binder, and film-former (Hypromellose Ph. Eur., 2025).

8. Methylcellulose (MC)

Category: Semi-Synthetic

Source: The methyl ether of cellulose, derived by treating cellulose with methyl chloride and an alkali (PubChem, 2024).

Relevant Properties: An non-ionic polymer that uniquely dissolves in cold water to form a viscous solution but exhibits thermal gelation (it gels upon heating). This property makes it valuable for certain processing techniques and drug release profiles.

9. Sodium Carboxymethyl Cellulose (NaCMC)

Category: Semi-Synthetic

Source: Produced by treating cellulose with an aqueous sodium hydroxide solution followed by monochloroacetic acid (Ataman Kimya, 2024).

Relevant Properties: A well-known anionic water-soluble polymer. It acts as a thickener and stabilizer, with its high molecular chains forming a flexible, long-chain structure that imparts viscoelastic properties to solutions. Its effectiveness is often affected by the presence of electrolytes (Jagau *et al.,* 2024).

10. Carboxymethyl Ethylcellulose (CMEC)

Category: Semi-Synthetic

Source: A complex derivative of cellulose, chemically modified to contain both carboxymethyl and ethyl groups. It shares the same natural cellulose origin and chemical modification process (etherification) as other cellulose derivatives (Jagau *et al.,* 2024).

Relevant Properties: CMEC possesses both hydrophobic (ethyl) and hydrophilic (carboxymethyl) groups, which gives it distinct properties regarding solubility and viscosity modification compared to its non-modified counterparts like NaCMC. It may show pH dependent solubility or swelling characteristics.

1.7 Research Gap and Rationale for this Study

Despite extensive literature on individual agents, gaps persist in systematic rankings of specific sets like sodium alginate, Eudragit L-100, HPMC, NaCMC, chitosan, carbopol, CMEC, HEC, MC, and PVP under uniform rheological criteria.

Previous studies often focus on one or two agents, making cross-comparisons difficult (patel *et al.,* 2019). Additionally, limited data exist on how synthetic vs. Semi-synthetic polymers perform under environmental stress conditions such as varying temperature and Ph. This study therefore seeks to address this gap by conducting a comprehensive evaluation of ten suspending agents, comparing their viscosity and Ph stability, under controlled conditions. The results will provide valuable insights for formulators in selecting the most appropriate suspending agents for stable and patient-friendly Pharmaceutical suspensions.

Technical and economic relevance of the study

a) Technical relevance

Suspending agents are essential components of pharmaceutical formulations, especially in suspensions where the active pharmaceutical ingredient (API) is insoluble in the dispersing medium. Synthetic and semi-synthetic polymers such as Carbopol, Eudragit-L100, NaCMC, CMEC, MC, HPMC, PVP, sodium alginate, chitosan, and HEC enhance viscosity, prevent sedimentation, and ensure uniform drug distribution throughout a product’s shelf life.

By evaluating the physicochemical properties (pH, density, sedimentation stability) and rheological characteristics (viscosity, flow behaviour) of these polymers, this study provides a systematic ranking of their performance under simulated formulation conditions. Such data-driven comparison directly addresses common challenges in suspension development, including particle settling, flocculation, and phase separation, which can compromise drug efficacy, bioavailability, and patient safety.

The study also advances formulation science by identifying polymers that demonstrate desirable behaviours such as pseudoplastic flow, thixotropy, and pH stability, properties that support better redispersibility, ease of administration, and improved controlled-release potential. These insights reduce trial-and-error during formulation development, support regulatory quality requirements, and guide formulators in selecting excipients that enhance product stability and performance.

b) Economic relevance

The pharmaceutical excipients market where suspending agents represent a significant category is a rapidly expanding global sector driven by increased demand for advanced formulations and the rising prevalence of chronic diseases. In this context, rational selection of cost-effective and high-performing suspending agents offers substantial economic advantages.

By ranking the agents based on stability and efficiency, this study helps manufacturers choose excipients that minimize material usage, reduce production losses from unstable batches, and extend product shelf life. These improvements lower manufacturing and quality assurance costs, reduce R&D expenses associated with repeated reformulation, and accelerate time-to-market.

For pharmaceutical companies particularly in resource-limited settings the findings support informed procurement strategies, promote the adoption of widely available and economically viable excipients, and encourage sustainable formulation practices by limiting the need for excess stabilizers. Ultimately, this contributes to more affordable medication, improved competitiveness for manufacturers, and positive economic impacts across the pharmaceutical supply chain

1.8 Significance of the Study

This study is significant as it provides a systematic ranking of suspending agents based on their rheological properties, addressing a critical need in Pharmaceutical formulation development. By identifying agents that offer optimal viscosity, and stability, the study will assist formulators in selecting appropriate excipients to enhance suspension quality, ensuring uniform drug delivery and improved patient compliance. The findings will be particularly valuable for developing oral suspensions, guiding evidence-based selection of suspending agents during formulation design, where ease of pouring and redispersion are essential for patient acceptability. Additionally, the study contributes to the scientific literature by synthesizing data on suspending agents, offering a reference for researchers and Pharmaceutical professionals seeking to optimize suspension formulations.

1.9 Aim and Objectives of the study:

Aim:

to evaluate and rank different suspending agents used in Pharmaceutical formulations based on their rheological properties.

Objectives:

1. To prepare suspensions using selected semi-synthetic, and synthetic suspending agents.
2. To evaluate their rheological behaviour (including viscosity) of commonly used suspending agents in Pharmaceutical suspensions.
3. To compare and rank the suspending agents according to their rheological performance and Pharmaceutical suitability.
4. To provide recommendations for selecting suspending agents in Pharmaceutical formulation development.

CHAPTER TWO

MATERIALS AND METHOD

2.1. Study Design

This study employs an experimental approach to prepare Pharmaceutical suspensions. The suspending agents investigated include chitosan, sodium alginate, sodium carboxymethyl cellulose (NaCMC), hydroxyethylcellulose (HEC), hydroxypropylmethyl cellulose (HPMC), Carbopol, Eudragit L-100, carboxymethylethyl cellulose (CMEC), polyvinylpyrrolidone (PVP) and methylcellulose(MC).

The methodology focuses on formulating suspensions at varying concentrations expressed in grams per 100 ml (w/v), ensuring complete dissolution and hydration, to enable subsequent rheological and stability testing for ranking the agents based on their performance in Pharmaceutical suspensions. The study was carried out in two phase; Phase I: Suspending agents in vehicles and Phase II: Ibuprofen formulations. All experiments were conducted under controlled laboratory conditions to ensure consistency and reproducibility.

2.2. Materials

The suspending agents used in this study are: Chitosan, Sodium Alginat, Sodium Carboxymethylcellulose (NaCMC), Hydroxyethylcellulose (HEC), Carbopol, Carboxymethylethyl Cellulose (CMEC), Hydroxypropylmethylcellulose (HPMC), Methyl Cellulose (MC), Eudragit L-100 and Polyvinylpyrrolidone (PVP) obtained from pyrex IG Ltd, ibuprofen, sodium citrate, sodium benzoate obtained from pharmaceutics laboratory, university of Benin,, absolute ethanol and polysorbate 80 obtained from safety medicals, sulfuric acid ($H2SO4$) from pharmaceutical chemistry laboratory

All materials were sourced from certified suppliers and comply with British Pharmacopoeia (bp) standards. Distilled water was used as the primary solvent unless otherwise specified.

2.3. Phase I: sample preparation

Formulations were prepared for each suspending agent at specified weight/volume (w/v) concentrations, with dissolution facilitated using a magnetic stirrer and followed by a hydration period to ensure complete gel formation. The preparation methods for each agent are detailed below. All formulations were prepared in 100 ml volumes.

2.3.1. Preparation of **chitosan**

Chitosan formulations were prepared at concentrations of 0.5%, 1.0%, 1.5%, and 2.0% w/v (corresponding to 0.5 g, 1.0 g, 1.5 g, and 2.0 g per 100 ml).

Solvent preparation: a 1% h2so4 solution was prepared by diluting concentrated h2so4 with distilled water to achieve a final concentration of 1% v/v.

Dissolution: chitosan (0.5 g, 1.0 g, 1.5 g, or 2.0 g) was weighed using an analytical balance and gradually added to 100 ml of 1% h2so4 solution in a 250 ml beaker placed on a magnetic stirrer. (Zamani & Taherzadeh, 2010). The mixture was stirred at room temperature (approximately 25°c) for 30 to 60minutes until complete dissolution was achieved.

Hydration: the resulting solutions were allowed to stand at room temperature for an additional 30 minutes. This standing period facilitated complete hydration, polymer swelling and ensured formation of a clear and homogenous viscous solution.

2.3.2 Preparation of Hydroxyethylcellulose (HEC) and Hydroxypropylmethylcellulose (HPMC) Formulations

Formulations of Hydroxyethylcellulose (HEC) and Hydroxypropylmethylcellulose (HPMC) were prepared using the hot-water dispersion method, as both polymers require elevated temperature to achieve complete hydration and uniform dispersion. (Katayama *et al.,* 1992).

Concentrations: HEC formulations were prepared at 0.5%, 1.0%, 1.5%, and 2.0% w/v (corresponding to 0.5 g, 1.0 g, 1.5 g, and 2.0 g per 100 ml), while HPMC formulations were prepared at 0.5%, 1.2%, 2.6%, 3.0%, and 9.0% w/v (corresponding to 0.5 g, 1.2 g, 2.6 g, 3.0 g, and 9.0 g per 100 ml).

Dissolution**:** For each concentration, 60 ml of distilled water was heated to above 80°C using a hot plate. The weighed polymer (HEC or HPMC) was gradually added to the hot water in a 250 ml beaker placed on a magnetic stirrer to prevent clumping and ensure uniform dispersion. The mixture was stirred for 20–30 minutes while hot until complete dispersion was observed, then removed from heat and allowed to cool to room temperature.

Cooling and Volume Adjustment**:** As cooling progressed, gel formation was observed, indicating proper hydration of the polymer. The final volume of each formulation was made up to 100 ml with distilled water, followed by an additional 20 minutes of stirring to obtain a homogeneous gel.

Hydration: All formulations were allowed to stand at room temperature for 30 minutes to ensure complete hydration before further evaluation.

2.3.3. Preparation of Carbopol

Carbopol was formulated using a similar hot-dispersion technique (Lubrizol, 2012). Carbopol formulations were prepared at concentrations of 0.5%, 1.0%, 1.5%, and 2.0% w/v (corresponding to 0.5 g, 1.0 g, 1.5 g, and 2.0 g per 100 ml).

Dissolution: about 60ml of distilled water was heated to above 80°c using a hot plate and placed in a 250 ml beaker on a magnetic stirrer. The polymer (carbopol; 0.5 g, 1.0 g, 1.5 g, or 2.0 g) was weighed and gradually added to the hot water under continuous stirring to prevent clumping. Gel formation occurred immediately upon addition. Stirring continued for 30 minutes, after which the mixture was made up to 100 ml using room-temperature distilled water and stirred further to obtain a homogenous dispersion.

Volume Adjustment: after cooling to room temperature, the volume was made up to 100 ml with room-temperature distilled water, followed by additional stirring for 20 minutes to ensure uniformity.

Hydration: the formulations were allowed to stand at room temperature for 30 minutes to ensure complete hydration.

2.3.4. Preparation of EUDRAGIT L-100

Eudragit L-100 formulations were prepared at concentrations of 1.0%, 2.0%, 5.0%, and 7.5% w/v (corresponding to 1.0 g, 2.0 g, 5.0 g, and 7.5 g per 100 ml). Eudragit L-100 was prepared using absolute ethanol as the vehicle due to its insolubility in water (Cetin *et al.,* 2010).

Dissolution: Eudragit L-100 (1.0 g, 2.0 g, 5.0 g, or 7.5 g) was weighed and gradually added to 100ml of absolute ethanol in a 250 ml beaker on a magnetic stirrer. The mixture was stirred at room temperature for 30–60 minutes until complete dissolution was achieved.

Hydration: the formulations were allowed to stand at room temperature for 30 minutes to ensure complete hydration.

2.3.5 Preparation of Sodium Carboxymethyl Cellulose (NaCMC), Sodium Alginate, Carboxymethyl Ethyl Cellulose (CMEC), Methyl Cellulose (MC), and Polyvinylpyrrolidone (PVP) Formulations:

Formulations of Sodium Carboxymethyl Cellulose (NaCMC)**,** Sodium Alginate**,** Carboxymethyl Ethyl Cellulose (CMEC)**,** Methyl Cellulose (MC)**,** and Polyvinylpyrrolidone (PVP) were prepared using the cold-water dispersion method**,** as these polymers readily hydrate and swell at room temperature (Ogaji & Hoag, 2011).

Concentrations: NaCMC, CMEC, MC, and PVP were prepared at 0.5%, 1.0%, 1.5%, and 2.0% w/v (equivalent to 0.5 g, 1.0 g, 1.5 g, and 2.0 g per 100 ml). Sodium Alginate was prepared **at** 0.5%, 2**.7**%, 5.0%, and 10.0% w/v (equivalent to 0.5 g, 2.7 g, 5.0 g, and 10.0 g per 100 ml).

Dissolution**:** For each concentration, the accurately weighed quantity of the respective polymer was gradually added to 100 ml of room-temperature distilled water in a 250 ml beaker under continuous stirring using a magnetic stirrer to prevent clumping and ensure uniform dispersion. Stirring was continued for 30–60 minutes until complete dissolution or uniform dispersion was achieved.

Hydration: The prepared dispersions were then allowed to stand at room temperature for 30 minutes to ensure complete swelling and stabilization of the polymers before further testing.

General notes;

Storage: All formulations were stored in glass bottles at 25°c pending further testing.

API And Excipients: Incorporation of the active Pharmaceutical ingredient (paracetamol) and excipients (e.g., sodium benzoate, sucrose) was not performed during this preparation Phase and will be detailed in subsequent sections.

Quality Control: all weights were measured using a calibrated analytical balance, and volumes were measured using calibrated measuring cylinders to ensure accuracy.

All formulations were prepared in clean, dry beakers using distilled water as the solvent, except for Eudragit L-100 and chitosan. The use of a magnetic stirrer throughout the process ensured uniform mixing and minimized air entrapment. After preparation, each formulation was covered and allowed to stand undisturbed for hydration prior to evaluation for their Physicochemical properties such as viscosity, Ph, and density.

2.4. Phase II: Ibuprofen formulations.

2.4.1. Preparation of Control Suspension (No Suspending Agent):

A control formulation containing no suspending agent was first prepared to serve as a baseline for comparison (Ogaji & Hoag, 2011)

Step 1: Preparation of Buffer/Preservative Solution (Preparation 1)

0.1 g of sodium benzoate and 0.5 g of sodium citrate were accurately weighed and transferred into a beaker containing 75 ml of distilled water. The mixture was stirred continuously until complete dissolution was achieved.

Step 2: Preparation of Wetting Agent Solution (Prep 2)

10 ml of Prep 1 was transferred into another beaker and mixed with 5 ml of polysorbate 80. The solution was stirred for a few minutes to ensure uniform mixing.

Step 3: Incorporation of the Active Ingredient

Preparation 2 was then transferred into a clean mortar and 2g of ibuprofen was gradually incorporated while triturating with a pestle to form a smooth slurry. The slurry was then transferred into the remaining Prep 1 and stirred thoroughly to obtain a homogeneous mixture.

Step 4: Final Dilution

The formulation was made up to the final volume with distilled water, mixed thoroughly, transferred into a clean bottle, and labelled as Control Suspension.

2.4.2. Preparation of ibuprofen Suspensions with Hydroxypropyl Methylcellulose (HPMC):

Hydroxypropyl methylcellulose (HPMC) requires hot dispersion and cold gelation for complete hydration. Suspensions were formulated using HPMC at concentrations of 0.5% and 1% w/v.

Step 1. Polymer Dispersion:

0.5 g and 1 g of HPMC were separately weighed and added to 40 ml of distilled water pre-heated to above 80 °C. The mixture was stirred using a magnetic stirrer for 20-30 minutes to ensure proper dispersion and allowed to cool to room temperature, during which HPMC hydration and gel formation occurred.

Step 2. Preparation of Buffer and Preservative Solution (Preparation 1):

0.1 g of sodium benzoate and 0.5 g of sodium citrate were dissolved in a beaker containing 40 ml of distilled water with stirring until complete dissolution

Step 3. Preparation of Wetting Agent Solution (Preparation 2):

10 ml of Preparation 1 was combined with 5 ml of polysorbate 80 and stirred thoroughly.

Step 4. Incorporation of the API:

Preparation 2 was then transferred into a clean mortar and 2g of ibuprofen was gradually incorporated while triturating with a pestle to form a smooth slurry.

Step 5. Final Formulation:

The remaining 30 ml of Preparation 1 was added to the hydrated HPMC suspension and mixed thoroughly. The ibuprofen slurry (Prep 2) was incorporated into the combined buffer/preservative/HPMC mixture and stirred thoroughly for homogeneity. The formulation was made up to the final volume with distilled water, mixed thoroughly, transferred into a clean bottle, and labelled appropriately

2.4.3. Preparation of ibuprofen Suspensions with Carbopol

Carbopol requires neutralization and hydration at elevated temperatures to form a stable dispersion. Suspensions were formulated using Carbopol at concentrations of 0.5% and 1% w/v.

Step 1. Polymer Dispersion:

0.5 g and 1 g of Carbopol were separately added to 40 ml of distilled water pre-heated to above 80 °C. The dispersion was stirred with a magnetic stirrer for several minutes until uniform and then allowed to cool to room temperature for complete hydration.

Step 2. Preparation of Buffer and Preservative Solution (Prep 1):

0.1 g of sodium benzoate and 0.5 g of sodium citrate were weighed and dissolved in a separate beaker containing 40 ml of distilled water at room temperature with stirring until complete dissolution

Step 3. Preparation of Wetting Agent Solution (Prep 2):

10 ml of Prep 1 was mixed with 5 ml of polysorbate 80 and stirred thoroughly.

Step 4. Incorporation of Ibuprofen:

Preparation 2 was then transferred into a clean mortar and 2g of ibuprofen was gradually incorporated while triturating with a pestle to form a smooth slurry.

Step 5. Final Formulation:

The remaining 30 ml of Preparation 1 was added to the prepared carbopol suspension and mixed thoroughly. The ibuprofen slurry (Prep 2) was incorporated into the combined buffer/preservative/carbopol mixture and stirred thoroughly for homogeneity. Distilled water was added to make up the final volume, mixed thoroughly, transferred into a clean bottle, and labelled appropriately

2.4.4 Preparation of Ibuprofen Suspensions Containing CMEC, Sodium Alginate, NaCMC, and MC

Ibuprofen suspensions were formulated using Carboxymethyl Ethyl Cellulose (CMEC), Sodium Alginate, Sodium Carboxymethyl Cellulose (NaCMC), and Methyl Cellulose (MC) at 0.5% and 1.0% w/v concentrations to evaluate their suspending properties.

Step 1: Preparation of Polymer Dispersions

Accurately weighed quantities of each polymer (0.5 g and 1.0 g) were dispersed separately in 40 ml of distilled water contained in 250 ml beakers. The mixtures were stirred on a magnetic stirrer for approximately 30 minutes to ensure proper wetting and hydration of the polymer. Each dispersion was then allowed to stand until a uniform gel-like consistency was obtained.

Step 2: Preparation of Buffer and Preservative Solution (Prep 1)

A mixture of **0.**1 g sodium **benzoate** and 0.5 g sodium citrate was dissolved in 40 ml of distilled water under continuous stirring until complete dissolution occurred.

Step 3: Preparation of Wetting Agent Solution (Prep 2)

From Prep 1*,* 10 ml was withdrawn and mixed with 5 ml of polysorbate 80 to aid in the dispersion of the hydrophobic drug (ibuprofen). The solution was stirred to ensure uniform mixing.

Step 4: Incorporation of the Active Pharmaceutical Ingredient (API)

The wetting agent solution *(*Prep 2*)* was transferred into a clean mortar**.** 2 g of ibuprofen was gradually added while triturating with a pestle to form a smooth, uniform slurry.

Step 5: Final Formulation

The remaining Prep 1 (approximately 30 ml) was poured into the previously prepared polymer dispersion and mixed thoroughly. The ibuprofen slurry was then incorporated into the combined buffer/preservative/polymer mixture and stirred until homogenous. Distilled water was added to make up the final volume to 100 ml. The final suspensions were transferred into labelled bottles and stored at room temperature for subsequent analysis.

Table 2.1 Formulations Table of ibuprofen suspension with different suspending agents and varying concentrations

Suspending agents	Concentration (%w/v)	Ibuprofen (g)	Preservative (Na benzoate, g)	Buffer (Na citrate, g)	Polysorbate 80 (ml)	Final volume (ml)
None (Control)	0	2.0	0.1	0.5	5	100
Nacmc	0.5	2.0	0.1	0.5	5	100
	1.0	2.0	0.1	0.5	5	100
CMEC	0.5	2.0	0.1	0 5	5	100
	1.0	2.0	0.1	0.5	5	100
Na Alginate	0.5	2.0	0.1	0.5	5	100
	1.0	2.0	0.1	0.5	5	100
MC	0.5	2.0	0.1	0.5	5	100
	1.0	2.0	0.1	0.5	5	100
HPMC	0.5	2.0	0.1	0.5	5	100
	1.0	2.0	0.1	0.5	5	100
Carbopol	0.5	2.0	0.1	0.5	5	100
	1.0	2.0	0.1	0.5	5	100

2.5. Evaluation of Formulations

Following the preparation of the suspending agent formulations, the prepared suspending agent formulations were subjected to Physicochemical evaluation to determine the effect of the different suspending agents and their concentrations on formulation quality. These parameters were measured to assess the rheological and stability characteristics of the formulated suspensions. These tests were performed using calibrated laboratory equipment, with each measurement conducted in duplicate for all formulations. All tests were performed at room temperature (25 ± 2 °c) and in duplicates to ensure accuracy and reproducibility.

2.5.1. Determination of Density

The density of each suspension was determined using a 25 ml borosilicate glass specific gravity bottle (Pycnometer), the procedure involved:

Calibration: the empty, clean and dry density bottle was weighed using an analytical balance to obtain its tare weight (w_1).

Water Reference: the bottle was filled with distilled water at room temperature, and the combined weight (w_2) was recorded. The density of water at 25°c (0.997 g/ml) was used as a reference to verify the bottle's volume.

Sample Measurement: each test suspension formulation was gently poured into the density bottle until the 25 ml mark was reached, ensuring no air bubbles were trapped. Excess formulation was removed, the bottle was wiped clean, and the combined weight (w_3) was recorded.

2.5.2. Determinatuon Of PH

The Ph of the prepared suspensions was measured using a digital Ph meter **(**Hanna Instruments Hi 2215 Ph/Orp Meter). The procedure included:

Calibration: The Ph meter was calibrated using a standard buffer solution of Ph 4.0 prior to testing each set of preparations to ensure accurate readings. Calibration was verified with the buffer solution, and the electrode was rinsed with distilled water and blotted dry with tissue paper between uses to prevent cross-contamination .

Sample Preparation: A 50 ml aliquot of each formulation was transferred to a clean beaker and allowed to equilibrate to room temperature (approximately 25°c).

Measurement: The Ph electrode was immersed in the sample, and the reading was recorded after stabilization (typically within 1–2 minutes).

Repetition: Ph was measured in duplicates for each concentration, with results reported as mean ± standard deviation.

2.5.3. Determination Of Viscosity

Viscosity was assessed using an NDJ-5S Viscometer equipped with interchangeable spindle probes of varying sizes to accommodate the range of formulation viscosities. The procedure was adapted based on the thickness of the suspensions, as follows:

Spindle and speed selection:

- For formulations with lower viscosity (e.g., lower concentrations of each agent), the largest spindle (typically ndj-5s spindle l2) was used at 30 rpm.
- As viscosity increased with intermediate concentrations, the speed was reduced to 12 rpm, and the medium spindle (typically ndj-5s spindle l3) was employed.
- For the thickest formulations (e.g., highest concentrations of agents like chitosan or HEC), the smallest spindle (typically ndj-5s spindle l4) was used at 12 rpm.
- Spindle selection and rpm adjustments were determined through preliminary trials to ensure readings remained within the viscometer's measurable range (typically 1–2,000,000 mpa·s, depending on spindle and speed).

Sample Preparation: approximately 100 ml of each formulation was transferred to a clean beaker and allowed to equilibrate to 25°c, with temperature monitored using the viscometer's built-in sensor.

Measurement: the selected spindle was attached to the viscometer, lowered into the sample, and rotated for 1 minute or until a stable reading was obtained. Viscosity was recorded in millipascal-seconds (mpa·s)

Repetition: viscosity was measured in duplicates for each concentration, with results reported as mean ± standard deviation. Any spindle or speed changes were noted for each measurement to ensure consistency in data interpretation.

General Notes

Equipment Calibration: The hi 2215 Ph meter, ndj-5s viscometer, and analytical balance were calibrated according to manufacturer guidelines prior to use. The density bottle's volume was validated using distilled water.

Storage Conditions: Post-measurement, formulations were stored in glass bottles at 25°c for further testing (e.g., stability or sedimentation), to be detailed in subsequent sections.

Data Recording: All measurements were recorded with precision to two decimal places, and any deviations or anomalies were noted for further investigation.

CHAPTER THREE

RESULT AND DISCUSSION

This chapter presents the experimental data collected for the prepared suspending-agent formulations. The results are divided into two main phases: the initial assessment of suspending agents dissolved in their respective vehicles without the active pharmaceutical ingredient (API) or additional excipients, and the subsequent evaluation of formulations incorporating ibuprofen as the API. All measurements were carried out at ambient temperature (25–28 °C) unless otherwise stated. pH measurements were performed with a calibrated pH meter and recorded on Days 1, 14 and 30. Viscosity measurements were made using an NDJ-5S viscometer and are reported in mPa·s; spindle and rpm used for each reading are shown in the viscosity tables.

3.1 Organoleptic Properties of the Suspending Agents

Organoleptic evaluation is an important preliminary test used to assess the physical characteristics of excipients, as these properties can influence the appearance, acceptability, and stability of pharmaceutical formulations. Parameters such as colour, odour, texture, and solubility give valuable information about the identity and potential usability of each suspending agent. Table 3.1 shows the organoleptic characteristics of the ten suspending agents used in this study.

Table 3.1: Organoleptic Properties of the Suspending Agents

Suspending agents	Colour	Smell	Form/texture	Solubility
Chitosan	Light yellow	Faint characteristics odor	Soft brittle flakes	Insoluble in water, solunle in aqueous acidic solutions
Sodium alginate	Brownish yellow	Faint odor	Granular powder	High solubility in water
Cmec	Off-white	Odorless	Smooth, soft and easy to compress, fine powder	High solubility in water
Pvp	White	Odorless	Fine powder	High solubility in water
Eudragit L100	White	Odorless	Fine powder	Insoluble in water, solunle in ethanol
Nacmc	White	Almost odorless	Fine powder	High solubility in water
Methyl cellulose	Off-white	Odorless	Granular/pelleted form	High solubility in water
Carbopol	White	Characteristics slightly odor	Fine white powder	High solubility in water
Hpmc	Off white	Odorless	Granular powder	Soluble in water, exhibit thermal gelation
Hec	White	Odorless	Fine powder	Soluble in water, exhibit thermal gelation

The organoleptic properties of the suspending agents examined were consistent with literature descriptions and confirm their identities and suitability for pharmaceutical use. Most of the agents appeared as white to off-white fine powders, which is desirable in pharmaceutical formulation since it ensures uniform blending with other ingredients and does not impart colour to the final suspension.

Chitosan differed slightly in its light yellow colour and faint odour, attributable to its natural origin (derived from chitin in crustacean shells). Its poor water solubility but solubility in acidic media aligns with previous findings that chitosan dissolves only in dilute acids such as acetic or hydrochloric acid due to protonation of amino groups. This property influences its pH-dependent application as a suspending or gelling agent. Chitosan's acid-dependent solubility reflects its cationic nature, enabling pH-triggered behaviors useful in controlled-release suspensions but complicating neutral pH formulations

Sodium alginate exhibited a brownish-yellow colour and high water solubility, reflecting its marine algal source and the hydrophilic nature of its polysaccharide chains. Its easy dispersibility makes it a preferred natural polymer for aqueous suspension systems.

The synthetic and semi-synthetic polymers such as CMC, NaCMC, PVP, HPMC, HEC, and Carbopol **were** white to off-white, odourless, and fine powders, consistent with their commercial grades. These properties are beneficial for pharmaceutical formulations as they ensure chemical stability and compatibility with various active ingredients.

Eudragit L100**,** being insoluble in water but soluble in ethanol, differs from others due to its methacrylic acid copolymer structure, making it useful for enteric-coated systems rather than aqueous suspensions.

HPMC and HEC were noted to exhibit thermal gelation, an important characteristic that affects their rheological behaviour and gel strength at elevated temperatures, enhancing suspension stability upon storage.

Overall, the organoleptic evaluation indicates that the suspending agents used were of good pharmaceutical quality, showing acceptable physical characteristics with no objectionable odour or discoloration that could affect formulation quality or patient acceptability, this evaluation highlights the diversity among suspending agents, guiding selection based on the target suspension's requirements. For general pharmaceutical suspensions, agents like NaCMC or HPMC may be preferred for their balanced organoleptic profile, while specialized needs (e.g., acid-resistant) favor chitosan. These findings set the foundation for subsequent rheological and physicochemical assessments, where solubility and texture will likely correlate with viscosity and sedimentation behaviors.

3.2 pH Variation of Formulations Over Time

Monitoring pH variation over time is essential in assessing the stability and compatibility of suspending agents in aqueous systems. The pH of a formulation affects the ionization state, solubility, and viscosity of polymers and may influence the chemical stability of active ingredients when incorporated later. pH variation can also indicate potential polymer degradation or microbial growth during storage (Aulton and Taylor, 2018). The results presented in Table 3.2 show the pH changes of methyl cellulose, hydroxypropyl methylcellulose (HPMC), hydroxyethyl cellulose (HEC), carboxymethyl cellulose (CMC), and sodium carboxymethyl cellulose (NaCMC) formulations over a period of 30 days.

Table 3.2. Ph variation OF methyl cellulose, hydroxypropyl methylcellulose (HPMC), hydroxyethyl cellulose (HEC), carboxymethyl cellulose (CMC), and sodium carboxymethyl cellulose (NaCMC) formulations OVER TIME

Suspending agents	Concentration (%)	pH Day 1	pH Day 14	pH Day 30
Methyl cellulose	0.5	6.92	7.07	7.29
	1.0	7.10	7.21	7.33
	1.5	7.09	7.29	7.35
	2.0	7.07	7.37	7.68
Hpmc	0.5	6.63	6.43	6.50
	1.2	5.83	6.45	6.59
	2.6	5.28	6.43	6.54
	3.0	5.23	6.41	6.44
	9.0	4.84	6.47	6.50
Hec	0.5	6.63	5.91	5.45
	1.0	6.18	5.71	5.40
	1.5	6.11	5.53	5.28
	2.0	6.06	5.23	5.01
Cmec	0.5	7.08	6.78	6.73
	1.0	6.86	6.32	6.26
	1.5	6.96	6.83	6.69
	2.0	6.99	6.91	6.73
Nacmc	0.5	7.04	6.97	7.22
	1.0	7.05	6.99	7.19
	1.5	6.92	6.91	7.04
	2.0	6.58	6.90	7.14

The pH of all suspending agents tested ranged between 4.8 and 7.7 throughout the 30-day observation period, indicating that all formulations remained within the acceptable pH range (4.0–8.0**)** for oral pharmaceutical preparations (Allen and Ansel, 2020). None of the formulations showed abrupt or extreme pH fluctuations, suggesting good chemical stability of the polymers in aqueous media.

Methyl cellulose maintained a slightly alkaline pH (6.9–7.7) across all concentrations, with a gradual increase over time. This upward trend may be attributed to mild hydrolytic rearrangement **or** ion exchange interactions with dissolved ions in water (Kulkarni *et al.,* 2002). The stable and near-neutral pH supports its suitability for oral suspension systems, as it minimizes drug degradation risks.

HPMC formulations initially exhibited a **sl**ightly acidic pH (4.8–6.6)**,** particularly at higher concentrations, which later rose gradually towards neutrality over time. The increase may be due to hydration and equilibrium polymer relaxation**,** allowing more uniform dispersion (Rowe *et al.,* 2009). The pH stability suggests that HPMC solutions are chemically inert and unlikely to produce acidic degradation products during storage (Zhang *et al.,* 2014).

HEC showed a slight pH decline from near-neutral (6.6) to mildly acidic (5.0) over the 30 days. This downward shift could indicate minor oxidative degradation or microbial activity in the aqueous medium since no preservative or API was included (Müller *et al.,* 2017). Despite the drop, the pH remained within acceptable limits, showing that HEC maintains moderate stability under neutral storage conditions.

CMC solutions were initially neutral (≈7.0) but showed **a** minor pH reduction (≈6.7) by day 30. This could be attributed to hydrolysis of carboxymethyl groups in water over prolonged storage (Kulkarni *et al.,* 2002). Nevertheless, the pH remained within a stable range, confirming CMC’s resilience as a suspending and thickening agent in aqueous formulations.

NaCMC maintained excellent pH stability, ranging narrowly between 6.9–7.2 throughout the 30-day period. This stability aligns with literature reports that sodium substitution confers enhanced resistance to hydrolytic degradation and microbial attack compared with unmodified CMC (Rowe *et al.,* 2009). The near-neutral pH and low variation demonstrate NaCMC's strong potential for maintaining long-term suspension stability.

Among the celluloses tested, NaCMC and methyl cellulose showed the highest pH stability, while HEC demonstrated a slight downward drift over time. HPMC exhibited an adaptive pH rise toward neutrality, and CMC showed minimal change. Since rheological behaviour can be influenced by pH due to ionization of functional groups (Tadros, 2013), these results provide an important foundation for understanding the rheological stability and viscosity performance discussed in later sections.

Overall, the findings indicate that all tested suspending agents are chemically stable in aqueous systems over the study period, making them suitable for use in oral suspension formulations without risk of rapid pH-induced degradation.

Table 3.3. PH Variation OF sodium alginate, chitosan, eudragut L-100, carbopol, and polyvinylpyrrolidone Formulations Over Time

Suspending agents	Concentration (%)	pH Day 1	pH Day 14	pH Day 30
Sodium Alginate	0.5	5.20	6.54	6.52
	2.7	4.82	6.14	6.54
	5.0	4.74	5.95	6.49
	10.0	4.52	5.35	6.42
Chitosan	0.5	3.46	3.44	3.40
	1.0	3.83	3.77	3.71
	1.5	4.00	3.93	3.84
	2.0	4.13	4.06	4.03
EUDRAGIT L-100	1.0	4.56	4.31	4.42
	2.0	4.54	4.46	4.42
	5.0	4.62	4.53	4.61
	7.5	4.63	4.61	4.67
Carbopol	0.5	3.34	3.09	2.98
	1.0	3.20	2.97	2.90
	1.5	3.07	2.82	2.76
	2.0	2.91	2.69	2.66
Polyvinylpyrrolidone	0.5	6.43	6.03	5.97
	1.0	6.32	5.97	5.84
	1.5	6.12	5.82	5.79
	2.0	5.92	5.74	5.71

The pH stability of a suspension formulation plays a critical role in determining the chemical stability, solubility, and compatibility of both the suspending agent and any active pharmaceutical ingredient (API) that may later be incorporated (Allen & Ansel, 2021).

From the results, sodium alginate exhibited a steady increase in pH from slightly acidic (4.5–5.2) on Day 1 to near-neutral levels (6.4–6.5) by Day 30. This gradual rise may be due to ion exchange between alginate's carboxylate groups and environmental ions in solution, leading to the formation of sodium salts that slightly elevate pH over time (Garg *et al.,* 2019). This trend suggests excellent long-term stability, as alginates generally perform well within a pH range of 4–10 (Rowe *et al.,* 2009).

In contrast, chitosan formulations remained acidic throughout (pH 3.4–4.1) with only minor fluctuations. This is consistent with chitosan's weakly basic amino groups that are protonated in acidic conditions, making it soluble only under acidic pH (Dash *et al.,* 2011). The small decrease in pH with time indicates limited hydrolytic degradation, showing good stability in acidic medium.

Eudragit L-100**,** an anionic copolymer of methacrylic acid and methyl methacrylate, also maintained a stable mildly acidic pH (4.3–4.6)**,** which aligns with its solubility profile in organic solvents rather than water (Elder & Delaney, 2020). The minimal pH change suggests it remains chemically inert in aqueous environments, making it suitable for enteric formulations.

Carbopol suspensions exhibited the lowest pH values (2.6–3.3) and showed a slight decline over time**.** This acidic behavior arises from the carboxylic acid groups in the polymer backbone (Florence & Attwood, 2015). The gradual pH drop may result from polymer chain rearrangement or incomplete neutralization, which can slightly increase hydrogen ion concentration over time. However, this does not necessarily indicate instability, as Carbopol remains functionally stable under acidic to neutral conditions.

Lastly, polyvinylpyrrolidone (PVP) formulations displayed moderate pH values (5.7–6.4) that slightly decreased during the 30-day period. PVP's neutral to slightly acidic pH range reflects its amphiphilic nature and its known stability across a wide pH range (Ogunjimi *et al.,* 2020). The marginal pH decrease suggests minor environmental interactions or oxidative processes, but overall, PVP demonstrated excellent pH stability**.**

Overall, the pH variation observed across the suspending agents falls within the acceptable range (3–8) for most oral suspension formulations (Aulton & Taylor, 2018). Stability over 30 days implies that these agents can be considered chemically stable under room temperature storage, especially sodium alginate, chitosan, and PVP which exhibited the least pH fluctuations.

3.3 Viscosity Determination

Viscosity measurements were performed using an NDJ-5S viscometer at room temperature, with readings recorded at torque percentages between 20% and 90%. Data were collected at Week 1 and Week 3 for each suspending agent at varying concentrations, using appropriate spindles and RPM settings.

3.3.1. Viscosity Studies of Carbopol Formulations

The viscosity of Carbopol formulations was determined at varying concentrations (0.5–2.0%) using appropriate spindle types and a constant rotational speed (mostly 30 rpm). Table 3.4 below presents the mean viscosity values obtained at Weeks 1 and 3.

Table 3.4 Viscosity of Carbopol formulations

	CONC (%)	SPINDLE	RPM	VISCOSITY (mPa.s)
Week 1	0.5	L2	30	5.29
	1.0	L2	30	7.00
	1.5	L2	30	17.30
	2.0	L2	12	40.10
Week 3	0.5	L3	30	4.33
	1.0	L3	30	4.65
	1.5	L3	30	7.72
	2.0	L3	30	13.40

The viscosity of Carbopol formulations increased with polymer concentration, consistent with the formation of a more extensive three-dimensional gel network as polymer chains hydrated and swelled in water. At Week 1, the 0.5% and 1.0% formulations displayed relatively low viscosities (5.29–7.00 mPa·s), while the 1.5% and 2.0% samples exhibited higher viscosities (17.30–40.10 mPa·s), indicating concentration-dependent thickening behavior.

After three weeks, a general reduction in viscosity was observed across all formulations, which could be attributed to partial structural relaxation, polymer rearrangement, or microstructural degradation over time. The 2.0% Carbopol formulation, for instance, decreased from 40.10 mPa·s to 13.40 mPa·s, suggesting that higher polymer concentrations are more prone to viscosity loss upon standing, possibly due to trapped air release or polymer chain disentanglement.

The use of different spindle types (L2 and L3) reflected the need to accommodate the viscosity range of the samples; however, the observed trend clearly shows that Carbopol exhibits non-Newtonian pseudoplastic behavior, where viscosity decreases under constant or prolonged shear. This behavior is advantageous in pharmaceutical suspensions because it allows for ease of pouring and redispersion while maintaining high viscosity at rest to prevent sedimentation (Rowe *et al.,* 2012; Tadros, 2010).

Overall, Carbopol demonstrated desirable rheological properties as a suspending agent, particularly at concentrations between 1.0–1.5%, where the viscosity was sufficient for physical stability without being overly viscous or gel-like.

3.3.2 Viscosity Studies of Chitosan Formulations

The viscosity of chitosan formulations was determined at varying concentrations (0.5–2.0%) and measured using appropriate spindles (L2 and L3) at a constant speed of 30 rpm. The viscosity readings were recorded during Week 1 and Week 3 as presented in Table 3.5 below.

Table 3.5. viscosity of Chitosan formulation

	CONC (%)	Spindle	RPM	Viscosity (mPa.s)
Week 1	0.5	L2	30	5.51
	1.0	L2	30	10.9
	1.5	L2	30	13.6
	2.0	L3	30	8.92
Week 3	0.5	L3	30	4.53
	1.0	L3	30	4.85
	1.5	L3	30	5.45
	2.0	L3	30	7.57

The viscosity of chitosan formulations showed a concentration-dependent trend during Week 1, with viscosity increasing from 5.51 mPa·s at 0.5% to a peak of 13.6 mPa·s at 1.5%. This reflects the typical behavior of polymeric systems where viscosity rises as polymer chain entanglement and molecular interactions increase with concentration (Rinaudo, 2006). However, at 2.0%, the viscosity slightly decreased to 8.92 mPa·s, which could be attributed to incomplete polymer solubilization or molecular aggregation at higher concentrations. Since chitosan dissolves in dilute acidic media and not in neutral water, incomplete protonation of amino groups may have led to partial precipitation and reduced chain mobility (Kumar *et al.,* 2004).

After three weeks, all chitosan formulations exhibited a decline in viscosity, with values ranging from 4.53 to 7.57 mPa·s. This reduction may indicate time-dependent polymer degradation, structural relaxation, or sedimentation of undissolved particles. The higher concentration formulations (1.5–2.0%) maintained relatively higher viscosities compared to the lower ones, signifying that even though there was viscosity loss over time, the formulations retained some level of stability.

The change in spindle type from L2 to L3 was necessary to accommodate the varying viscosities as the formulations aged, but within the same spindle conditions, the results consistently showed that viscosity correlates with polymer concentration. The relatively moderate viscosity values suggest that chitosan behaves as a pseudoplastic (shear-thinning**)** polymer — a rheological property desirable for pharmaceutical suspensions because it provides ease of redispersion and pourability while preventing sedimentation during storage (Tadros, 2010).

Overall, chitosan demonstrated suitable rheological behavior for use as a suspending agent, particularly at concentrations between 1.0% and 1.5%**,** where viscosity was optimal and stable enough to provide adequate suspension characteristics without forming overly viscous gels.

The viscosity profile of chitosan formulations indicated that viscosity increased with polymer concentration up to 1.5% and declined thereafter, both over time and with higher concentration. This suggests that chitosan's optimal concentration range for use as a suspending agent lies between 1.0–1.5%, where it provides a balance between flowability and stability. The time-dependent decrease in viscosity may necessitate the inclusion of stabilizers or pH control to maintain long-term rheological stability in suspension formulations.

3.3.3 Viscosity Studies of Carboxymethyl Ethylcellulose (CMEC) Formulations

The viscosity of CMEC formulations was determined at concentrations ranging from 0.5% to 2.0%, using spindle L2 at 30 rpm for Week 1 and spindle L3 at 30 rpm for Week 3. The viscosity values are presented in Table 3.6 below.

Table 3.6. viscosity of Carboxymethyl ethylcellulose (CMEC) formulation

	CONC (%)	SPINDLE	RPM	Viscosity (mPa.s)
Week 1	0.5	L2	30	5.86
	1.0	L2	30	7.20
	1.5	L2	30	9.49
	2.0	L2	30	10.9
Week 3	0.5	L3	30	4.27
	1.0	L3	30	4.57
	1.5	L3	30	5.32
	2.0	L3	30	5.95

The viscosity of Carboxymethyl Ethylcellulose (CMEC) formulations showed a consistent increase with concentration during Week 1, rising from 5.86 mPa·s at 0.5% to 10.9 mPa·s at 2.0%. This pattern reflects the polymeric nature of CMEC, where higher polymer concentrations lead to increased chain entanglement, intermolecular hydrogen bonding, and resistance to flow (Rowe *et al.,* 2009). Such a concentration-dependent increase is typical for cellulose derivatives used as suspending and thickening agents in pharmaceutical formulations.

By Week 3, a noticeable decrease in viscosity was observed across all concentrations, with values ranging from 4.27 to 5.95 mPa·s. The decline may be attributed to hydration instability, polymer chain relaxation, or partial breakdown of the macromolecular structure over time. Environmental factors such as pH fluctuations, temperature, and microbial contamination could also influence the viscosity stability of cellulose-based systems (Tadros, 2010).

The spindle change from L2 to L3 was due to the lower viscosity recorded after storage, ensuring better sensitivity and accuracy during measurement. Despite the reduction, the viscosity remained within a moderate range that is ideal for pourable suspensions**,** suggesting that CMEC maintains acceptable rheological stability for short- to medium-term formulations. CMEC exhibits pseudoplastic flow behavior, typical of cellulose derivatives, which ensures high viscosity at rest (reducing sedimentation) and low viscosity under shear (facilitating easy pouring and redispersion) (Martin *et al.,* 2020). This property is beneficial for pharmaceutical suspensions where uniform particle distribution and stability are critical.

Overall, the 1.5–2.0% CMEC concentrations provided optimal viscosity profiles, balancing flowability and stability. Lower concentrations (0.5–1.0%) produced thinner dispersions that may be less effective in minimizing sedimentation, while concentrations above 2.0% could lead to overly viscous or gel-like consistency.

The viscosity of CMEC formulations increased with concentration, reaching a maximum at 2.0%, but gradually declined after three weeks. This suggests that while CMEC provides good initial viscosity and stability, it may exhibit time-dependent reduction in consistency. Concentrations between 1.5% and 2.0% appear most suitable for use as suspending agents, providing an effective balance between suspension stability and ease of redispersion during storage.

3.3.4 Viscosity Studies of Eudragit L100 Formulations

The viscosity of Eudragit L100 formulations was measured at concentrations ranging from 1.0% to 7.5% using spindle L2 at 30 rpm for Week 1 and spindle L3 at 30 rpm for Week 3. The values are shown in Table 3.7

Table 3.7. viscosity of Eudragit-L100 formulation

	CONC (%)	SPINDLE	RPM	Viscosity (mPa.s)

Week 1	1.0	L2	30	4.78
	2.0	L2	30	4.98
	5.0	L2	30	5.29
	7.5	L2	30	8.96
Week 3	1.0	L3	30	4.29
	2.0	L3	30	4.36
	5.0	L3	30	4.87
	7.5	L3	30	6.85

The viscosity of Eudragit L100 formulations increased moderately with rising polymer concentration, ranging from 4.78 mPa·s at 1.0% to 8.96 mPa·s at 7.5% during Week 1. This trend indicates that increasing the polymer content enhances the internal resistance to flow, a reflection of higher chain interaction and polymer entanglement within the dispersion (Rowe *et al.,* 2009).

However, compared to natural and cellulose-based polymers such as carbopol or CMEC, Eudragit L100 exhibited relatively low viscosity values, even at higher concentrations. This may be attributed to its methacrylic acid copolymer structure, which is less hydrophilic and more rigid, resulting in limited water swelling and lower thickening capacity (Khan *et al.,* 2015).

By Week 3, there was a slight decrease in viscosity across all concentrations, which could be due to minor polymer precipitation, solvent evaporation, or reduced interaction between polymer chains upon storage. The spindle change from L2 to L3 for Week 3 was necessary to enhance measurement accuracy at lower viscosity ranges.

Eudragit L100 is insoluble in water but soluble in ethanol and alkaline media**,** and its dispersions often behave as non-Newtonian, slightly pseudoplastic fluids. The slight shear-thinning property ensures that while the dispersion remains stable at rest, it flows readily under agitation or when being poured (Tadros, 2010).

Although Eudragit L100 did not provide a substantial viscosity rise compared to hydrophilic gums, it remains a valuable suspending or coating polymer, particularly for **enteric** formulations where pH-dependent solubility is desired (Rowe *et al.,* 2009; Martin *et al.,* 2020). The relatively low viscosity also makes it easier to handle in processes requiring spray coating or solvent-based dispersion.

Eudragit L100 formulations displayed a modest increase in viscosity with concentration, maintaining stable yet low rheological profiles compared to other suspending agents. The polymer's low hydrophilicity limits its thickening potential but enhances its suitability for formulations requiring controlled release or pH-dependent solubility. Concentrations between

5.0% and 7.5% appear optimal for achieving moderate viscosity without compromising flow properties or dispersion uniformity.

3.3.5. Viscosity Studies of Hydroxyethyl Cellulose (HEC) Formulations

The viscosity of HEC formulations was evaluated at concentrations ranging from 0.5% to 2.0% using appropriate spindle and rpm combinations to ensure optimal torque readings. Measurements were taken at Week 1 and Week 3 to determine viscosity stability over time. The results are presented in Table 3.8.

Table 3.8. viscosity of Hydroxylethyl Cellulose (HEC) formulation

	CONC (%)	Spindle	RPM	Viscosity (mPa.s)

Week 1	0.5	L3	30	8.28
	1.0	L4	30	20.6
	1.5	L4	30	39.5
	2.0	L4	12	38.2
Week 3	0.5	L3	30	5.19
	1.0	L3	30	11.3
	1.5	L4	30	14.7
	2.0	L4	12	37.7

Hydroxyethyl Cellulose (HEC) exhibited a marked increase in viscosity with rising polymer concentration, reflecting its strong thickening capability and hydrophilic nature. At Week 1, viscosity rose sharply from 8.28 mPa·s (0.5%) to 39.5 mPa·s (1.5%), before stabilizing at

38.2 mPa·s (2.0%), suggesting that beyond a certain concentration threshold, further increases in polymer content did not substantially affect viscosity. This plateau effect is typical for cellulose ethers, where entanglement and hydrogen bonding among polymer chains reach saturation (Bajpai *et al.,* 2016).

At Week 3, a noticeable decrease in viscosity was observed at lower concentrations (0.5–1.5%), possibly due to hydration changes, minor polymer degradation, or microbial growth in the aqueous dispersion. However, the 2.0% formulation maintained a nearly constant viscosity (37.7 mPa·s), indicating good stability at higher polymer concentrations. This stability can be attributed to enhanced chain interactions and the formation of a more cohesive gel-like structure (Tadros, 2010).

The viscosity profile suggests that HEC dispersions display pseudoplastic (shear-thinning) behavior, where viscosity decreases under shear, facilitating better pourability and redispersibility—properties highly desirable in pharmaceutical suspensions (Martin *et al.,* 2020). The use of different spindles (L3–L4) reflects the increasing thickness of the dispersions as concentration rises, necessitating higher torque sensitivity for accurate measurement.

Overall, HEC proved to be a highly effective suspending agent, maintaining good rheological stability and viscosity consistency over time, especially at concentrations above 1.5%. Its performance aligns with established literature describing HEC as a nonionic, pH-stable, and temperature-tolerant polymer suitable for oral and topical formulations (Rowe *et al.,* 2009; Sahu *et al.,* 2018).

HEC formulations demonstrated a concentration-dependent increase in viscosity, with minimal decline over time, particularly at higher polymer levels. This confirms the polymer's effectiveness as a **viscosity** enhancer and stabilizer in pharmaceutical suspensions. The 1.5%–2.0% concentration range provided an optimal balance between flowability and structural stability, suggesting its suitability for long-term suspension systems where consistent rheology is required.

3.3.6 Viscosity Studies of Hydroxypropyl Methylcellulose (HPMC) Formulations

The viscosity of HPMC formulations was determined at concentrations ranging from 0.5% to **9.0%** using a Brookfield viscometer with appropriate spindle selection (L2–L3) and a constant speed of 30 rpm. Measurements were taken at Week 1 and Week 3 to assess viscosity changes over time. The results are summarized in Table 3.9.

Table 3.9. viscosity of HPMC formulation

	CONC (%)	Spindle	RPM	Viscosity (mPa.s)
Week 1	0.5	L2	30	4.85
	1.2	L2	30	4.73

	2.6	L2	30	4.99
	3.0	L2	30	4.96
	9.0	L2	30	5.21
Week 3	0.5	L3	30	4.09
	1.2	L3	30	4.07
	2.6	L3	30	4.13
	3.0	L3	30	4.15
	9.0	L3	30	4.39

The viscosity of HPMC formulations remained relatively stable across all tested concentrations, with only minor variations between 4.73–5.21 mPa·s during the first week and a slight decline by the third week. This modest viscosity increase at higher concentrations reflects the moderate thickening capacity of HPMC in aqueous systems compared to more cross-linked polymers such as Carbopol or HEC (Tadros, 2010).

The near-constant viscosity readings across concentrations suggest that polymer chain entanglement reached an equilibrium**,** and further increases in concentration did not substantially alter flow resistance. HPMC is known to exhibit pseudoplastic or shear-thinning behavior, where viscosity decreases under applied shear stress, contributing to better pourability and redispersibility of pharmaceutical suspensions (Martin *et al.,* 2020).

Over the three-week storage period, the slight reduction in viscosity (approximately 0.4–0.6 mPa·s across concentrations) could be attributed to structural relaxation of polymer chains, mild degradation, or environmental factors such as temperature and microbial activity (Rowe *et al.,* 2009). However, the overall decrease was minimal, indicating excellent rheological stability.

The transition from spindle L2 to L3 between Week 1 and Week 3 measurements reflects a viscosity reduction that allowed the use of a less sensitive spindle while maintaining accurate torque readings. This stability, coupled with consistent flow behavior, aligns with the established profile of HPMC as **a** nonionic cellulose ether known for maintaining viscosity over a broad pH range (4–8) and exhibiting excellent compatibility with a variety of APIs and excipients (Sahu *et al.,* 2018; Kamel *et al.,* 2008).

Overall, HPMC's stable viscosity profile and minimal temporal variation make it an ideal suspending agent for formulations requiring reproducible rheological behavior and good physical stability without significantly altering pH or taste characteristics.

HPMC demonstrated consistent viscosity behavior across different concentrations**,** with negligible change over the three-week observation period. This suggests that HPMC maintains good rheological stability, flow properties, and polymer integrity in aqueous formulations. The results confirm its suitability as a stable and efficient suspending agent in pharmaceutical suspensions where moderate viscosity and predictable flow are desirable.

3.3.7. Viscosity Studies of Methylcellulose (MC) Formulations

The viscosity of Methylcellulose (MC) formulations was evaluated at varying concentrations (0.5%–2.0%) using a Brookfield viscometer at a constant spindle speed of 30 rpm. Measurements were taken at Week 1 and Week 3 to assess temporal viscosity stability. The corresponding results are presented in Table 3.10

Table 3.10. viscosity of Methyl Cellulose (MC) formulation

	CONC (%)	SPINDLE	RPM	Viscosity (mPa.s)
Week 1	0.5	L3	30	4.51

	1.0	L3	30	6.42
	1.5	L3	30	14.1
	2.0	L4	30	11.5
Week 3	0.5	L3	30	4.31
	1.0	L3	30	5.32
	1.5	L3	30	8.85
	2.0	L3	30	9.53

The viscosity of MC formulations exhibited a direct relationship with polymer concentration, demonstrating a significant increase in viscosity from 4.51 mPa·s at 0.5% to 14.1 mPa·s at 1.5% during the first week. This behavior is characteristic of hydrophilic cellulose derivatives, where polymer chain entanglement and intermolecular hydrogen bonding increase as concentration rises (Khurana & Bansal, 2002). However, a slight drop in viscosity at 2.0% concentration in Week 1 (11.5 mPa·s) may indicate structural breakdown incipient **or** incomplete hydration, which sometimes occurs at high polymer loadings due to aggregation (Tadros, 2010).

After three weeks, a moderate decrease in viscosity was observed across all concentrations, with values declining by approximately 10–35%**.** This decline could be attributed to molecular relaxation**,** chain disentanglement**, or** microbial degradation over time. Despite this reduction, the formulations retained considerable viscosity, indicating reasonable rheological stability during the test period.

The results also suggest that MC formulations display pseudoplastic flow behavior**,** consistent with literature reports that methylcellulose solutions exhibit shear-thinning characteristics beneficial for suspension redispersibility (Martin *et al.,* 2020). This property ensures easy pourability during administration while maintaining adequate viscosity under static conditions to prevent sedimentation.

Moreover, the viscosity trend observed supports the use of MC as a moderate to strong thickening and suspending agent, especially in low-to-medium concentration ranges. Its non-ionic nature makes it compatible with a wide variety of APIs and electrolytes, reducing the risk of incompatibility or pH-related instability (Rowe *et al.,* 2009). The observed stability over three weeks also aligns with findings by Kamel et al. (2008), who reported that MC maintains viscosity effectively within neutral to slightly alkaline pH environments.

Methylcellulose exhibited a clear concentration-dependent viscosity increase with slight reduction over time, suggesting good initial thickening ability and moderate long-term stability. Although some decline was observed after three weeks, MC maintained sufficient viscosity to support its role as an effective suspending agent. Its rheological behavior indicates that MC can provide desirable flow properties, ensuring both suspension stability and ease of redispersion during storage and use.

3.3.8 Viscosity Studies of Sodium Alginate Formulations

Result

The viscosity of Sodium Alginate formulations was determined at different concentrations (0.5%–10.0%) using a Brookfield viscometer at 30 rpm. Readings were taken after Week 1 and Week 3 to monitor viscosity stability over time. The results are shown in Table 3.11

Table 3.11 viscosity of Sodium Alginate formulation

	CONC (%)	Spindle	RPM	Viscosity (mPa.s)
Week 1	0.5	L2	30	4.98
	2.7	L2	30	6.35

	5.0	L2	30	6.33
	10.0	L2	30	6.49
Week 3	0.5	L3	30	4.24
	2.7	L3	30	4.24
	5.0	L3	30	4.80
	10.0	L3	30	5.81

The results indicate that the viscosity of Sodium Alginate formulations increased slightly with polymer concentration during Week 1**,** ranging from 4.98 mPa·s at 0.5% **to** 6.49 mPa·s at 10.0%**.** This trend reflects the polyelectrolyte nature of Sodium Alginate, where viscosity rises due to increased polymer chain entanglement and the presence of hydrophilic carboxyl groups that promote water binding (Draget *et al.,* 2005).

After three weeks**,** a slight decrease in viscosity was observed across all concentrations. The most significant drop was seen at 2.7%**,** which decreased from 6.35 mPa·s to 4.24 mPa·s**,** suggesting minor molecular relaxation or partial depolymerisation over time. Despite this reduction, the viscosity values remained within acceptable limits for oral suspensions, maintaining sufficient flow resistance to minimize sedimentation (Rowe *et al.,* 2009).

The viscosity profile demonstrates that Sodium Alginate exhibits moderate thickening capacity and maintains good rheological stability during storage. Its gel-forming ability in the presence of divalent cations such as Ca^{2+} is well documented and contributes to improved suspension stability through three-dimensional network formation (Gombotz & Wee, 2012). However, the relatively low viscosity changes over time suggest that formulations were physically stable without significant syneresis or phase separation.

This aligns with the findings of Glicksman (1983), who reported that alginate solutions maintain a pseudoplastic flow behavior — where viscosity decreases under shear but restores when static — a desirable characteristic in pharmaceutical suspensions for easy pouring and redispersion.

Sodium Alginate formulations showed a concentration-dependent increase in viscosity during the first week, followed by a mild reduction after three weeks. The polymer maintained stable rheological characteristics over time, making it a suitable suspending agent for formulations requiring moderate viscosity and reversible gel strength. Its biocompatibility, natural origin, and pseudoplastic flow behavior further enhance its application in liquid dosage forms.

3.3.9. Viscosity Studies of Sodium Carboxymethyl Cellulose (NaCMC) Formulations

The viscosity of NaCMC formulations was determined at different polymer concentrations ranging from 0.5% to 2.0% using a Brookfield viscometer. Measurements were taken after

Week 1 and Week 3 to assess viscosity changes during storage. Results are presented in Table 3.12.

Table 3.12. viscosity of NaCMC formulation

	CONC (%)	Spindle	RPM	Viscosity (mPa.s)
Week 1	0.5	L2	30	11.9

	1.0	L3	12	24.8
	1.5	L3	12	11.8
	2.0	L4	12	32.5
Week 3	0.5	L3	30	4.52
	1.0	L3	30	5.40
	1.5	L3	30	8.88
	2.0	L3	30	10.40

The viscosity data revealed a concentration-dependent increase in viscosity during the first week of measurement, with values ranging from 11.9 mPa·s at 0.5% to 32.5 mPa·s at 2.0%**.**

This trend is typical of hydrophilic colloidal polymers**,** as increasing polymer concentration enhances molecular entanglement and chain overlap in the aqueous medium, thereby increasing resistance to flow (Rowe *et al.,* 2009).

However, by Week 3**,** there was **a** notable decrease in viscosity across all concentrations. The most substantial drop was observed in the 1.0% formulation, which declined from 24.8 mPa·s to 5.40 mPa·**s**. This reduction may be attributed to hydrolytic degradation **or a** loss of molecular integrity over time, particularly in aqueous systems where NaCMC's carboxymethyl groups can undergo chain scission under varying pH or temperature conditions (Kamel *et al.,* 2008).

The observed reduction in viscosity over time could also reflect partial sedimentation or polymer relaxation**,** which causes reduced polymer-polymer interaction and less network rigidity. Nonetheless, the formulations retained sufficient viscosity to act as effective suspending agents, particularly at higher concentrations (≥1.5%), ensuring adequate stability for pharmaceutical suspensions.

This finding aligns with the work of Talukdar and Kinget (1995)**,** who reported that NaCMC displays strong pseudoplastic flow behavior and high swelling capacity, both of which are desirable for improving the pourability and redispersibility of suspensions. The thixotropic nature of NaCMC ensures that suspensions maintain their viscosity at rest but become less viscous upon shaking, facilitating ease of administration (Martin *et al.,* 2021).

NaCMC formulations demonstrated high initial viscosity that increased with polymer concentration, confirming its strong thickening and suspending ability. However, the reduction in viscosity after three weeks indicates possible polymer relaxation or structural degradation during storage. Despite this, NaCMC maintained adequate viscosity within acceptable limits for oral suspensions, making it one of the more stable and effective cellulose-based suspending agents.

3.3.10 Viscosity Studies of Polyvinylpyrrolidone (PVP) Formulations

Viscosity measurements for PVP formulations were carried out at different concentrations (0.5–2.0%) using a Brookfield viscometer at 30 rpm. Data were collected at Week 1 and Week 3 **to** evaluate the influence of concentration and storage time on viscosity. The results are shown in Table 3.13

Table 3.13. viscosity of PVP formulation

	CONC (%)	SPINDLE	RPM	Viscosity (mPa.s)

Week 1	0.5	L3	30	5.86
	1.0	L3	30	7.20
	1.5	L3	30	8.49
	2.0	L3	30	10.9
Week 3	0.5	L3	30	4.13
	1.0	L3	30	4.92
	1.5	L3	30	6.34
	2.0	L3	30	7.63

The viscosity of PVP formulations exhibited a progressive increase with concentration during Week 1, ranging from 5.86 mPa·s at 0.5% **to** 10.9 mPa·s at 2.0%**.** This indicates that PVP forms a more viscous solution as polymer concentration increases, due to enhanced molecular chain entanglement and interaction with water molecules. PVP is a non-ionic, water-soluble synthetic polymer that shows excellent compatibility and solubilizing properties, which explains the smooth rise in viscosity with concentration (Rowe *et al.,* 2009).

By Week 3**, a** general decline in viscosity was observed across all formulations. The 2.0% PVP formulation, for instance, decreased from 10.9 mPa·s to 7.63 mPa·s. This slight drop in viscosity over time may result from temperature- or moisture-induced changes, mild polymer relaxation**, or** partial sedimentation of dispersed particles leading to reduced network density. Such changes are common in polymeric systems that undergo storage under ambient conditions (Aulton & Taylor, 2018).

Compared to natural gums and cellulose derivatives, PVP maintained moderate viscosity stability and good flow characteristics, suggesting that it could enhance suspension **re-**dispersibility and pourability without causing high resistance to flow. The polymer's Newtonian flow behavior ensures consistent performance during handling and administration (Martin *et al.,* 2021).

Furthermore, PVP's viscosity values remained within the acceptable range for oral pharmaceutical suspensions (approximately 4–20 mPa·s), indicating suitability as a suspending or stabilizing agent that ensures adequate physical stability while maintaining good patient acceptability (Jones & Medlicott, 1995).

PVP formulations displayed a concentration-dependent increase in viscosity, confirming its strong potential as a rheology modifier in suspension systems. Although a slight viscosity reduction occurred after prolonged storage, PVP maintained sufficient consistency for suspension stability. Its synthetic origin, inertness, and compatibility with a wide range of drugs make it an excellent alternative to natural polymers where controlled viscosity and smooth flow are desired.

3.4 Results for second set of formulations (Phase II: Ibuprofen formulations.)

The following results correspond to the formulations that included ibuprofen (API), sodium benzoate (preservative), polysorbate 80 (wetting agent), sodium citrate buffer and selected suspending agents. All pH readings were at room temperature. Viscosity for these formulations was determined using spindle L3 at 60 rpm.

3.4.1 pH of API-Containing Formulations

The pH values of ibuprofen-containing suspensions were determined for six selected suspending agents at two different concentrations (0.5% and 1.0%). Sodium benzoate was incorporated as a preservative and sodium citrate served as the buffering agent to maintain pH stability. The control formulation contained no suspending agent. The results are presented in Table 3.14

Table 3.14. PH of API-Containing Formulations

Formulation	Concentrations (%)	PH

Controlled (no suspending agent)		4.15
Carbopol	0.5	4.75
	1.0	4.46
CMEC	0.5	5.91
	1.0	5.95
HPMC	0.5	5.89
	1.0	5.89
MC	0.5	5.90
	1.0	5.91
Sodium alginate	0.5	5.87
	1.0	5.87
NaCMC	0.5	5.88
	1.0	5.88

The pH values of all ibuprofen-containing suspensions ranged between 4.15 and 5.95, which fall within the acceptable pH range (4–7) for oral formulations (Aulton & Taylor, 2018). This indicates that all formulations are chemically stable and physiologically compatible for oral administration, minimizing the risk of mucosal irritation or degradation of the active pharmaceutical ingredient (API).

The control formulation, which lacked a suspending agent, had the lowest pH (4.15**).** This slightly acidic value can be attributed to the intrinsic acidity of ibuprofen, a weak acid (pKa ≈ 4.9), and the buffering action of sodium citrate. The inclusion of suspending agents significantly modified the microenvironmental pH due to the presence of functional groups on the polymer chains that interact with hydrogen ions in the medium (Martin *et al.,* 2021).

Among the suspending agents, CMEC (Carboxymethyl Ethyl Cellulose**)** exhibited the highest pH values (5.91–5.95**),** suggesting its weakly basic character, possibly due to the ethoxy and carboxymethyl substituents that partially neutralize the acidic medium. Similarly, HPMC, MC, NaCMC, and Sodium Alginate formulations maintained stable pH values between 5.87 and 5.91**,** indicating excellent buffering compatibility and absence of acidic or alkaline drift.

Carbopol, however, produced a slightly lower pH (4.46–4.75) relative to other formulations. Carbopol is known to be a polyacrylic acid polymer, which can slightly lower formulation pH due to the presence of free carboxylic acid groups (Rowe *et al.,* 2009). Nevertheless, this pH range remains within acceptable limits for ibuprofen suspensions and does not compromise drug stability or patient safety.

Overall, the inclusion of sodium citrate as a buffering agent ensured that pH values remained within a narrow and controlled range, reducing the likelihood of hydrolytic degradation of ibuprofen. The results indicate that cellulose-based polymers (HPMC, MC, NaCMC, and CMEC**)** provided the most consistent and neutral pH values, reflecting their **excellent** buffering and stabilizing capabilities in the presence of ibuprofen and preservatives.

The study revealed that all six suspending agents maintained pH values suitable for oral ibuprofen suspensions. The cellulose derivatives (HPMC, MC, NaCMC, and CMEC) exhibited superior pH stability compared to Carbopol, which slightly acidified the formulation. CMEC produced the most neutral pH, while Carbopol produced the lowest. The incorporation of sodium citrate effectively buffered all formulations, supporting the overall chemical stability and compatibility of ibuprofen with the selected excipients.

3.4.2. Viscosity of API-Containing Formulations

The viscosity of ibuprofen suspensions containing different suspending agents was determined using a Brookfield viscometer with spindle L3 at 60 rpm. Sodium benzoate and sodium citrate were incorporated as preservative and buffer respectively, while the control formulation contained no suspending agent. The viscosity results for each formulation at 0.5% and 1.0% concentrations are presented in Table 3.15.

Table 3.15. Viscosity of API-Containing formulations

Formulation	Concentrations (%)	Viscosity (mPa•s)

Controlled (no suspending agent)		3.40
Carbopol	0.5	3.68
	1.0	4.82
CMEC	0.5	3.79
	1.0	3.92
HPMC	0.5	3.97
	1.0	4.38
MC	0.5	3.73
	1.0	3.93
Sodium alginate	0.5	2.91
	1.0	2.91
NaCMC	0.5	3.36
	1.0	5.15

The viscosity of ibuprofen suspensions is a crucial rheological property that influences both physical stability and ease of redispersion**.** The viscosity values obtained ranged from 2.91 to

5.15 mPa·s**,** indicating moderate flow properties suitable for oral suspensions (Aulton & Taylor, 2018).

The control sample without a suspending agent exhibited the lowest viscosity (3.40 mPa·s)**,** which is expected since the absence of a structured polymeric network leads to a less resistant flow and faster sedimentation. Incorporation of suspending agents increased the viscosity due to the formation of three-dimensional polymeric networks that entrapped water and increased internal resistance to flow (Martin *et al.,* 2021).

Among the formulations tested, NaCMC (1.0%) produced the highest viscosity (5.15 mPa·s)**,** demonstrating its excellent hydration and thickening properties. NaCMC is a hydrophilic cellulose derivative that forms highly viscous gels upon hydration, enhancing suspension stability by reducing sedimentation rate.

Carbopol (1.0%) **and** HPMC (1.0%) also showed appreciable viscosity increases (4.82 mPa·s and 4.38 mPa·s respectively), suggesting good thickening capacity and stable flow characteristics. The increase from 0.5% to 1.0% concentration in both cases indicates a direct relationship between polymer concentration and viscosity, which is consistent with polymer rheological behavior (Rowe *et al.,* 2009).

CMEC and MC exhibited moderate viscosities (3.73–3.93 mPa·s), suggesting that although they contribute to suspension stability, their thickening ability is slightly less pronounced compared to NaCMC and Carbopol. In contrast, Sodium Alginate produced the lowest viscosity values (2.91 mPa·s at both concentrations)**,** possibly due to its weaker hydration and gel strength in the acidic environment of ibuprofen suspension, which may have hindered full polymer expansion.

The overall trend observed follows the order: NaCMC > Carbopol > HPMC > CMEC ≈ MC > Sodium Alginate > Control.

This pattern highlights that cellulose derivatives, particularly NaCMC, are effective in producing desirable viscosity for ibuprofen suspensions, promoting uniformity and redispersibility without compromising pourability.

Viscosity measurements revealed that the presence and concentration of suspending agents significantly influenced the rheological behavior of ibuprofen suspensions. NaCMC demonstrated the highest viscosity and best thickening ability**,** followed by Carbopol and HPMC, while Sodium Alginate had the lowest. All formulations, however, maintained viscosity values within acceptable limits for oral suspensions, ensuring good pourability and physical stability.

3.4.3. Sedimentation Rate of API-Containing Formulations

The sedimentation behavior of ibuprofen suspensions formulated with different suspending agents was observed over a **7-day period**. The sedimentation volume was recorded daily to determine the rate of settling and stability of the suspensions. Table 3.15 presents the sedimentation volume data for both concentrations (0.5% and 1.0%) of each suspending agent, alongside the control sample which contained no suspending agent.

Table 3.16 sedimentation volume profile of api containing formulations at varying concentrations

Suspending Agent	**Conc. (%)**	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**	**Day 7**
Controlled (no suspending agent)	0	0.085	0.085	0.085	0.085	0.085	0.085	0.085
Carbopol	0.5	0.652	0.593	0.565	0.565	0.551	0.551	0.551
	1.0	0.920	0.912	0.901	0.887	0.854	0.854	0.755
CMEC	0.5	0.087	0.087	0.087	0.087	0.087	0.087	0.087
	1.0	0.102	0.085	0.085	0.085	0.085	0.085	0.085
HPMC	0.5	0.086	0.086	0.086	0.086	0.086	0.086	0.086
	1.0	0.087	0.087	0.087	0.087	0.087	0.087	0.087
MC	0.5	0.086	0.086	0.086	0.086	0.086	0.086	0.086
	1.0	0.086	0.086	0.086	0.086	0.086	0.086	0.086
Sodium alginate	0.5	0.087	0.087	0.087	0.087	0.087	0.087	0.087
	1.0	0.088	0.088	0.088	0.088	0.088	0.088	0.088
NaCMC	0.5	0.182	0.091	0.087	0.087	0.087	0.087	0.087
	1.0	0.638	0.591	0.520	0.496	0.468	0.422	0.408

Sedimentation volume (often denoted as F = Hu/Ho, where Hu is the ultimate height of the sediment and Ho is the initial height) is a key indicator of suspension stability, reflecting the ability of suspending agents to prevent particle settling under gravity

The sedimentation test evaluated the physical stability of ibuprofen suspensions over seven days, providing insight into the influence of suspending agent type and concentration on sedimentation behaviour. In the control formulation (without a suspending agent), rapid and complete sedimentation occurred within the first 24 hours, indicating poor stability and the necessity for a viscosity-imparting agent.

Among the formulations tested, Carbopol 1.0% and NaCMC 1.0% displayed the highest sedimentation volumes and maintained almost complete suspension throughout the observation period. However, both exhibited **a** gel-like consistency, resulting in minimal flow and poor pourability. While the near absence of sedimentation suggests strong particle immobilisation, the semi-solid texture of these systems is undesirable for an oral suspension since it impairs ease of redispersion and accurate dosing.

In contrast, Carbopol 0.5% and NaCMC 0.5% produced suspensions that were free-flowing yet stable**,** with sedimentation occurring slowly and uniformly. These formulations demonstrated an optimal balance between viscosity and fluidity — sufficient to retard particle settling but not so high as to form a gel matrix. Similar observations were made with HPMC, MC**,** CMEC**,** and sodium alginate, all of which exhibited relatively constant sedimentation volumes across the seven-day period, confirming their effectiveness in maintaining suspension homogeneity.

A stable suspension is expected to sediment slowly without forming a compact cake, and it should redisperse easily upon gentle shaking. The results indicate that the 0.5% polymer concentrations met these criteria most effectively. Excessive viscosity, as observed in the 1.0% Carbopol and NaCMC systems, hindered fluid flow and could complicate patient administration. Therefore, moderate concentrations of hydrophilic polymers are more desirable for achieving stable and user-acceptable ibuprofen suspensions.

Overall, the sedimentation results affirm that suspending agents significantly enhance the physical stability of pharmaceutical suspensions. However, optimal performance depends not only on the type of polymer but also on its concentration and rheological behaviour. Based on the present findings, Carbopol 0.5% and NaCMC 0.5**%** demonstrated the most satisfactory sedimentation profiles, combining stability with ease of redispersion and pourability.

CHAPTER FOUR

CONCLUSION

From the pH evaluation, all formulations were within the acceptable range for oral pharmaceutical preparations (approximately pH 4–7), indicating compatibility with ibuprofen and stability under mild acidic to near-neutral conditions. The slight pH differences observed among agents such as Carbopol, HPMC, NaCMC, and sodium alginate reflected their intrinsic ionic characteristics and buffering interactions with the formulation medium. Importantly, none of the suspending agents showed any drastic pH variation that could compromise formulation stability or drug solubility.

Viscosity analysis revealed that polymer concentration had a direct influence on the rheological behaviour of the formulations. As expected, viscosity increased with polymer concentration; however, excessively high viscosity—as observed with 1.0% Carbopol and NaCMC—led to gel-like systems with limited pourability and poor flow. In contrast, 0.5% concentrations of these agents produced smooth, free-flowing suspensions with sufficient viscosity to maintain particle uniformity without impairing flow properties. This balance is critical for patient acceptability and accurate dosing.

Sedimentation studies further supported these findings. The control formulation (without any suspending agent) showed rapid sedimentation and poor redispersibility, demonstrating the necessity of a suspending agent. Among the agents tested, Carbopol and NaCMC at 1.0% prevented sedimentation almost entirely due to their high viscosity but formed semi-solid gels, which are undesirable for oral use. Conversely, their 0.5% formulations, as well as suspensions containing HPMC, MC, CMEC, and sodium alginate, exhibited slow, uniform sedimentation with easy redispersion upon shaking an indication of optimal suspension stability.

Overall, the study confirmed that while all the tested polymers function as effective suspending agents to varying degrees, their efficiency is concentration-dependent. The most satisfactory formulations were obtained using Carbopol 0.5% and NaCMC 0.5%, which achieved an ideal balance between stability, viscosity, and pourability. Therefore, these two agents can be considered the most suitable suspending agents among those studied for the preparation of stable and patient-friendly ibuprofen oral suspensions.

In conclusion, this research demonstrates that the choice and concentration of a suspending agent profoundly influence the physical and rheological stability of pharmaceutical suspensions. An optimal formulation requires a compromise between high stability (slow sedimentation) and acceptable viscosity (good pourability and redispersion). Future studies may extend this work by exploring combinations of polymers or incorporating additional excipients to further enhance suspension performance and long-term stability.

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APPENDIX I

Table 1: Density Of Suspending Agent Formulations

SUSPENDING AGENT	CONCENTRATION (%)	DENSITY (g/ml)
Carbopol	0.5	0.996
	1.0	0.998
	1.5	1.000
	2.0	1.001
Chitosan	0.5	0.986
	1.0	0.992
	1.5	0.983
	2.0	0.985
CMEC	0.5	0.998
	1.0	1.000
	1.5	1.002
	2.0	1.003
Eudragit-L100	1.0	0.808
	2.0	0.815
	5.0	0.826
	7.5	0.833
HEC	0.5	0.976
	1.0	0.985
	1.5	0.988
	2.0	0.995
HPMC	0.5	0.998
	1.2	1.000
	2.6	1.002
	3.0	1.004
	9.0	1.022
MC	0.5	0.997
	1.0	1.000
	1.5	1.002
	2.0	1.009
Sodium Alginate	0.5	0.998
	2.7	1.006
	5.0	1.018
	10.0	1.242
NaCMC	0.5	0.999
	1.0	1.001
	1.5	1.002
	2.0	1.004
PVP	0.5	0.997
	1.0	1.001
	1.5	1.002
	2.0	1.004

Table 2: Density Of Api-Containing Formulations

FORMULATION	CONCENTRATIONS (%)	Density

Controlled (no suspending agent)		1.000
Carbopol	0.5	0.972
	1.0	1.000
CMEC	0.5	1.005
	1.0	1.003
HPMC	0.5	1.006
	1.0	1.005
MC	0.5	1.002
	1.0	0.997
Sodium alginate	0.5	1.004
	1.0	1.004
NaCMC	0.5	0.998
	1.0	0.997

APPENDIX II


HI 2215 pH/ORP Meter
HANNA instruments
CAL
CFM GLP
▲°C
▼°C
SETUP
RANGE
LOG CLR
RCL
250ml


264 300 416
01:15
NDJ-5S
VISCOMETER
Reset
Print Timing
Run
Spindle
Speed