EVALUATION OF SOME PROPERTIES OF ALOE VERA GEL AS A POTENTIAL PULP MUMMIFYING AGENT

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NOVEMBER, 2025

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A RESEARCH WORK SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE AWARD OF THE DOCTOR OF PHARMACY DEGREE BY THE FACULTY OF PHARMACY UNIVERSITY OF BENIN

NOVEMBER, 2025.

CERTIFICATION

This is to certify that this work was carried out by ELIZABETH OSASERE OWIE in the Department of Pharmaceutical Technology and Pharmaceutics, Faculty of Pharmacy, University of Benin, Benin city, Nigeria.

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DEDICATION

This work is dedicated to God Almighty.

ACKNOWLEDGEMENTS

My unreserved and profound gratitude goes to God Almighty, the greatest and most important personality in my journey. Also, my lovely mother for the hard sacrifices and her encouragement that saw me through to the completion of this work and throughout my journey in Pharmacy School, University of Benin.

I am grateful to my supervisor, Prof. Matthew I. Arhewoh, for his constructive corrections, sacrifices, enriched ideas, support and unwavering interest in this work, which was a great source of motivation.

My heart is full of love for my wonderful family for their loving care and support throughout my journey in Pharmacy school. My loving mother and my amazing siblings, Iyobosa Owie, Efe Owie, Odion owie, Joy owie, Osaretin Owie and Igbinosa Owie, your belief in me and endless display of love and support have been my greatest source of strength. My heart is filled with profound appreciation for each of you.

I am deeply grateful to my incredible friends, Ebere Nwonu, Ayomide Irekhore, Aniebiet Ikot, Martha Ogomini, Blessing Umukoro and Egah Lucky Oseghale. Your unwavering support and companionship have been a beacon of light on this journey. Words cannot express the depth of my gratitude for your genuine friendship. I cherish each of you immensely!

Finally, my warm appreciation goes to all my colleagues and classmates, especially to my project partners for their support and co-operation as we navigated our way from start to finish of the project work.

ABSTRACT

Background: Aloe vera gel, like other natural products, is prone to microbial contamination hence highlighting the need for effective stabilization to enhance its shelf life. This study Evaluate the stability of Aloe vera gel as a potential pulp mummifying agent and also investigates its antimicrobial activity against oral pathogen.

Method: Fresh Aloe vera leaves (105.84 g) were harvested, thoroughly washed with distilled water, and filleted to remove the outer rind. The inner mucilaginous gel was scooped into a beaker, homogenized, and filtered to obtain 60 ml of clear *Aloe vera* sap. This extract was incorporated into different gel bases prepared using varying concentrations of Carbopol 990, Sodium Carboxymethyl cellulose (Na-CMC), Hydroxypropyl methylcellulose (HPMC), and Gelatin. Calculated amounts of Tween 80, Vitamin E, Methyl paraben, and Propyl paraben were added. The Carbopol-based gels were neutralized with Triethanolamine to a pH of 6–7 to achieve optimal consistency. All formulations were evaluated for physicochemical properties including pH, viscosity, density for a period of 8 weeks and antimicrobial evaluation was carried out against *Streptococcus mutans and Lactobacillus acidophilus.* The gels were stored for two months, and the physiochemical parameters were re-evaluated after 4 and 8 weeks; variations over time were an index of their stability

Results: pH values of the various formulation ranged between 3.69 ± 0.00 and 7.83 ± 0.00, with most formulations within the physiological range of 5.5–8.0. Carbopol gels showed excellent pH stability, HPMC formulations became slightly more acidic over time, while Na-CMC and Gelatin gels exhibited an alkaline change over time.

Viscosity values ranged from 4.38 ± 0.01 to 17.10 ± 0.14 mPa·s. Carbopol gels retained consistency, HPMC gels demonstrated a slight increase, whereas Na-CMC and Gelatin formulations demonstrated viscosity loss during storage.

The Specific gravity ranged from 0.9984 to 1.0217 g/ml, indicating good physical uniformity across all formulations. The Antimicrobial testing revealed no inhibitory zones for Aloe vera gel or sap against the tested organisms, while formocresol showed a 55 mm inhibition zone.

Conclusion: Carbopol-based formulations exhibited superior stability in both pH and viscosity, making them the most suitable gelling agents for Aloe vera dental gels. Although the formulations showed no antimicrobial activity, their favorable physicochemical properties indicate potential for dental therapeutic applications. Further long-term stability studies are recommended.

TABLE OF CONTENT

COVER PAGE.....1
TITLE PAGE.....2
CERTIFICATION.....3
DEDICATION.....4
ACKNOWLEDGEMENTS.....5
ABSTRACT.....6
TABLE OF CONTENT……7
CHAPTER ONE.....1
1.1 Introduction.....1
1.1.1 An overview of pulp mummification.....1
1.2 Pulp Mummifying Agents:.....2
1.3 Statement of the Problem.....3
1.4. Aloe vera: A Natural Alternative for Pulp Mummification.....3
1.5. Advantages of stabilizing Aloe vera gel.....5
1.6 Gels.....5
1.6.1 Characteristics of gels.....6
1.6.2. Advantages of a gel.....6
1.6.3. Gelling agents.....7
1.7 Preservatives.....8
1.7.1 Properties of an ideal preservative.....8
1.7.2 Classification of preservatives.....9
1.8. Overview of the antimicrobial activity of Aloe vera.....10
1.9. Measure to check the stability of gels.....11
1.10. Alternative Plant-Based Pulp Mummification Agents.....12
1.11. Aim and Objectives.....13
CHAPTER TWO.....15
2.1. Materials.....15
2.2. Method:.....15
2.2.1. Extraction of Aloe vera.....15
2.2.2. Preparation of the gel base (Carbopol 990).....15
2.2.3. Preparation of the gel base (Na-CMC and HPMC).....16
2.2.4. Preparation of the gel base (Gelatin).....16
2.2.5. Evaluation of gel.....16
2.3. Statistical Analysis:.....18
CHAPTER THREE.....20
3.1. pH:.....20

3.2. Viscosity (mPa.s):..... 22
Figure 1: Time dependent change in the Viscosity of Carbapol across different concentrations... 24
Figure 2: Time dependent change in the Viscosity of HPMC across different concentrations.. 25
Figure 3: Time dependent change in the Viscosity of CMC across different concentrations.....26
Figure 4: Time dependent change in the Viscosity of Gelatin across different concentrations..27
3.3 Specific gravity (g/ml):.....29
3.4. Antimicrobial assessment:.....31
CHAPTER FOUR.....34
4.1. Conclusion..... 34
4.2. Recommendations.....34
REFERENCES.....36
APPENDIX.....43
Appendix 1: CMC Formulation (A7- A8)..... 43
Appendix 2: Carbopol Formulation (A1 - A3)..... 44
Appendix 3: HPMC Formulations (A4- A5)..... 45
Appendix 4: Gelatin Formulations (A11- A12).....46
Appendix 5:.....47

LIST OF TABLES

Table 2.1: Formula for the Preparation of the Various Batches of Aloe vera Gel 19

Table 3.1: pH Values of Aloe vera Dental Gel Formulation at Different Storage Periods 20

Table 3.2: Density Values of Aloe vera Dental Gels Formulation at Different Storage Periods. 30

Table 3.3: Zone of Inhibition(mm) of Aloe vera Gel, Sap And Formocresol Against Selected Oral Pathogens 33

LIST OF FIGURES

Figure 1: Time dependent change in the Viscosity of Carbapol across different concentrations 24

Figure 2: Time dependent change in the Viscosity of HPMC across different concentrations 25

Figure 3: Time dependent change in the Viscosity of CMC across different concentrations 26

Figure 4: Time dependent change in the Viscosity of Gelatin across different concentrations 27

CHAPTER ONE

1.1 Introduction

1.1.1 An overview of pulp mummification

The dental pulp is a connective soft tissue which consists of odontoblasts, immune cells , fibroblasts and vascular components.The pulp is significant as it plays a role in tooth nutrition, defense and development. It is classified as coronal pulp when located within the crown and radicular pulp when located between the cervix of the tooth to its apex. When exposed to microbial invasion or trauma, the pulp can become irritated and inflamed, leading to reversible or permanent pulpitis or necrosis (Ghannam *et al.,* 2023). In order to preserve tooth vitality, procedures such as pulpotomy is employed, which involves the removal of the inflamed coronal pulp while maintaining the vitality of the radicular pulp (Subramanyam and Somasundaram, 2020).

In endodontics, pulp mummification is significant as it renders the pulp inactive to alleviate pain and maintain the integrity of dental pulp during dental procedures. It is carried out using suitable mummifying agents which acts by removing moisture and inducing hardening of the pulp and root canal (Reshmi and Jayalakshmi, 2020). Examples of such agents include formocresol (FC), ferric sulphate (FS), sodium hypochlorite (SH), calcium hydroxide (CH), formaldehyde and cresol. However the use of FC has raised concern as it is reported from previous studies to be cytotoxic, mutagenic, and carcinogenic (Igna, 2021). Thus there is an increase in demand to explore safer, biocompatible and environmentally friendly alternatives. Natural products such as Aloe vera gel have gained increased awareness due to their accessibility, biocompatibility and minimal side effects. Aloe vera (*Barbadensis miller*) is a well known medicinal plant renowned for its antimicrobial, anti-inflammatory, antioxidant, antibacterial, antifungal and wound healing properties has emerged as a potential candidate for pulp mummification (Subramanyam and Somasundaram, 2020). The gels extracted from Aloe vera leaves have been shown to inhibit

microbial growth and promote dehydration as it contains bioactive components such as polysaccharide, enzymes, phenolic compounds and anthraquinones (Gupta *et al*, 2010). However, as with other natural formulations Aloe vera gel is prone to microbial contamination due to their high water content and organic composition. In order to alleviate this, gelling agents, preservatives and neutralizers are incorporated into the formulation.

This study involves the formulation and stability evaluation of Aloe vera gel as a potential pulp mummifying agent.

1.2 Pulp Mummifying Agents:

I. Iodoform: This is a yellow crystalline solid from the family of organic halogen compounds. It is used as an antiseptic in certain preparations. This property is due to the ability to liberate iodine slowly upon decomposition. It can be used with tannic acid, glycerine, phenol, eugenol, cinnamon in pulp Mummification (Reshmi and Jayalakshmi, 2020).

II. Paraform: This is a polymer of formaldehyde. They are used for intracanal dressing and also used to blunt pains in sensitive dentin. It can be mixed with mastic zinc phosphate (cement), gutta percha and any other temporary fillings. It is not to be applied in tooth pulp or irritant teeth (Reshmi and Jayalakshmi, 2020).

III. Formaldehyde: this is a natural constituent of the human cell that plays a role in cellular processes. Several researchers have debated on the connection between formaldehyde and cancer in humans. Further more studies have shown that it is only a course for concern at high concentration (Reshmi and Jayalakshmi, 2020).

IV. Cresol: This is a phenolic compound called hydroxy toluene. They have a melting point not far from room temperature and can be solid or liquid depending on the temperature. They oxidize slowly in the presence of air (Reshmi and Jayalakshmi, 2020).

V. Formocresol: Formocresol is a combination of formaldehyde and cresol, and a potent antibacterial agent and is recognized for its use in pediatric dentistry for pulpotomy procedures. It acts through the aldehyde group of the formaldehyde, which inhibits the action of inflammatory enzymes preventing further enzymatic degradation. The other component, Cresol, enhances tissue fixation and damages cellular structures (Issrani *et al*., 2022).

1.3 Statement of the Problem

The use of formocresol, despite its effectiveness, has been linked to potential systemic toxicity; it has been classified as a potential carcinogen by the International Agency for Research on Cancer. It has other adverse effects such as degeneration, necrosis, inflammation and undesirable tissue changes in the pulp or periapical tissues (Abirami *et al.,* 2020). Studies indicate that formaldehyde which is a component of formocresol can cause tissue irritation, systemic toxicity and immunologic effect hence it is cytotoxic (Issrani *et al*., 2022). This may lead dentists to consider alternative treatments or more closely monitor patients who have undergone Formocresol pulpotomies and these highlight the need for exploration of natural alternatives that can achieve similar superior clinical outcomes while minimizing risk. However, as with other natural products Aloe vera is prone to microbial contamination due to their high water content and organic composition. Also Post-harvest, Aloe vera leaves begin to lose biological activity within 36 hours thus the need for stabilization (Ahlawat and Khatkar, 2011). Different stabilizing or gelling agents, preservatives and neutralizers are incorporated to increase the shelflife of the formulation.

1.4. Aloe vera: A Natural Alternative for Pulp Mummification

Aloe vera (*Aloe barbadensis* Miller) is a succulent plant belonging to the Liliaceae family. It is known for its antimicrobial (Matei *et al.,* 2025), biodegradability, biocompatibility, low toxicity properties (Rahman *et al.*, 2017) and It has gained popularity in food and cosmetics as acemannan

have been recorded to have beneficial effects (López *et al.*, 2022). They are found growing in arid climatic areas like the desert and the tropics. In ancient times it has been used in countries such as Egypt (known as the plant of immortality), Rome and China (known as the elixir of youth) as medicine. The plant contains bioactive compounds such as:

I. Anthraquinones: These are phenolic compounds that Provide analgesic and antibacterial activity (Nandal and Bhardwaj, 2012). Examples of anthraquinone are; Barbaloin (aloin A and B), ester of cinnamic acid, Aloe-emodin, anthranol, and emodin (Ahlawat and Khatkar, 2011).
II. Acemannan: increases wound healing, Antineoplastic and immunomodulatory activity (Ahlawat and Khatkar, 2011).
III. Saponins: antimicrobial activity (Nandal and Bhardwaj, 2012).
IV. Hormones such as Bradykinase which has an anti-inflammatory effect (Ahlawat and Khatkar, 2011), Auxin and gibberellin which promote wound healing and have anti-inflammatory properties (Nandal and Bhardwaj,2012).
V. Vitamins such as vitamin B1, B2, B6, C, E and folic acid (B9) (Ahlawat and Khatkar, 2011).

Aloe vera carry out preservative effect on dental pulp via its antimicrobial, Stimulation of Healing and anti inflammatory effects. It gel inhibit bacteria growth, preventing pulpal necrosis and damage as it contains bioactive components such as the anthraquinones. (Nandal and Bhardwaj, 2012; Jain *et al.,* 2016). In addition, Aloe vera demonstrate notable anti-inflammatory and analgesic actions by inhibiting the production of prostaglandins E2 on the arachidonic acid pathway via cyclooxygenase enzyme, thus preventing the Inflammatory process (Vázquez *et al.*, 1996; Matei *et al.,* 2025). The plant also support tissue preservation and healing, largely owing to

Glucomannan, a polysaccharide that stimulate and support fibroblast development and boost collagen synthesis to promote wound healing (Indira *et al*., 2025). Another study verified that Aloe vera enhances wound contraction and collagen synthesis as it contains mannose-6-phosphate that is Known to promote collagen synthesis and fibroblast activity (Subramanian *et al* ., 2006).

1.5. Advantages of stabilizing Aloe vera gel

I. Stabilization helps to improve shelf life and consistency of Aloe vera gel
II. It enhances Antimicrobial, anti-inflammatory, and wound healing effects on dental tissues.
III. It helps to maintain Antimicrobial efficacy of Aloe vera gel
IV. It provide gentler and biocompatible formulation for sensitive dental tissues

1.6 Gels

Wikipedia, (2014) defined a Gel as a semi-solid whose qualities can range from soft and weak to strong and durable. Gels are characterized as a substantially dilute cross-linked system that exhibits no flow when in the steady state, yet the liquid phase may still diffuse through this system. The United States Pharmacopeial Convention (2009) defines gels as semisolid systems that comprise either suspensions of small inorganic particles or large organic molecules penetrated by a liquid. Gels with a network of small fragments are considered two-phase systems. In a two-phase system, if the dispersed phase comprises large particles, the gel mass is referred to as magma. Single-phase gels are made up of organic macromolecules that circulate uniformly throughout a liquid, leaving no visible boundaries between them and the liquid. Gels are widely used in pharmaceutical and cosmetics because of their ability to deliver drugs locally, transdermally, orally, and even ophthalmically (Rathod and Mehta, 2015).

1.6.1 Characteristics of gels

I. Swelling: This is the first stage of dissolution.Gel-solvent interactions take the role of gel-gel interactions as the solvent permeates the gel matrix. A certain amount of cross-linking in the gel matrix that inhibits complete breakdown typically causes limited swelling (Rathod and Mehta, 2015)

II. Ageing: This involves a delayed spontaneous aggregation by a colloidal system. Ageing gels cause the gelling agent to build a dense network over time (Rathod and Mehta, 2015).

III. Syneresis: This involves contraction of the gel upon standing and the expulsion of water or liquid at the surface of the gel. The relaxation of elastic strains created during the gel's setting has been linked to the contraction process. The release of these tensions results in less interstitial space for the solvent, which forces fluid expression (Rathod and Mehta, 2015).

1.6.2. Advantages of a gel

According to previous study by (Reshmi and Jayalakshmi, 2020;) the advantages of gels include:

I. It promotes a non-greasy and comfortable application.

II. It exhibits a strong force of adhesion to the application site

III. Active ingredient can be easily incorporated to the formulation

IV. It maintain stability and increase shelflife of the formulation

V. It can be applied evenly on the site of application

1.6.3. Gelling agents

Stabilizers also known as thickeners or gelling agents. They are stability enhancers added to food and pharmaceutical formulations.They improve the shelf life and prevent separation (Nguyen, 2025). They improve the consistency of gels. Common gelling agent include:

I. Gelatin: This is a light-amber to faintly yellow-colored, brittle and coarse solid powder. It is odorless and tasteless.This is used in various pharmaceutical formulations as a gelling agent, suspending agent and viscosity enhancer and binding agent (Rowe *et al*., 2009).

II. Carbopol: These are synthetic products of acrylic acid polymer that can be used in various formulations as a binding agent, stabilizing agents, controlled release agents and emulsifying agents. It is used in various formulations such as gels, lotions, ointments and paste. They form acidic dispersion in water and when neutralized, they form viscous gels. Neutralization is done by adding a base such as sodium hydroxide, sodium bicarbonate and inorganic amines such as triethanolamine. It should be noted that One gram of Carbapol is neutralized by approximately 1.5g of triethanolamine. The addition of an antioxidant is necessary as they become less viscous on exposure to ultraviolet light.minimized by the addition of a suitable antioxidant. They are stable at extreme temperatures below 104°c for up to 2 hours (Rowe *et al*., 2009)

III. Carboxymethylcellulose sodium(CMC): This is used in pharmaceutical preparation as it increases their viscosity. It is used as a stabilizing agent, coating agent, suspending agent, and disintegrant. Aqueous solutions are most stable and viscous between pH 7 and 9. If the pH drops below 2, precipitation can occur. Conversely, when the pH rises above 10, the solution's viscosity rapidly decreases (Rowe *et al.,* 2009)

IV. Hydroxypropyl methylcellulose (HPMC): It is also known as Hypomellose. It is a white, odorless and tasteless fibrous powder. This is widely used in oral , topical Nasal and ophthalmic preparation as a stabilizing, gelling, and binding agent, Bioadhesive material; controlled-release agent; dissolution enhancer; emulsifying agent; coating agent;extended-release agent; solubilizing agent; thickening and viscosity-increasing agent.

To form it into a gel using aqueous solution, it is appropriate to disperse Hypomellose in hot water of about 80-90 C while continuously stirring it. It should be noted that the heat source can after thorough dispersion into the hot water. sufficient cold water is added to make up to volume. creasing agent (Rowe *et al.,* 2009)

1.7 Preservatives

Preservatives are additives used in the prevention of microbial growth throughout the shelflife of a product. They are used in non sterile dosage forms to inhibit microbial growth and protect against bacteria that might be introduced during the course of production. Preservatives are frequently added to pharmaceutical and cosmetic products and serve the purpose of preventing bacteria growth that can occur from repeated withdrawal of individual doses from a multi dose container (Malik Al-Rubaye, 2022).

1.7.1 Properties of an ideal preservative

I. A good preservative should be effective at low concentrations against many different microbes.
II. To ensure it remains active during manufacturing, storage and use, It should be stable across a wide range of pH and temperature conditions.
III. The preservative must also be water-soluble at the required concentrations
IV. It is compatible with a variety of pharmaceuticals and inactive ingredients.
V. it should not possess noticeable odor, taste, or color.

1.7.2 Classification of preservatives

Preservatives are classified based on the mechanism of action, chemical class and based on sources.

I. Based on mechanism of action :

A. Antioxidants: These are substances that protect the active ingredients and other additives from oxidation, a process which is caused by exposure to light and oxygen. They function as "self-sacrificing" agents, which means that they get oxidized themselves to prevent other, more critical components from degrading. Common examples include Vitamin E (Nazemi *et al.,* 2017; Keen *et al.,* 2016), Vitamin C, butylated hydroxytoluene (BHT), and butylated hydroxyanisole (BHA) (Malik Al-Rubaye, 2022).

B. Sorbates/Chelating agents are agents that stabilize a drug by binding to metal ions that would otherwise cause it to break down. They form complexes with these ions, essentially neutralizing them and preventing them from degrading pharmaceutical products. Common examples include EDTA, polyphosphates, and citric acid (Malik Al-Rubaye, 2022).

II. Based on chemical class:

A. Organic acid: These include; Benzoic acid, Sodium benzoate and Sorbic acid

B. Esters of p-hydroxylbenzoic acid (*parabens)*: One example of this is methyl paraben. Methyl paraben is an odorless, white crystalline powder that is widely used as an antimicrobial preservative in cosmetic and pharmaceutical preparations. It has a broad spectrum of antimicrobial activities and is very effective against yeast and molds. It is used in oral solution and suspension at a concentration of 0.015-0.2 (Rowe *et al.*, 2009). Another example of this is Propyl paraben. It is also an odorless, tasteless and white crystalline power which is used alone or in combination with other paraben esters. It is widely used in pharmaceutical preparations as an antimicrobial preservative. Parabens are more active against yeast and mold than against bacteria but they are effective against gram positive and gram negative bacteria (Rowe *et al.*, 2009).

III. Based on sources

A. Natural preservatives: These are preservatives obtained from natural sources like plants and animals.examples include; honey, neem oil, salt etc (Malik Al-Rubaye, 2022).

B. Synthetized preservatives: These are preservatives synthesized in the laboratory. Examples include; sodium benzoates, sorbates, nitrites etc (Malik Al-Rubaye, 2022).

1.8. Overview of the antimicrobial activity of Aloe vera

Dental caries remains one of the most prevalent oral diseases and it is driven primarily by acidogenic bacteria such as *Streptococcus mutans* and *Lactobacillus acidophilus*. Interest for natural alternative agents for oral care has increased as they can offer safer and broad-spectrum antimicrobial activity. Aloe vera gel and extracts contain multiple bioactive components and has been evaluated in numerous in vitro studies for activity against common cariogenic organisms. Aloe vera has demonstrated promising antibacterial effects against both *S. mutans* and *Lactobacillus acidophhilus* across Various literatures.

In one study to reduce *S. mutans* contamination of tooth brush, dentifrice containing Aloe vera and propolis was compared with chlorhexidine and fluoride as control. They found significant reduction of *S. mutans* for Aloe vera and propolis dentifrice. But this did not differ significantly from the control (Bertolini *et al.,* 2012). Though the study demonstrated antimicrobial activity, the effect of Aloe vera alone was not isolated.

Another study compared the ethanolic extract of Aloe vera and propolis with 2% chlorhexidine against *S. mutans* and *L.acidophilu*s and found that Aloe vera exhibited bacteriostatic activity (not bactericidal) against the tested organism but with lesser potency as compared to chlorhexidine

(Mahabala *et al*., 2016). In the Evaluation of antibacterial potential of Aloe vera extracts against *Streptococcus mutans* and *Lactobacillus acidophilus* it was found that the ethanolic extract from the leave and gel of Aloe vera did not produce activity against *S mutans* but possess significant activity against *L.acidophilus* (Yavagal *et al.*, 2012).

In a more recent study, commercially available dentifrice and Aloe vera based products were evaluated against *S mutan*s. findings suggest that there was significant activity of Aloe vera but it had lesser potency compared to commercially available dentifrice (Tonguç-Altin *et al*., 2024).

1.9. Measure to check the stability of gels

To determine the stability of a gel, several key properties are measured. These include; pH, viscosity and specific gravity. These provide insight on the physical and chemical stability of gels over time.

I. pH: The pH of a gel plays a role in its stability as it affects the rate of release of a drug, its residence time as well as its physical properties. Gels vary depending on their intended use and composition for example carbomer based gel which are often used in topical and dental preparation requires neutralization with an alkali to achieve a desired pH. Oral formulations should ideally have a pH within the normal saliva range which falls between 5.5-8.0. Outside this range, formulation can negatively affect oral health and effectiveness of the product (Maslii *et al.,* 2020).

II. Viscosity: This gives information about the stability of pharmaceutical preparation in terms of its composition, bioavailability and rate of release of the drug. It is measured using a viscometer (Vilimi *et al*., 2024) studies have shown that an increase in the viscosity of the emulsion gel increases its stability (Oppermann *et al*., 2015; Lee, Wi *et al*., 2023),

increases its diffusion rate, reduction in color change and dental erosion (Torres *et al*., 2022)

III. specific gravity (SG): According to (Salsabila *et al.,* 2015) the formula for calculating the specific gravity is given in equation 1:

$$SG = \frac{M3 - M1}{M2 - M1}$$

Equation 1:1

where M_1 = Mass of the dry empty density bottle

M_2 = Mass of the bottle filled with gel

M_3 = Mass of the bottle filled with distilled water

1.10. Alternative Plant-Based Pulp Mummification Agents

Several natural substances have been explored for their potential in pulp mummification

I. Turmeric: Turmeric (*Curcuma longa*), renowned for its anti-inflammatory and antimicrobial properties, has been explored as a potential agent in dental procedures, particularly in pulpotomy treatments for primary teeth. Several studies have investigated the efficacy of turmeric as a pulpotomy medicament. An in vivo study evaluated the use of turmeric powder as a pulpotomy agent in primary teeth. The results indicated that turmeric powder demonstrated excellent clinical success, acceptable radiographic outcomes, and good survival rates, positioning it as a promising biocompatible material for pulpotomy procedures (Purohit *et al.,* 2017; Mashal *et al*., 2024). Another study assessed both turmeric gel and turmeric powder as pulpotomy medications. Both forms exhibited excellent clinical success, acceptable radiographic success, and favorable survival rates, suggesting their potential as viable alternatives in pulpotomy treatments.

II. *Allium sativum*: *Allium sativum,* commonly known as garlic, has been investigated for its potential use in dental procedures, particularly in pulpotomy treatments for permanent teeth. This is due to its antimicrobial, anti-inflammatory property. Several studies have evaluated the efficacy of *Allium sativum* oil as a pulpotomy medicament, one of such findings indicates that *Allium sativum* oil could serve as an effective alternative to formocresol, offering comparable antibacterial effects, and clinical outcomes (Mohammad *et al.,* 2015).

III. Neem (*Azadirachta indica*): It has Antibacterial, antifungal, and anti-inflammatory properties. These properties are as a result of Azadirachtin and nimbidin it contains. Neem has been explored for its potential in endodontic treatments due to its antimicrobial activity against oral pathogens hence it is a potential pulp mummifying agent (Lakshmi *et al.*, 2015).

1.11 Aim and Objectives

The aim of the study is to formulate Aloe vera gel as a Potential Pulp Mummifying agent.

The specific objectives are;

I. To formulate a stable Aloe vera gel using appropriate gelling agents and preservatives,

II. To evaluate the physicochemical stability parameters such as pH, viscosity, and specific gravity of the formulated gels,

III. To determine the antimicrobial potential of the Aloe vera gel against *Streptococcus mutans* and *Lactobacillus acidophilus.*

CHAPTER TWO

MATERIAL AND METHOD

2.1. Materials

Aloe vera plant harvested from Egah Farm, Iyoba college, Nigeria. Polysorbate 80 (as tween 80) obtained from PARK Scientific Limited, Northampton, UK. HPMC (Hydroxypropyl methyl cellulose) obtained from PARK Scientific Limited, Northampton, UK. Carbopol 990 (carbomer) obtained from the Product of Monomer Chemical Industrial Limited, India. Na-CMC (Sodium Carboxymethyl Cellulose) obtained from ANQUI Eagle Cellulose. Co., Limited, China. Methyl and propyl paraben (SALIGIN MP, Salicylates and Chemicals Pvt. Ltd., India),Vitamin E USP (Tocopheryl Acetate, Product of UK). Triethanolamine, Gelatin and Distilled water (Pyrex I.G Limited).

2.2. Method:

2.2.1. Extraction of Aloe vera Sap

Three years old Fresh Aloe vera leaves were harvested from Egah farm in the month of August. 105.84 g of the leaves were accurately weighed and washed thoroughly with distilled water. The outer rind was carefully removed with a sharp knife and the inner succulent sap was scooped out, blended and filtered into a beaker. 60ml of Fresh Aloe vera sap was obtained and stored in a refrigerator (Afza *et al.,* 2022).

2.2.2. Preparation of the gel base (Carbopol 990)

Carpobol 990 was carefully dispensed in hot distilled water and was continuously stirred using a magnetic stirrer until it swelled completely. Calculated amount of Triethanolamine was added to adjust the pH (Kamble *et al.*, 2023). Methyl and propyl parabens were dissolved in hot water, after which Vitamin E and Tween 80 was added to this preservative solution (Khan *et al*., 2013). The resulting mixture was incorporated into the previously prepared gel base (Kamble *et al.*, 2023).

Thereafter, 60 ml of Aloe vera was then added and stirred for 20 minutes to ensure uniformity. The final weight was made up to a 100 g with sufficient water (Khan *et al.,* 2013).

2.2.3. Preparation of the gel base (Na-CMC and HPMC)

The gelling agents (Na-CMC and HPMC) were carefully dispensed in distilled water. Na-CMC was continuously stirred using a stirrer until it swelled completely, while HPMC was left to hydrate (Kamble *et al.*, 2023; Majumder *et al* 2016). Methyl and propyl parabens were dissolved in hot water, after which Vitamin E and Tween 80 was added to this preservative solution (Khan *et al*., 2013). The resulting mixture was introduced into the previously prepared gel base (Kamble *et al.*, 2023). Thereafter, 60 ml of Aloe vera was then added and stirred for 20 minutes to ensure uniformity. The final weight was made up to a 100 g with sufficient water (Khan *et al.,* 2013).

2.2.4. Preparation of the gel base (Gelatin)

Gelatin was carefully dispensed in hot distilled water, stirred until dissolution and left to stand for about 15 minutes. Methyl and propyl parabens were dissolved in hot water, after which Vitamin E and Tween 80 was incorporated to this preservative solution (Khan *et al*., 2013). The resulting mixture was introduced into the previously prepared gel base (Kamble *et al.*, 2023). Thereafter, 60 ml of Aloe vera was then added and stirred for 20 minutes to ensure uniformity. The final weight was made up to a 100 g with sufficient water (Khan *et al.,* 2013).

2.2.5. Evaluation of gel

The gel was evaluated using the pH. Viscosity, specific gravity and Antimicrobial activities

I.pH:

A. flowing gels; the pH of the gels were measured using a digital pH meter by inserting the electrode directly into the gels. The pH was calibrated before use, using a buffer of 4.02 and 6.84. The average of the two readings measured were calculated (Khan *et al*., 2013).

B. Stiff gel: 1g of the gels were accurately weighed and dissolved in 100ml of distilled water. The pH was measured using a digital pH meter which was calibrated using a buffer of 4.02 and 6.84. The average of two readings measured were calculated (Khan *et al.,* 2013).

II. Viscosity: The viscosity of the various formulations were measured using the brookfield viscometer (NDJ 5S). The gels were rotated at 30 rotations per minute (rpm). At each speed, the average of two readings were calculated (Dantas *et al*., 2016).

III. Specific gravity (SG):

A 25 mL density bottle was used to measure the gel's specific gravity. First, the clean and empty bottle was weighed and recorded as W_1. After that, the bottle is filled with distilled water at 25 °C, capped and cleaned to get rid of any excess water on the bottle. The bottle with water was weighed and recorded as W_2. The bottle was drained and gels of the different gelling agents were added. Its weight was recorded as W_3 after it was capped and cleaned. The masses of the gel and water were computed as ($W_3 - W_1$) and ($W_2 - W_1$), respectively. The specific gravity was determined using EQUATION 2.1 below and the measurement was done in duplicate.

$$SG = \frac{W3 - W1}{W2 - W1}$$

EQUATION 2.1

IV. Antimicrobial Activity:

The antimicrobial properties were determined using the Agar well diffusion method. Culture of *Streptococcus mutans and lactobacillus acidophilus* were streaked on a plate of blood agar and MRS agar respectively. Five wells which measure 10mm were made with a 10mm sterile cork borer. 0.1 ml of the gels were pipetted into four of the individual wells. 0.1 ml of the control (positive control) were added to the fifth well on the individual plates.The plates were incubated

for 24-48 hours at a temperature of 37°C. The antibacterial activities were evaluated by the zone of inhibition.

2.3. Statistical Analysis:

The data collected were analyzed using descriptive statistics (mean ± standard deviation). Mean values were visually compared using bar graphs generated in Microsoft Excel

TABLE 2.1: Formula for the Preparation of the Various Batches of Aloe vera Gel

Batch code	Aloe vera sap (ml)	Carbopol (g)	HPMC (g)	CMC (g)	Gelatin (g)	Methyl-paraben (g)	Propyl-paraben (g)	Triethanolamine (ml)	Tween 80 (ml))	Vitamin E (ml)	Distilled Water to (ml)
A1	60	0.3	-	-	-	0.2	0.02	0.45	0.5	0.5	100
A2	60	0.5	-		-	0.2	0.02	0.75	0.5	0.5	100
A3	60	0.75	-	-	-	0.2	0.02	1.125	0.5	0.5	100
A4	60	-	0.5	-	-	0.2	0.02	-	0.50	0.5	100
A5	60	-	1	-	-	0.2	0.02	-	0.5	0.5	100
A6	60	-	1.5	-	-	0.2	0.02	-	0.5	0.5	100
A7	60	-	-	0.75	-	0.2	0.02	-	0.5	0.5	100
A8	60	-	-	1	-	0.2	0.02	-	0.5	0.5	100
A9	60	-	-	1.5	-	0.2	0.02	-	0.5	0.5	100
A10	60	-	-	-	5	0.2	0.02	-	0.5	0.5	100
A11	60	-	-	-	6	0.2	0.02	-	0.5	0.5	100
A12	60	-	-	-	7	0.2	0.02	-	0.5	0.5	100
A13	-	0.3	-	-	-	0.2	0.02	0.45	0.5	0.5	100
A14	-	-	0.5	-	-	0.2	0.02	-	0.5	0.5	100
A15	-	-	-	0.75	-	0.2	0.02	-	0.5	0.5	100
A16	-	-	-	-	5	0.2	0.02	-	0.5	0.5	100

HPMC= Hydroxylpropyl methylcellulose

CMC= Carboxylmethylcellulose

CHAPTER THREE

RESULTS AND DISCUSSION

3.1. pH:

The Evaluation of pH of Aloe vera dental gels Formulation ranges from 3.67-7.83 as shown in Table 3.1

Table 3.1: pH Values of Aloe vera Dental Gel Formulation at Different Storage Periods

Batch Code	Week 1	Week 4	Week 8
A1	7.065 ± 0.007	7.050 ± 0.003	7.620 ± 0.06
A2	6.365 ± 0.021	6.350 ± 0.014	6.400 ± 0.014
A3	6.765 ± 0.007	6.560 ± 0.000	6.715 ± 0.007
A4	4.625 ± 0.007	4.115 ± 0.021	4.105 ± 0.007
A5	4.500 ± 0.000	4.060 ± 0.000	3.690 ± 0.000
A6	4.515 ± 0.007	4.050 ± 0.014	3.715 ± 0.007
A7	4.475 ± 0.035	4.965 ± 0.007	7.685 ± 0.007
A8	5.480 ± 0.000	7.615 ± 0.021	7.830 ± 0.000
A9	5.625 ± 0.007	7.175 ± 0.021	7.615 ± 0.035
A10	5.010 ± 0.028	5.025 ± 0.007	7.135 ± 0.007
A11	4.990 ± 0.014	5.075 ± 0.007	5.020 ± 0.014
A12	5.160 ± 0.000	5.185 ± 0.007	7.450 ± 0.410
A13	5.940 ± 0.014	5.625 ± 0.049	5.580 ± 0.014
A14	6.365 ± 0.092	N/A	N/A
A15	8.090 ± 0.014	N/A	N/A
A16	5.885 ± 0.077	N/A	N/A

Note: Value of pH are expressed in Mean ± S.D (n =2)

The pH of Aloe vera dental gel formulations was evaluated at three storage periods (Week 1, Week 4, and Week 8) to evaluate their chemical stability and suitability for oral application. An ideal Pulp Mummifying agent should be near neutral pH or the pH should be within the normal range of the saliva (5.5-8.0) to avoid ineffectiveness, additional pulp irritation and negative effects from the formulation (Maslii *et al*., 2020). Most formulations fell within this acceptable range, with slight

variations observed over the eight-week storage period. These fluctuations reflect the effects of polymer type, concentration, and storage time on gel stability.

A1–A3 (Carbopol-Based Formulations) At Week 1, pH values ranged between 6.36 and 7.07 which was all within the acceptable range. Over time A1 increased slightly from 7.065 ± 0.007 to 7.620 ± 0.060, A2 remained stable (6.365 ± 0.021 - 6.400 ± 0.014) while A3 showed minimal change (6.765 ± 0.007 - 6.715 ± 0.007). Thus all Carbopol gels remained within the physiological pH range, with minor variations suggesting excellent pH stability. The slight alkaline drift observed in A1 could be due to neutralization during storage.

At week For Batch A4–A6 (HPMC-Based Formulations), the Initial pH values ranged from 4.50 ± 0.000 to 4.63 ± 0.007, which are slightly below the acceptable range. Over the 8-week period, a gradual decrease in pH was observed, with the lowest value in A5 (3.69 ± 0.00). This implies that all HPMC values became more acidic over time, dropping further below the physiological range. This decline suggests acidic degradation or an interaction between HPMC and *Aloe vera* components. Although the low SD values indicate consistent readings, the continuous pH drop implies chemical instability and limited buffering capacity. Hydroxypropyl methylcellulose (HPMC) is a chemically neutral polymer and typically maintains stability across pH 3–11 in simple systems (Rowe *et al.,* 2009; Vlad *et al.,* 2025). However, because HPMC has no intrinsic buffering capacity, the final pH of gel systems depends largely on added components. The lower pH of the Aloe-containing HPMC batches in comparison to the control suggests that the *Aloe vera* extract contributed to increased acidity within the gel matrix. Aloe vera gel contains organic acids, such as malic and citric acids, which can shift the pH downward when insufficiently neutralized. Hence the differences observed likely reflect the influence of Aloe vera constituents rather than polymer instability (Vlad *et al.*, 2025).

Na-CMC-based formulations (A7–A9) initially displayed mildly acidic pH (≈4.5–5.6) but shifted markedly toward alkaline values (≈7.6–7.8) by Week 8. The CMC control (A15) started strongly alkaline (8.09) which implies that Aloe vera 0R other additives reduced the inherent alkaline pH of Carboxymethyl cellulose sodium (Na-CMC). The observed alkaline drift in the test formulations may result from chemical changes in the polymer network. These findings underscore the need for rigorous pH control and buffering when formulating CMC-based Aloe vera gels.

Gelatin-based formulations started moderately acidic (5.0–5.2), with one batch (A11) remaining stable, while others (A10, A12) increased to alkaline pH (7.1–7.45) by Week 8. The gelatin control (A16) remained moderately acidic (5.88).

Gelatin-based Aloe vera gel formulations (A10–A12) showed distinct pH behaviour over the 8-week storage period when compared with their control sample (A16). All gelatin batches (A10–A12) were slightly more acidic (5.0-5.2) than the control A16 (5.9) at Week 1, indicating that the presence of Aloe vera extract influenced the pH moderately. All three batches show slight increases in pH at week 3 relative to Week 1 and this indicates moderate pH stabilization toward neutral levels. A10 and A12 show substantial upward pH drift into alkaline range, indicating instability or degradation of the gel matrix (7.1 – 7.45) at week 8, while A11 remained stable, maintaining near-initial pH (5.02), suggesting better buffering or higher stability. Importantly all gelatin formulations were not within the physiological acceptable range of oral formulations (5.5 - 8.0).

3.2. Viscosity (mPa.s):

The Evaluation of Viscosity of Aloe vera dental gels Formulation is represent by the bar graph below:

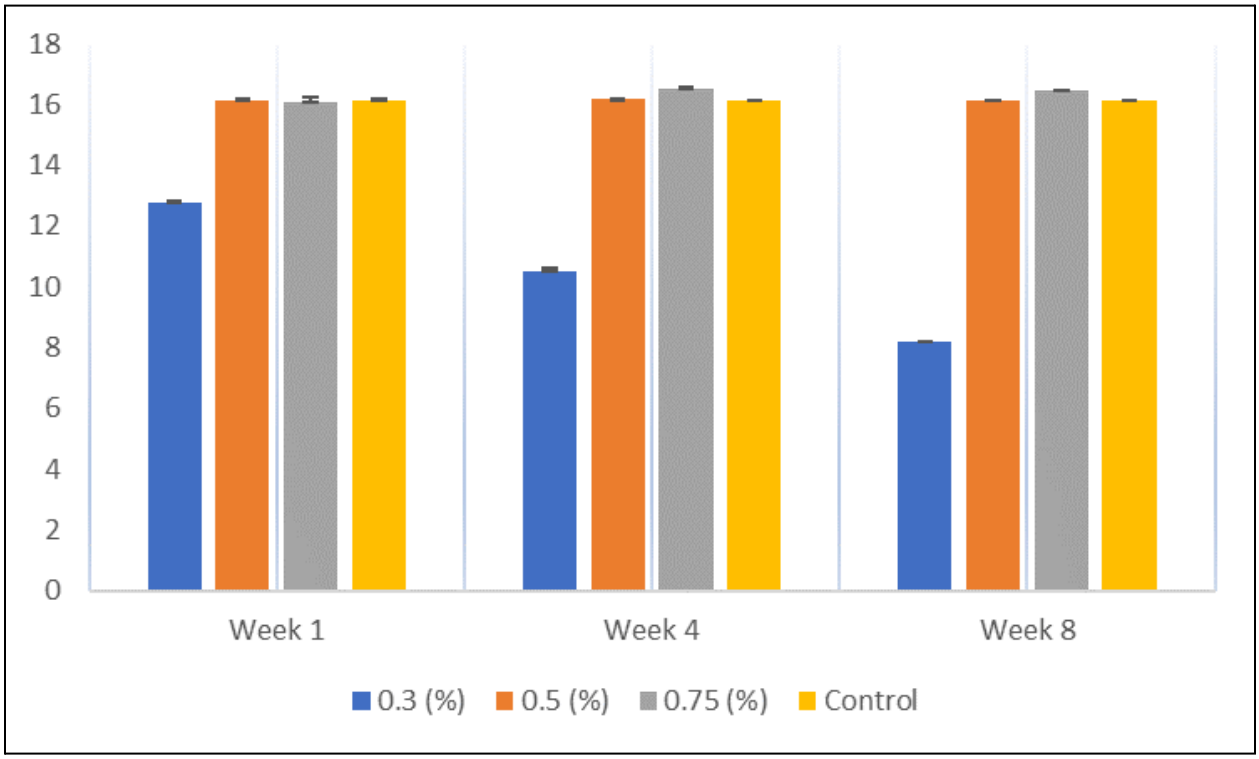

Figure 1: Time dependent change in the Viscosity of Carbapol across different concentrations

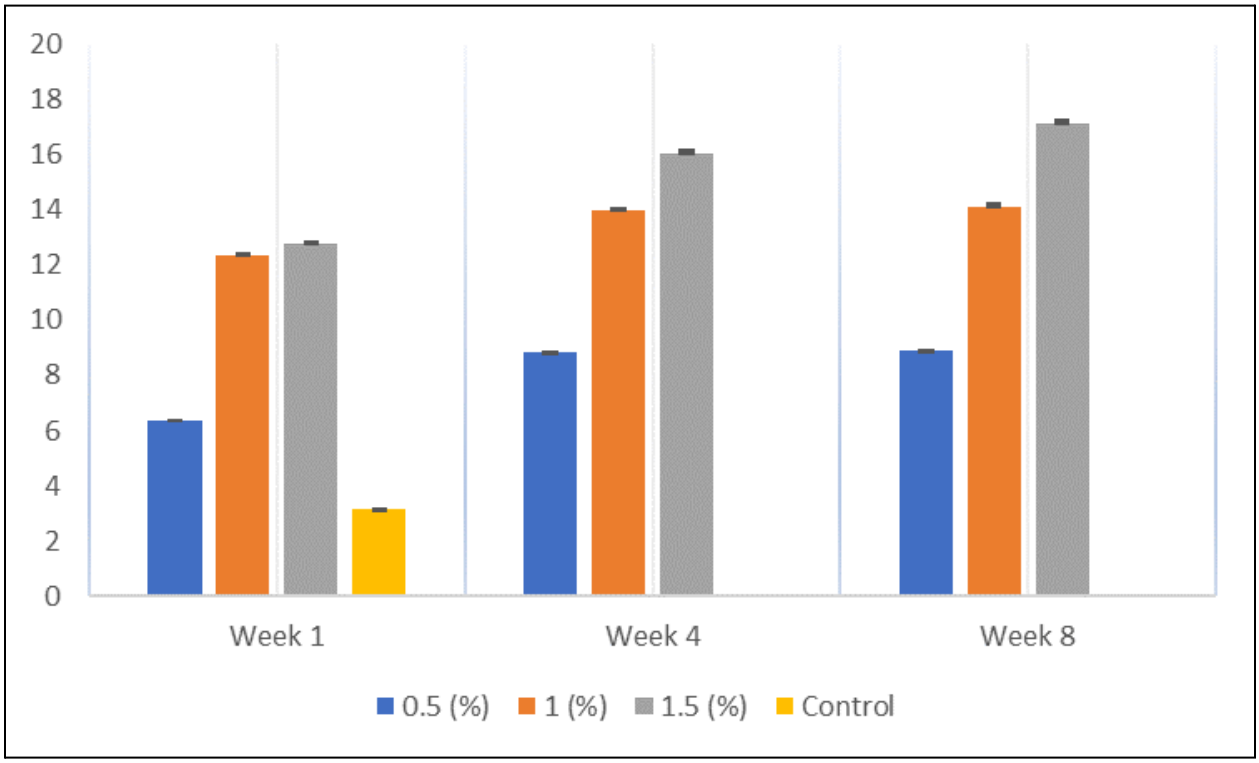

Figure 2: Time dependent change in the Viscosity of HPMC across different concentrations

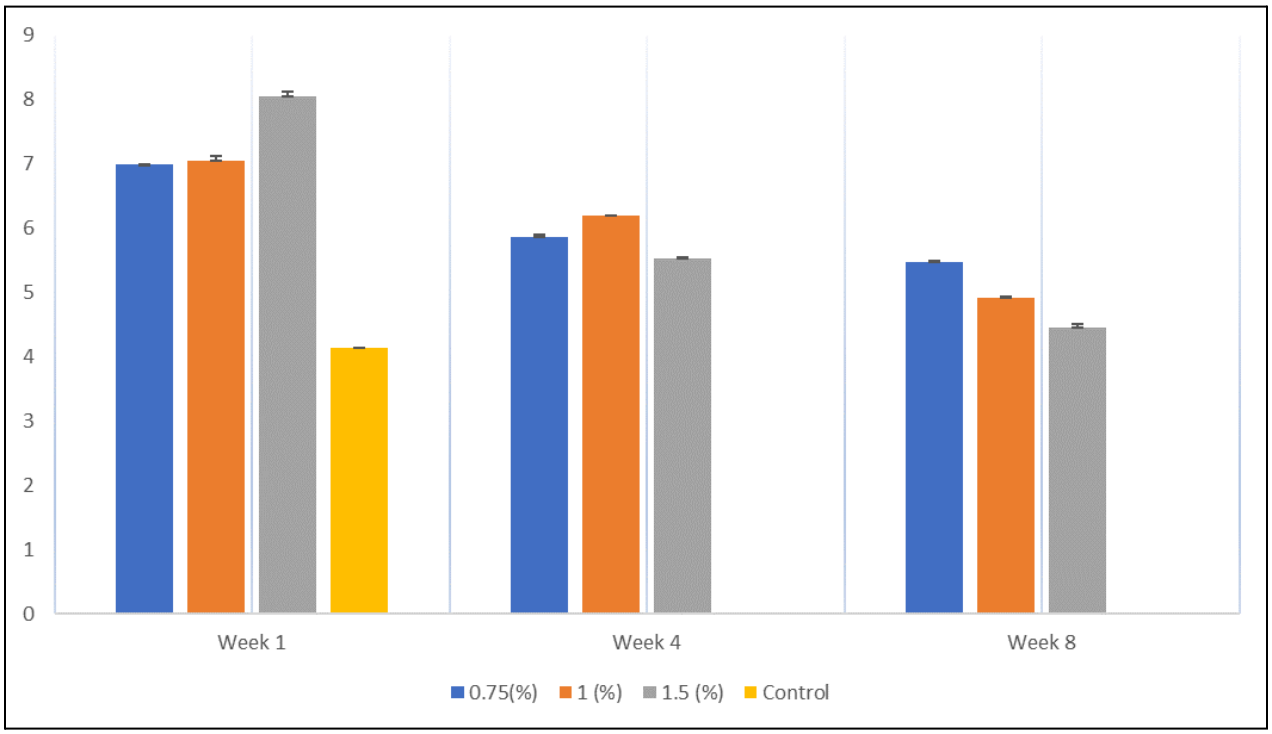

Figure 3: Time dependent change in the Viscosity of CMC across different concentrations

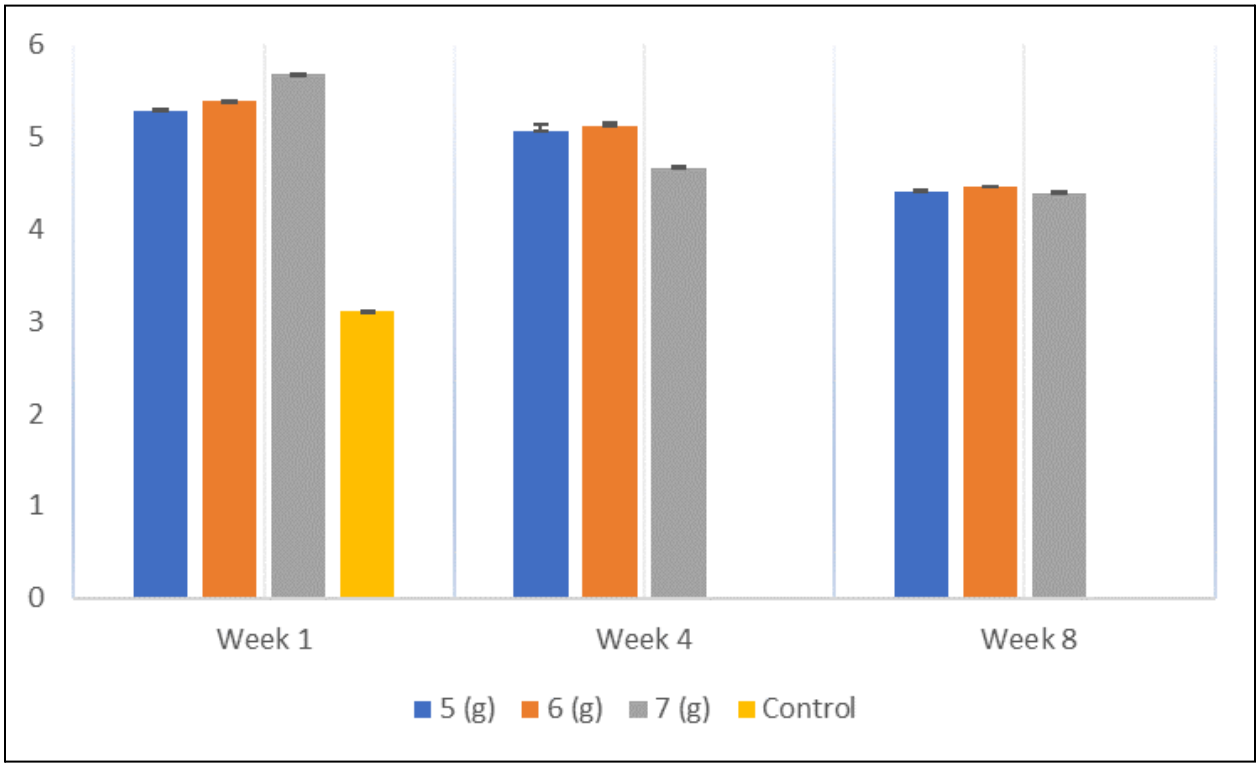

Figure 4: Time dependent change in the Viscosity of Gelatin across different concentrations

The viscosity of the formulated dental gels (A1–A16) was determined at Weeks 1, 4, and 8 to assess the effect of storage duration and polymer type on the rheological stability of the formulations. According to (Torres et al., 2022), the viscosity of an ideal pulp mummifying gel should be sufficiently high to allow the material to remain in place within the pulp chamber, yet not so high as to inhibit adequate diffusion of active ingredients.

Formulations A1 - A3 (Carbopol-based) as well as the control (13) displayed relatively high and stable viscosity values throughout the eight-week period. A1 showed a gradual decrease from 12.75 ± 0.07 to 8.17 ± 0.09, while A2 and A3 maintained stability between 16.10–16.50 mPa·s. The slight decline observed in A1 may be due to lower polymer concentration and partial relaxation of the gel matrix over time. A2 and A3, containing higher Carbopol levels, maintained stable viscosity due to the presence of a well-developed three-dimensional network that resisted structural breakdown.

HPMC-based formulations (A4–A6) showed a progressive increase in viscosity with time. A4 increased from 6.38 ± 0.00 at week 1 to 8.90 ± 0.01 at week 8, A5 increased from 12.35 ± 0.07 at week 1 to 14.10 ± 0.14 at week 8, and A6 from 12.75 ± 0.07 to 17.10 ± 0.14. This gradual increase in viscosity may be attributed to polymer hydration and further swelling of the gel matrix. Although this increase enhances gel firmness and retention at the site of application, excessively high viscosity could potentially reduce the diffusion of the active ingredient.

Formulations containing Na-CMC (A7–A9) demonstrated a consistent decrease in viscosity over the storage period. A7 demonstrated a decline from 6.98 ± 0.01 to 5.47 ± 0.01, A8 from 7.05 ± 0.07 at week 1 to 4.92 ± 0.02 at week 8, and A9 from 8.05 ± 0.07 to 4.45 ± 0.06. All the formulations exhibited a continuous decline in viscosity, suggesting polymer degradation or weakening of hydrogen bonds within the gel structure. The decrease below 5 mPa·s at the eight

week indicates poor retention ability and reduced mechanical strength. This result implies that CMC may require viscosity enhancers to maintain its stability over time. CMC control formulation A15 demonstrated a very low viscosity compared to A8-A10 implying that *Aloe vera* increases the rheological property of the CMC.

Similarly, Gelatin-based formulations (A10–A12) also showed a reduction in viscosity with time, ranging from approximately 5.050 ± 0.071 to 4.38 ± 0.01 which was more viscose than the control. This reduction is likely due to partial hydrolysis or breakdown during storage. but was more viscous than the control. Hence, the incorporation of *Aloe vera* into formulation A10 - A12 leads to an increase in their viscosity. This is confirmed by the bar graph given above.

3.3 Specific gravity (g/ml):

The Evaluation of specific gravity of *Aloe vera* dental gels Formulation ranges from 0.9984 - 1.0217 as shown in Table 3.3 below

weight of empty 25ml density bottle(W1) = 20.58g

weight of bottle + distilled water (W2) = 45.45g

weight of bottle + Gels(W3)

specific gravity(SG) = W3 - W1 /W2 - W1

Table 3.2:Density Values of Aloe vera Dental Gels Formulation at Different Storage Periods.

Batch Code	W3	S.G (g/ml)
A1	45.41	0.9984
A2	45.46	1.0004
A3	45.48	1.0012
A4	45.47	1.0008
A5	45.50	1.0020
A6	45.56	1.0044
A7	45.69	1.0096
A8	45.70	1.0101
A9	45.75	1.0121
A10	45.85	1.0161
A11	45.77	1.0129
A12	45.99	1.0217

The individual batches have density measurement values ranging from 0.9984 g/ml - 1.0217 g/ml. These values were closely related to the density of water (1 g/ml). These findings are expected from the formulations as Aloe vera constitutes about 99.5% of water, with polymer and additives constituting to the overall mass -volume relationships.

Overall, the gradual increase in specific gravity from Carbopol < HPMC < CMC < Gelatin suggests that polymer type and concentration influence gel compactness and internal structure. Since all S.G values were within the acceptable range for dental gels (≈1.0 g/mL) (Chenna *et al*., 2025), the formulations can be considered physically uniform, stable, and suitable for oral application

3.4. Antimicrobial assessment:

Table 3.4 shows the antimicrobial assessment result of *Aloe vera* dental gel formulations, *Aloe vera* sap and formocresol(control)

Table 4: Zone of Inhibition(mm) of Aloe vera Gel, Sap And Formocresol Against Selected Oral Pathogens

organisms	***Aloe vera* gel**	***Aloe vera* sap**	**Formocresol**
Streptococcus mutans	No zone	No zone	55mm
Lactobacillus acidophilus	No zone	No zone	55mm

Findings revealed that neither the Aloe vera sap nor the formulated gels demonstrated inhibitory activity against the test cariogenic organisms which are Streptococcus mutans and lactobacillus acidophilus. This tells us that Aloe vera based formulations do not possess significant antimicrobial activity in these cariogenic organisms.

Nevertheless, several literature have reported the wound healing, anti-inflammatory and tissue properties of Aloe vera. For example, (Khan *et al.,* 2013; Raj *et al* 2024)) in Formulation development, optimization and evaluation of Aloe vera gel for wound healing, found that Aloe vera gel significantly shortened the healing time in wounds surgically induced in wistar rats compared with control treatments manifested as an increase in rate of contraction of wound area. Additionally, (Subramanian *et al.,* 2006; Fox *et al.,* 2017) verified that Aloe vera gel enhances wound contraction and collagen synthesis. This is attributed to the mannose-6-phosphate found in Aloe vera leaf gel. Formulations known to contain mannose have been demonstrated to promote collagen synthesis, fibroblast activity and boost macrophage activity.

Although the formulations of both the formulations and sap did not show direct antimicrobial effect against *S.mutans* and *L.acidophilus*, the capacity of Aloe vera to support tissue healing is nevertheless important in the context of pulp treatment.Preservation of dental pulp may not only

rely on the antimicrobial activity but also on the wound healing, inflammation reduction and promotion of regeneration processes. Despite having no direct antimicrobial activity, Aloe vera wound healing and regenerative mechanism may help preserve dental pulp in this way.

CHAPTER FOUR
CONCLUSION AND RECOMMENDATION

4.1. Conclusion

Stable Aloe vera dental gels were successfully developed using various polymer bases to evaluate their physicochemical and antimicrobial properties. Carbopol-based formulations demonstrated superior stability in terms of pH, viscosity, and specific gravity, making them most suitable for oral applications. Although the gels did not exhibit antimicrobial activity against *Streptococcus mutans* or *Lactobacillus acidophilus*, their physicochemical stability supports their potential use in dental formulations.

4.2. Recommendations

Long-term stability studies should be conducted over a period of 6–12 months to monitor changes in pH, viscosity, and microbial integrity under both in accelerated and real-time storage conditions. Additionally, the polymer concentration of sodium Carboxymethyl Cellulose (Na-CMC) and Gelatin should be increased to enhance the overall viscosity and structural stability of the formulations. Suitable viscosity enhancers is advised to maintain optimal and to improve retention at the site of application of CMC-based gels maintain optimal rheological properties and improve retention at the site of application.

Furthermore, the inclusion of an appropriate neutralizing agent in the HPMC-based formulations is advised to adjust and stabilize the pH within the physiologically acceptable range (5.5–8.0), thereby enhancing compatibility and reducing the risk of pulp irritation.

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APPENDIX

Appendix 1: CMC Formulation (A7- A8)

Appendix 2: Carbopol Formulation (A1 - A3)

Appendix 3: HPMC Formulations (A4- A5)

Appendix 4: Gelatin Formulations (A11- A12)

Appendix 5:

Table 3.2: Viscosity Values of Aloe vera Dental Gels Formulation at Different Storage Periods

Batch Code	Week 1	Week 4	Week 8
A1	12.750 ± 0.071	10.500 ± 0.141	8.170 ± 0.099
A2	16.125 ± 0.035	16.170 ± 0.042	16.130 ± 0.014
A3	16.100 ± 0.141	16.500 ± 0.000	16.450 ± 0.071
A4	6.380 ± 0.000	8.840 ± 0.014	8.895 ± 0.007
A5	12.350 ± 0.071	13.950 ± 0.071	14.100 ± 0.141
A6	12.750 ± 0.071	16.000 ± 0.141	17.100 ± 0.141
A7	6.980 ± 0.014	5.860 ± 0.028	5.470 ± 0.014
A8	7.050 ± 0.071	6.190 ± 0.000	4.915 ± 0.021
A9	8.050 ± 0.071	5.530 ± 0.014	4.445 ± 0.063
A10	5.280 ± 0.014	5.050 ± 0.071	4.410 ± 0.014
A11	5.375 ± 0.007	5.120 ± 0.028	4.460 ± 0.000
A12	5.670 ± 0.014	4.655 ± 0.247	4.380 ± 0.014
A13	16.125 ± 0.035	16.130 ± 0.014	16.150 ± 0.000
A14	3.155± 0.007	N/A	N/A
A15	4.13± 0.000	N/A	N/A
A16	3.105± 0.007	N/A	N/A

Note Values of viscosity are expressed in Mean ± S.D (n =2), N/A: Not Available.