

Design and evaluation for an eco-friendly hemostatic agent using bioactive natural components

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ABSTRACT

The primary objective of the present research work was to formulate an herbal hemostatic agent with highly efficacious as well as cost effective characteristics. This agent should have the capability of accelerating the process of the human body's normal blood clotting as well as imparting a degree of protection against microbes. A mixture of bioactive ingredients of *Blumea balsamifera* (Sambong) and *Moringa oleifera* was trialled in combination with Alum, which possesses powerful astringent properties, as the basis of a Carbopol 940 gel formulation in the creation of three distinctive batches of the product. Neem and Tulsi were added as excipients to impart greater anti-bacterial as well as anti-inflammatory activity. Results of this formulation provides the information about the presence of the vital secondary metabolites that are demanded for towel rejuvenescence and platelet aggregation was verified by the chemical analysis's findings. Following the process, an examination of each batch's physical characteristics verified the results, which showed that the product had a harmonious, smooth and non-greasy texture. Also, the product's pH value was discovered to vary between 5.95 to 6.48. The product that showed the most promising results on the spherometer readings of 1.33 gm.cm/sec was Batch III, as verified by the results on its spreadability. It's important that it's less precious and safer than synthetic medicines.

Keywords: Herbal hemostatic gel, Blood coagulation treatment, Natural materials used in the process of blood coagulation, *Blumea balsamifera*, *Moringa oleifera*, Alum, Tulsi and Neem extract, Carbopol 940, Phytochemical screening, Evaluation of topical gels.

INTRODUCTION

Coagulation or clotting is the mechanism by which blood changes from a liquid state to a gel like state to form a blood clot. The result of this mechanism is haemostasis or the cessation of blood flow from a damaged vessel and the repair process follows. The mechanism of coagulation involves fibrin deposition and maturation, as well as platelet activation, adhesion and aggregation.^[1] The physiological mechanism of blood coagulation is a complex system of coordination between various blood components such as cells and coagulation factors.^[2] The term "Haemostasis", which means "To halt bleeding", is a

Greek term consisting of "Haeme" meaning "Blood" and "Stasis" meaning "To stop".^[3] The haemostatic system is activated in pathological conditions requiring surgery, anesthesia or any other invasive procedure. This balance may also be disturbed by stress, cytokines and infectious pathogens. Consequently, there is a high risk of hemorrhagic and prothrombic disorders in the perioperative period.^[4] The cells termed haemocytes are concerned with haemostasis. Haemocytes release the blood clotting factors C and G, which together with hemolymph proteins, bring about coagulation in a calcium dependent reaction.^[5]

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

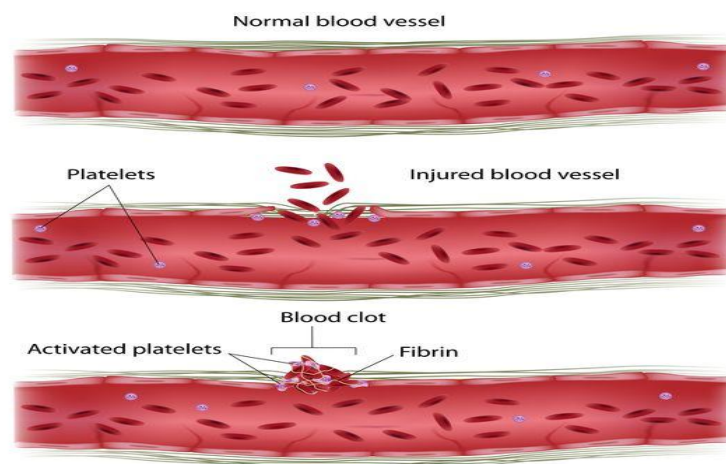


Figure 1 : Process of blood coagulation

Concomitant with injury to the endothelium of a blood artery, coagulation begins. Two processes are triggered by blood exposure to the subendothelial space: platelet alteration and exposure of subendothelial platelet tissue factor to coagulation factor VII, which ultimately results in the formation of cross linked fibrin. Primary haemostasis is the process by which platelets instantly form a plug at the site of injury. At the same time, secondary haemostasis takes place as other coagulation factors, apart from factor VII, interact in a cascade fashion to produce fibrin strands that support the platelet plug.^[6]

1.2 Classification:

Classification of topical hemostatic agents:

External dressings, mechanical hemostats, synthetic/semisynthetic sealants, and active or sticky agents are the numerous forms of hemostats that are used topically. Topical active substances, like fibrinogen and thrombin, function by actively contributing to the fibrin clot's development.^[7]

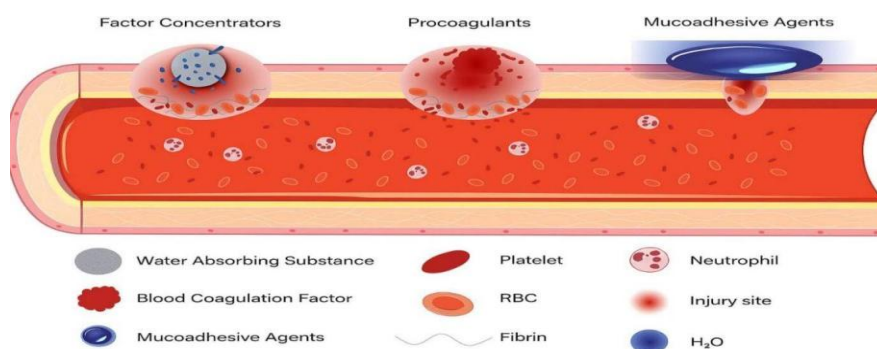


Figure 2 : Application and outlook of topical hemostatic agents

Usually, they are offered in liquid formulation (fibrin glue) or in combination with collagen (fibrin patch). These substances are sometimes called sticky hemostats because of their hemostatic and adhesive sealing properties. Topical mechanical hemostats consist of plant-based polysaccharide spheres, bovine collagen-oxidized cellulose, and pig gelatin. By increasing platelet activation and aggregation, these topically given medicines generate a clotting matrix at

the site of bleeding. These hemostats are known as passive hemostats, and they can improve the coagulation system's ability to function. Topical synthetic/semi-synthetic sealants are generally supplied as low-viscosity solutions that bind tissue surfaces by polymerizing into a solid film.^[8,9]

1.3 Mechanism Of Action:



The mammalian coagulation system is commonly divided using the intrinsic and extrinsic pathways (fig 6). Each of these cascades generates the extrinsic tissue factor (TF): The prothrombinase complex (FXa : FVa) development and finally thrombin production is supported by the intrinsic (FIXa : FVIIIa) tenase complex and factor (FVIIa). The independent activation of the intrinsic and extrinsic pathways, which then coverage into a single pathway (FX, FV, FII), is explained by the standard cascade coagulation model. The reviews give a thorough explanation of

the coagulation cascade.^[10,11] The coagulation cascade of secondary hemostasis has two basic pathways. Which causes fibrin to develop. These are the contact activation pathway, also called the intrinsic pathway, and the tissue factor pipeline, also called the extrinsic pathway, which lead to the same fundamental processes for fibrin production. It was believed that the two pathways of the coagulation cascade were of equal relevance, but it is now acknowledged that tissue factor (extrinsic) pathway is the predominant pathway in the initiation of blood coagulation.^[12]

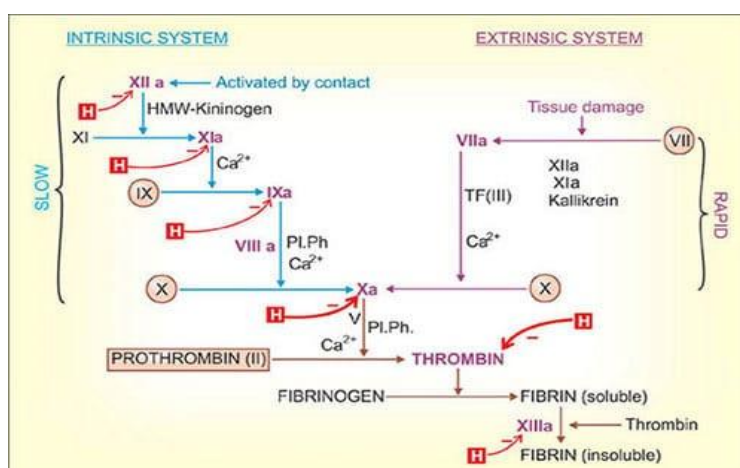


Figure 3 : Mechanism of blood coagulation

Our body's capacity to regulate bleeding is significantly influenced by the extrinsic tissue factor pathway. The principal role is to generate a "thrombin burst", which is when thrombin, the "star player" of the coagulation cascade, bursts out to further stimulate the cascade. Interestingly, FVIIa, one of the active coagulation factors, is present in considerable numbers relative to others.

This is how it functions:

1. FVII escapes from the blood when a blood artery is damaged and combines with tissue factor found on leukocytes and stromal fibroblasts, which are cells that contain tissue factor, to produce an active complex known as TF-FIIa.
2. FX and FIX are activated by TF-FVIIa; FXIa, FXII, FXa, and thrombin all contribute to the activation of FVII.

3. The activation of FX to create FXa by TF-FVIIa was significantly decreased by tissue factor pathway inhibitors (TFPI).
4. The prothrombinase complex, composed of FXa and its co-factor FVa, transforms prothrombin to thrombin.
5. Other components of the coagulation cascade that thrombin subsequently activates are FVIII and FV, which form a complex with FIX.
6. Additionally, FVIII is released from its link with VWF by thrombin.
7. The cycle continues with FVIIIa, FIXa's co-factor, and the "tenase" complex they create, which activates FX ("tenase" is combination of "ten" and enzyme suffix-"ase").

1.4 Rationale:



In order to avoid complications that may result from injuries and minor wounds, bleeding should be controlled as quickly as possible. Conventional methods of managing bleeding are very costly and may cause irritation of the area where they were applied. There was a great need to discover cheaper and safer methods of controlling bleeding that are derived from herbs. *Blumea balsamifera*, alum and moringa seed powder have already been established for hemostatic, astringent and wound-healing activities and therefore can be used as active ingredients for fast blood coagulation. Neem leaf extract and tulsi extract are added as excipients and it is assumed that it will increase antimicrobial

properties and have lesser chances of getting infected, resulting in fast healing of the wounds. Rationale for using gel form of dosage : Easy application, localized action and higher compliance rate. Carbopol was used as the gelling agents for the preparation of the optimum viscosity, stability and spreadability of the gel. Thus, the current study has been undertaken to formulate and test the herbal gel for fast blood coagulation, which can be considered safe, effective as well as cost-effective.

1.5 Literature Review:

Table 1 : Literature review

Sr.no	AUTHORS	TITLE OF PAPER	JOURNAL DETAILS	FINDING AND INNOVATION
1.	Mika-ella Harinder C. Wahani, Jay brian T. Monino, Orly Q. gantala, Sharifa c. Mahamod, Bainara B. Acot	Arugabon : A formulated organic open wound-healing ointment using sambong (<i>Blumea Balsamifera</i>) leaf extracts with guava scent	International journal of novel research and development (IJNRD)	The anti-bacterial, anti-inflammatory, and restorative properties of <i>blumea balsamifera</i> , popularly known as sambong, have long been established. It has long been proven that <i>blumea balsamifera</i> has anti-bacterial, anti-inflammatory, and healing attributes. It was observed in studies that sambong leaves have a significant effect in improving tensile strength and wound contraction, which signifies effective regeneration of tissue. Sambong extract was combined in the preparation of an organic ointment for the treatment of wounds. This organic ointment caused a reduction in the size of wounds similar to betadine, but its tensile strength was higher, indicating the effectiveness of the healing. Moreover, it portrayed a slight anti-bacterial property against <i>staphylococcus aureus</i> .
2.	Masyudi masyudi, Muhammad hanfiah, said usman and marlina marlina	Effectiveness of gel formulation of (capa leaf) <i>Blumea Balsamifera</i> L. on wound healing in white rats	Veterinary world	Because of the anti-bacterial and anti-inflammatory properties of <i>blumea balsamifera</i> L., it has been widely employed in the trade of wound healing agents. As reported in recent studies, the leaf extract of <i>B. balsamifera</i> has been successfully utilized in the preparation of a carbopol 940 gel, and in incision wound in rats, the 10% concentration showed better results in wound contraction, fibroblast cell proliferation, angiogenesis, and IL-2 levels. The efficacy of the B.



				balsamifera gel in acting as an effective herbal drug in the treatment of wounds is proved.
3.	Ashish Kumar Bind, Pawan Jain, Manoj Goyal and Ashok Goyal.	Development and assessment of an anti-acne hydrogel formulation containing Moringa oleifera leaf powder	World journal of Advanced Research and Reviews (WJARR)	Propionibacterium acnes bacteria are the causative agents of acne vulgaris. The increasing demands for natural substitutes have arisen due to the fact that the long-term use of semi-synthetic acne drugs tends to cause skin irritation and anti-biotic resistance. Due to the flavonoids and phenolic compounds, the leaves of the moringa oleifera have a high anti-bacterial and anti-inflammatory value. The extracts of the moringa oleifera have been shown to inhibit the growth of the bacteria that leads to acne. Hydrogels based on carbopol have been widely preferred due to its high spreadability, stability, and patient compliance. The herbal hydrogels have shown better safety and efficiency for the treatment of acne. There have been no significant studies. Conducted for the hydrogels that use moringa oleifera leaf powder.
4.	Mythili suresh, sri kessav Mukundan, Sivaraman Rajasekar, Sangavi gokulkrishnan, Navesh purushothaman, Sakthi priyadarsini sethuraman.	Development and Assessment of a multipurpose herbal cream with moringa oleifera lam.	Cureus part of springer nature published via MHS-SRMIST.	Moringa oleifera seed kernel oil is rich with bioactive compounds that have already been proven to exhibit anti-inflammatory, anti-bacterial, and anti-oxidant properties. Based on recent research findings, a well-formulated moringa oil with proper PH and homogeneity can be efficiently applied for making stable and non-greasy herbal creams. Like gentamycin, the proposed creams have also shown excellent anti-bacterial properties against E.coli and staphylococcus aureus. The denaturation test of albumin also confirmed its anti-inflammatory properties.
5.	Mahsa Shahbandeh, Mahsa Amin salehi, Maryam Soltanyzadeh, Mehrnaz Mirzaei, Ali	Evaluation of the Anti-bacterial and Wound Healing Properties of a Burn		An effective topical preparation is required for burn wounds in order to promote healing and prevent infection. Potassium alum has astringent and anti-bacterial properties. Curcumin and honey possess strong anti-microbial and anti-inflammatory properties with low cytotoxicity. When combined, it provides a synergistic effect, which accelerates

	Maleki, Abdolkarim Chehregani rad, Mohammad javad Fatemi, Reza Mirnejad, Mostafa Dahmardehei.	Ointment Containing Curcumin, Honey, and Potassium Aluminium.		re-epithelialization and healing of wounds. This provides an alternative treatment of burn wounds.
6.	Abdulkarim K. Alzomor, Ahmad safe Moharram, Nahlah Mansour Al Absi.	Formulation and evaluation of potash alum as deodorant lotion an after shaving astringent as cream and gel.	International current pharmaceutical journals	Because of the astringent and deodorizing properties of potash alum, it has been recognized as one of the natural agents. Studies have revealed that with an effective strength of 2%, it has antibacterial properties with a bacteriostatic action upon the axillary microbiota. Potash alum is converted into various preparation of lotions, creams, and gels so that the ease of use and retention can be improved. Use of these in pharmaceutical and cosmetic formulations is preferred due to the correct physicochemical properties and stability.

1.6 Drug Profile:

A.) Name: *Blumea (sambong)*^[13,14]

- **Botanical name:** *Blumea balsamifera*
- **Kingdom:** Plantae
- **Family:** Asteraceae
- **Genus:** *Blumea*



Figure 4 : *Blumea balsamifera*

- **Species:** *Blumea balsamifera*
- **Chemical constituents:** Monoterpenes, sesquiterpenes, diterpenes, flavonoids, organic acid, esters, alcohols, dihydroflavone, sterols, volatile oils, etc.
- **Solubility:** Methanolic extract, ethanolic extract, Aqueous extract.
- **Use:** Platelet aggregation, wound healing, anti-microbial, anti-inflammation, anti-plasmodial, disease and resistance activities, anti-oxidant, etc.
- **Category:** Platelet aggregation, wound healing, anti-microbial.

B.) Name: *Moringa seeds (saragva ni sing, drumstick seed)*^[15]

- **Botanical name:** *Moringa olifera* Lum.
- **Kingdom:** Plantae

- **Family:** Moringaceae
- **Genus:** Moringa
- **Chemical constituents:** Flavonoids, Quercetin, Phenolic acids, Tannins, etc.
- **Solubility:** Soluble in organic solvent such as chloroform, hexane
- **Use:** Wound healing, anti-inflammatory, anti-oxidant, anti-microbial.
- **Category:** Wound healing, anti-inflammatory, anti-microbial.



Figure 5 : Moringa seeds

C.) Name: Alum (phatkari)^[16]

- **Botanical name:** Potas alum
- **Kingdom:** Inorganic mineral substance
- **Chemical constituents:** $XAl(SO_4)_2 \cdot 12H_2O$, aluminium sulphate, monovalent cation, etc.
- **Solubility:** It is soluble in water
- **Use:** Help in blood coagulation, wound healing, skin treatment, oral hygiene, etc.
- **Category:** Hemostatic agent, anti-septic, astringent.



Figure 6 : Alum

D.) Name: Neem (margosa)^[17]

- **Botanical name:** Azadirachta indica
- **Kingdom:** Plantae
- **Family:** Maliaceae
- **Genus:** Azadirachta
- **Species:** Azadirachta indica
- **Chemical constituents:** Nimbidin, Nimbin, Azadirachtin, Polysaccharides, Nimbiol, etc.
- **Solubility:** Slightly soluble in water, readily soluble in organic solvent such as ethanol, methanol, ethyl acetate.
- **Use:** Anti-bacterial, anti-inflammatory, Anti-fungal, anti-tumour, immuno-modulatory, etc.
- **Category:** Anti-bacterial, anti-inflammatory.



Figure 7 : Neem

E.) Name: Tulsi (VishnuPriya)^[18,19,20]



- **Botanical name:** Ocimum sanctum (linn)
- **Kingdom:** Plantae
- **Family:** Labiatae
- **Genus:** Ocimum
- **Species:** Ocimum Sanctum
- **Chemical constituents:** It contain eugenol, Phenolic compound such as cirsilineol, circimaritin, rosameric acid, etc.
- **Solubility:** Soluble in water, ethanol, and methanol.
- **Use:** Anti-bacterial, anti-inflammatory, anti-microbial, anti-oxidant
- **Category:** Anti-microbial, anti-inflammatory.



Figure 8 : Tulsi

F.) Name: Carbopol 940

- Carbopol 940 is a synthetic polymer and does not belong to any biological Classification.
- It chemically classified as a carbomer, which is a homopolymer of acrylic acid cross- linked with allyl ethers.^[21]
- Carbopol appears as a white, fluffy powder and is widely used in pharmaceutical and cosmetic formulation.^[22]
- **Chemical constituents:** Carbomer polymer are formed from repeating units of acrylic acid.

- Carbomers are synthetic high-molecular weight polymers of acrylic acid that are cross linked with either alkyl sucrose or alkyl ether of pentaerythritol.^[23]
- **Solubility:** Soluble in water, glycerin, alcohol (partially), and insoluble in oils.^[24]

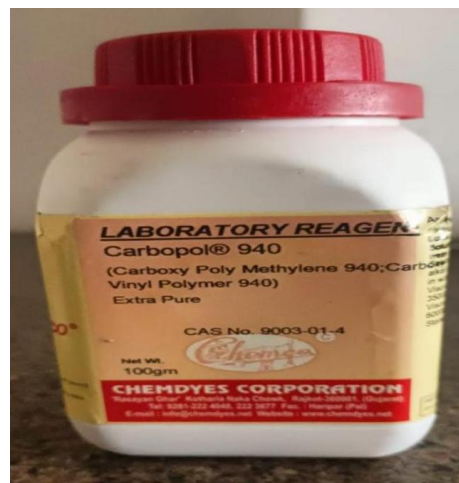


Figure 9 : Carbopol 940

- **Use:** Carbopol 940 is widely used as thickening, suspending and emulsifying agent in various industries.
- **Category:** Cross linked polyacrylics acid polymer^[25]

G.) Name: Propylene glycol

- **Name:** Propylene Glycol
- **IUPAC name:** Propane-1,2-diol
- **Synonyms:** 1,2-prpanediol^[26]
- **Category:** Diol (aliphatic glycol), Polyol, Pharmaceutical excipients.^[26]
- **Chemical nature:** Synthetic dihydric alcohol with –OH groups.
- **Structure and Properties:** Low molecular weight, Hygroscopic.
- **Solubility:** Completely miscible with water and alcohol.



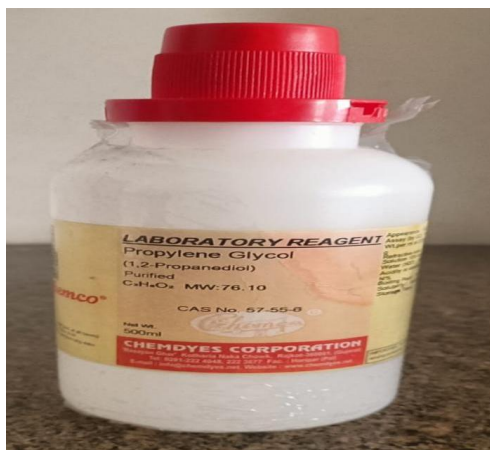


Figure 10 : Propylene glycol

- **Characteristics:** Colorless, Odorless, slightly viscous, stable, non-toxic at pharmaceutical concentration.^[27]
- **Uses:** Used as solvent, Humectant, and penetration enhancer in topical gels, creams, oral and injectable formulation.^[26]

2. Introduction (Formulation Related):

2.1 Introduction Of Gel:

The term “gel” comes from “gelatin”, and both “gel” and “jam” may be traced back to the Latin words “gelu” for “ice” and “gel” for “freeze” or “harden”. This introduction demonstrates the basic concept of a fluid setup to key regions of strength for a texture that doesn’t drift but is adaptable and retains certain fluid aspects.^[28] According to the USP, Gels also known as jellies, are semisolid systems that comprise either large organic molecules interpenetrated by a liquid or suspensions composed of small inorganic particles. The gel is categorised as a two-phase system when the gel mass contains a network of tiny distinct particles. The gel mass in a two-phase system is sometimes referred to as a magma if dispersed phase’s particle size is comparatively big. Organic macromolecules are evenly distributed throughout a liquid in single-phase gels so that there are no discernible boundaries between the dispersed macromolecules and the liquid.^[29] Gel is a homogeneous, semi-solid preparation that typically consists of a solution or dispersion of one or more medications in bases that are either hydrophilic or hydrophobic. Typically, Appropriate gelling agents are used in their

preparation. They are meant to be used for therapeutic, preventive or protective purposes on the skin or certain mucous membranes. Anti-oxidants, stabilizers, antimicrobial agents and preservatives are examples of appropriate additional substances that can be added to gel. Sterile gel should be used only on big open wounds or badly damaged skin.^[30] Applying a chemical to the skin in order to treat or cure skin disorders is known as topical medicine delivery.^[31] The drug or active component was released freely because gels are hydrophilic. A gel is composed of two factors a three-dimensional, cross-linked material that has enough liquid in it to form a rigid network that immobilises the liquid nonstop phase. The structural network of gel is made up of both inorganic patches and organic macromolecules.^[32] A gel is made up of a synthetic or natural polymer that forms a three-dimensional matrix in a hydrophilic liquid or dissipation medium. The medicine is contained in a thin subcaste of the gel forming matrix that physically covers the skin because the liquid evaporates as soon as it’s applied.^[33] It can improve absorption by penetrating the skin more thoroughly. The presence of a network formed by the interlocking of gelling agent particles is what gives a gel its flexibility.^[34] The gels are made by mixing an organic, inorganic or aqueous solvent or solvent systems with a gelling agent (gelator), which may be a natural, synthetic or semi-synthetic polymer or low molecular weight small molecules.^[35-38] In order for a gel to form, viscosity is essential. For a gel to become more viscous in its solution form, a certain concentration of polymer is needed.^[39]

2.2 Classification Of Gel:

Colloidal phases, solvent type, physical characteristics and rheological characteristics can all be used to categorise gels :

1. Based on colloidal phases :^[40]

They are classified into:

- A. Inorganic (Two phase system)
- B. Organic (Single phase system)

Inorganic (Two phase system):



Instead of bigger molecules, the system is made up of floccules of tiny particles and if the dispersion phase phase partition size is particularly large, the gel structure will become unstable and acquire a three-dimensional must be structure. They must be thixotropic, meaning that they change from a semisolid to a liquid when distributed. Two examples are bentonite magma and aluminium hydroxide gel.

Organic (Single phase system):

Large organic molecules are constantly dissolving on the twisted strands. Most organic gels are single-phase solutions composed of gelling agents like tragacanthin and carbomer and organic liquids like plastic base.

2. Based on nature of solvent :^[40]

Hydrogels (Water-based):

Because of the chemical or physical cross-linking of individual polymer chains, a hydrogel is a three-dimensional network of hydrophilic polymers that can develop in water and hold a sizable amount of water without losing its structural integrity. An example would be hydrophilic colloids such as silica, bentonite, tragacanth, pectine, sodium alginate, etc. The hydrogel can be used as a rectal drug delivery system, a sustained release drug delivery system or an ECG medical electrode.

Organogel (Using a non-aqueous solvent):

An organogel is a kind of gel that contains a liquid organic phase inside a three-dimensional, cross-linked network. Lecithin solution in organic solvents gels or organogels when a polar solvent is added.

Xerogels:

Xerogels are solid-formed gels made by letting materials shrink freely while gently drying at room temperature. When a xerogel is heated above a particular point, viscous sintering occurs, transforming the porous gel into a thick glass. Tragacanth ribbons, dry cellulose and polystyrene are a few examples. Gels that exhibit non Newtonian flow are sometimes classified as plastic gels, pseudoplastic gels and thixotropic gels.

3. Based on physical nature :^[40]

Elastic gels:

Gels made of alginates, agar, pectin and guar gum are elastic. The fibrous molecules are connected at the junction by relatively weak interactions like dipole attraction and hydrogen bonding. A salt bridge of the type -COO-X-COO creates an additional bond between two neighbouring strand networks if the molecule has a free -COOH group. For instance, carbopol and alginate.

Rigid gels:

Macromolecules having main valence bonds joining the framework can be used to create rigid gels. For example, the Si-O-Si-O bond holds silic acid molecules together in a silica gel, creating a polymer structure with a network of pores.

4. Based on rheological properties :^[41]

According to their rheological qualities, gels usually exhibit non-Newtonian flow properties. They fall into the following categories:

- A. Plastic gels
- B. Pseudoplastic gels
- C. Thixotropic gel

Plastic gels:

For instance, the rheogram plot for Bingham bodies, flocculated solutions of aluminium hydroxide that exhibit plastic flow, displays the yield value of the gels, which is the point at which the elastic gel bends and starts to flow.

Pseudoplastic gels:

For instance, a pseudo-plastic stream is shown by fluid scattering from materials such as sodium alginate, tragacanth, CMC and others. Regardless of production value, these gels become less consistent as shearing costs rise. When the long chain particles of the straight polymers shear, the rheogram is produced. The damaged atoms starts to shift their



extended hub towards skin when the shearing force is repeated, releasing dissolvable from the gel network.

Thixotropic gels:

The incredibly weak bonds that hold the gel particles together can be broken by shaking. The final configuration will gel again as a result of the particles

colliding and re-connecting (The reversible isothermal gel-sol-gel transition). In a colloidal framework with non-round particles, this produces a platform like design. For example, agar, bentonite and kaolin.

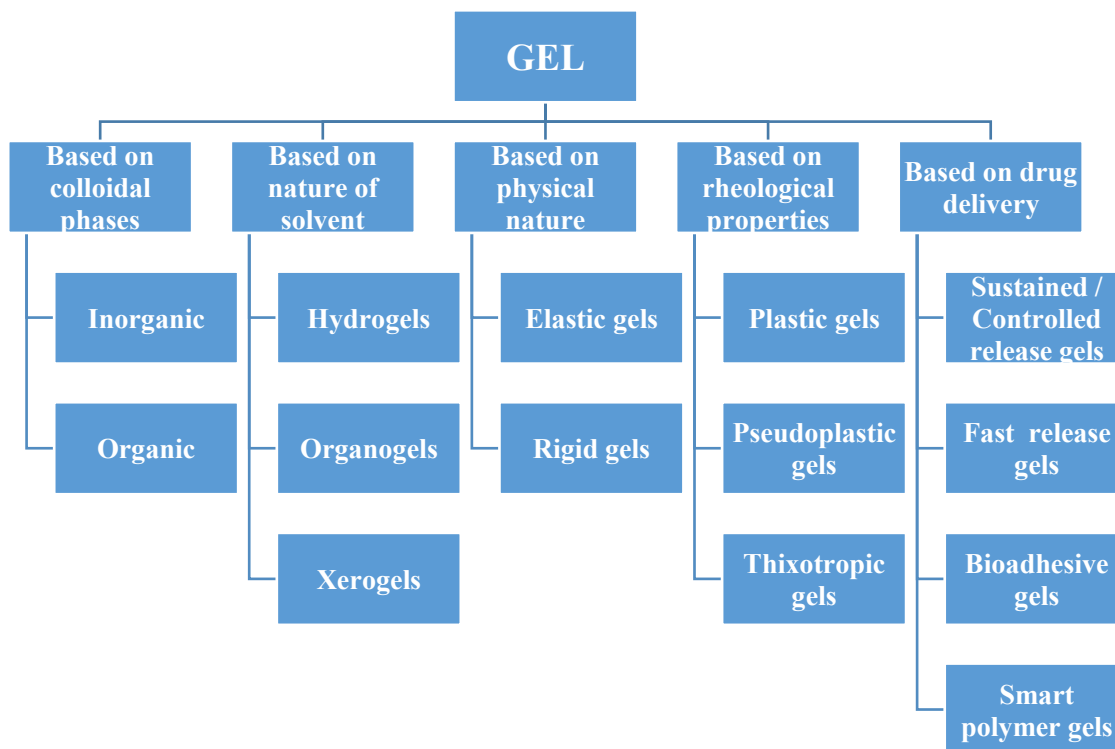


Figure 11 : Classification of gel

5. Based on drug delivery:

Pharmaceutical gels are commonly used as carriers in drug delivery system. These gels could be classified as:

Sustained / Controlled release gels:

Controlled medication delivery system offer a number of benefits, such as decreased dose recurrence, which enhances patient compliance, restricted / designated drug delivery and significantly fewer side effects. They also maintain blood levels within a desired range by limiting fixation fluctuation. Because of its dispersion component, which delivers medication via a polymer network (a network that is insoluble in water) or supply system (a water-insoluble polymeric layer), gels serve as controlled drug delivery systems. In the pharmaceutical industry,

hydrogels, aerogels and organogels are used as supported or controlled drug delivery systems.^[42]

Fast release gels:

Superabsorbent and rapidly expanding gels can be used to dissolve tablets quickly. Fast release gels can be used to treat acute conditions that require an immediate start to treatment.^[43]

Bioadhesive gels:

The bioadhesive frameworks limit nearby medications and extend the duration of the medication's home season in the oral cavity. Ophthalmic, mucoadhesive, transdermal, vaginal and cutaneous drug are administered using bioadhesive gels. Cross-connected polyacrylic corrosive gel framing bioadhesive polymers can exhibit controlled drug distribution at the swallowing site and stick to



mucosal surfaces for prolonged durations of time. Several hydrogel based bioadhesive frameworks for regulated drug release have been considered in this article. These kinds of polymer gel frameworks function as controlled drug delivery devices and bioadhesive frameworks that can deliver medications with enhanced bioavailability at a designated location.^[44]

Smart polymer gels:

Natural cunning or cunning gels are other names for smart polymer gels. Managed or self-directed distribution solutions for boosts responsive gel are gaining popularity among specialised specialists. Improved “shrewd” or sensitive gels have a superb physiochemical shift in response to minor alterations in their current surroundings, such as pH, temperature, light, appealing area and ionic components. Because these changes are reversible, the machine may revert to its original nation once the indicator or cause is eliminated. Hydrogels, which mimic smart gels, generally respond to natural fluctuations.^[45]

2.3 Method Of Preparation Of Gel:^[46]

1. Thermal change:

Due to the lipophilic nature of the colloids (solvated polymers) when thermal changes are introduced, gelatin forms. Some hydrogen formers are more soluble in heat than in cold water. With the lowering of temperature, the amount of moisture reduces and gelatin is formed (A gel may be obtained by cooling a concentrated hot solution). For example, cellulose derivatives, gelatin, agar, sodium oleate and guar gum. In some compounds, like cellulose ethers, the water solubility is because of hydrogen bonding. The lower solubility and disrupting of hydrogen bonds in the solutions lead to gel formation with the rise in temperature. Hence, this method may not be used as a reference method for the formulation of gels.

2. Flocculation:

In this respect, gelatin is introduced through the addition of a suitable amount of salt that precipitates an age state, but without reaching complete precipitation. In this case, in order to avoid such a high

concentration of precipitant, rapid mixing must be ensured. For example, a gelification of ethyl cellulose, polystyrene solutions in benzene can be affected by quickly mixing them with a suitable amount of non-solvent, such as petroleum ether. Salts, when added to hydrophobic colloids, cause coagulation, while salted gelification takes place when salts are added to hydrophobic colloidal solutions. Gels obtained from the process of flocculation show thixotropic properties. The hydrophilic colloids, such as gelatin, proteins and acacia, are affected due to a high concentration of electrolytes; usually, salting out of colloidal solution takes place, along with prevention of gelification.

3. Chemical reaction:

This method creates gel by chemical interactions between the solute and solvent. In case of higher concentration of the reactants, the result will be a gel structure as in the case of formation of aluminium hydroxide gel by interaction of an aluminium salt and sodium carbonate in an aqueous solution. A few more instances in which the polymeric chain has been cross-linked include PVA, cyanoacrylates with glycidol ether (Glycidol), toluene diisocyanates (TDI) and methane diphenyl isocyanide (MDI).

4. Fusion method:

In this process, all the medication, vehicles and gelling ingredients are combined under very high temperatures until a semisolid consistency is formed, which does not happen.

5. Cold method:

In this method, all ingredients, except the drug or active pharmaceutical ingredient are heated and mixed together. After reducing the temperature of the formulation, the drug is added and the mixing process continues until the gel form is not obtained.

6. Dispersion method:

In this method, the drug is dissolved in the medium and added to it the gelling agent which is stirred with water until it swells. If needed, buffer solutions are added to the gel to alter pH.



2.4 Advantages Of Gel:^[36,39,47,48,49]

Some of the main advantages of gel formulation over other semisolid dosage forms are as follows:

- Compared to other formulations, gels are simpler to make.
- The gel has a lovely, non-greasy composition.
- Gels stick to the application location rather effectively.
- Gels are biocompatible and safe for the environment.
- A high level of stress tolerance.
- The polymer can be used as a controlled release formulation by entwining it several times.
- Gels have a longer retention time than other topical dosage forms.
- They erect a barrier on the application site.
- They may be washed and are safe.
- They provide better spreadability and cooling effects because of solvent evaporation.
- They have very little long-term stability issues.
- They can be used to administer both polar and non-polar drugs.

2.5 Disadvantages Of Gel:^[36,39,49]

Despite several benefits, In adding to this, gel preparation has some demerits.

- The action of the gel is slower and more prolonged.
- The additives or gelators may cause irritation to the skin.
- The content of water in the gel increases the chance of microbial or fungal contamination.
- The loss of solvent in the gel preparation will result in drying.

- Some gels will become unstable because of flocculation.
- The gels may experience syneresis or the loss of solvent from the gel matrix.
- The gels with some covalent bonds are not penetrating. These make the drug entrapped in the gel matrix.
- Environmental conditions can alter the rheology of different gels.
- There is also the possibility of the gelling material forming precipitation and salting out.
- The use of polymers in gel preparation may result in the decomposition of some medications.

2.6 Ideal Properties Of Gel:^[50]

- The gel should be clear and homogenous.
- The nature of the gel should be inert.
- The gel should be non-sticky.
- The gel should not interact with any other ingredients of formulation.
- The gel must be stable.
- It has to be non-irritate, which would not be irritating to the skin or to any part where the gel is applied.
- The viscosity should be optimum.
- It should exhibit anti-microbial activity.
- If shear or force is applied during shaking of the container, it should break easily.
- The gel must be reliable.

2.7 CHARACTERISTICS OF GEL:

1. Swelling:

Gels can grow in size while absorbing fluids. Once could consider this to be the start of the disintegration process. Solvent penetrating the gel matrix causes gel-



solvent interactions to take the role of gel-gel interactions. Limited swelling results from normal cross-linking in the gel matrix, which prevents total breakdown. This gel swells considerably when the solvent combination shares a solubility feature with the gellant.^[51]

2. Syneresis:

Then, compression may follow in the gel structures that have stood. The interstitial fluid has communication and collection at the top layer of the gel. This is because the process is referred to as syneresis. The process has also occurred in other gels, such as organogels and inorganic hydrogels, besides natural hydrogels. Several concerns that arise during the setting of the gel have been associated with the use of the constriction tool. This is due to the amount of space left for the dissolvable that diminishes with the feeling that the loads are much better, leading to the release of the liquid. Osmosis phenomena have been observed in the syneresis of the ionically formed gels from either the gelatin or the psyllium seed gum. pH and electrolyte fixation phenomena have also been observed.^[52]

3. Ageing:

Slow spontaneous aggregation can easily be expected as a characteristic of colloidal system. The process described above can also be referred to as ageing. As a consequence of ageing, a network of gelling active ingredient starts to form in gels. The timer notices that since the fluid medium is lost from the newly formed gel, the process must be similar to the initial gelling process.^[40]

4. Structure:

The network created by the interlinking of the gelling agent particles gives a gel its flexibility. The gel's characteristics and the network's architecture are determined by the kind of particles and the force used to create the connections.^[53]

5. Rheology:

The non-newtonian flow characteristics of gelling agent and flocculated solid dispersion solutions are typified by a reduction in viscosity with an increase in

shear rate. They are hence called pseudoplasticity, or pseudo-plastic solutions. The fragile structure of inorganic particles scattered in water is disturbed when shear force is applied, and the breakdown of interparticle connection results in a greater propensity to flow. Similarity, when macromolecules are subjected to shear stress, they align along the direction of the tension.^[54]

3. Material And Methodology:

3.1 Extraction Process Of Herbs:

1. Extraction process for *Blumea balsamifera* leaves :^[55,56]

There were multiple processes involved in the manufacture of blumea balsamifera leaf extract. We started by cleaning the leaves to get rid of any dirt, insects, and other plants that were affixed to them. After that, we cleaned and dried them without leaving them in the sun. The dried leaves are then crushed into a powder using a blender. After that, we put 2000g of the powder in a container, submerged it in 1000ml of ethyl acetate, and allowed it to macerate for whole day. The filtrate was then obtained by filtering the extracts via filter paper. After that, we soaked the residues in the solvent once more, repeating the procedure until the solvent turned colorless.

2. Extraction process for *Moringa seed* :^[57]

The leaves of moringa oleifera were stripped from their stalks, and seeds were taken out of the pods and dehusked. They were shade dried for two weeks at an average room temperature, turning the seeds regularly to prevent fungal growth. They were kept out of direct sunlight to protect the active compounds. The white seed kernels and the leaves were each ground into a powder using a blender. The powdered seeds and leaves were stored in clean, sterile, airtight containers until Further processing. The extraction were conducted using four different solvents: Water, petroleum ether, ethyl acetate, and pure ethanol. Solvents were employed to soak the powdered plant material at a ratio of 1:5 (W/V), which is 1:4 to 1:16. For 72hours, the soaked plant material were let to stand in order to extract plant compound filtrates.



3. Extraction process for Alum :^[58]

Alum are freely soluble in water (especially hot water)

4. Extraction process for Neem leaves :^[59]

To get rid of dust and debris, the gathered *Azadirachta indica* leaves were rinsed with sterile distilled water and cleaned under running tap water. After washing, the leaves were sorted, divided, and allow to dry in a shed. A dry mechanical grinder was used to grind the dried leaves that had been shed. To get the fine powder, the dry powder was run through a mesh screen. 250 millilitres of distilled water were combined with fifty gram of powdered leaves. This conical flask was tightly sealed and allowed to macerate for 48 hours at room temperature. The contents of the flask were shaken every two hours throughout this time. A muslin cloth was used to filter the contents of the conical flask. Whatman number 1 filter paper was used to filter the small amount of filtrate that was remained in the flask after it had been rinsed twice. The filtrate was moved to a sterile evaporating dish and left under a fan to allow the solvent to evaporate. The extract that remained in the bowl after the solvent had completely evaporated was transferred to sealed screw-cap vials and kept in the refrigerator until it was needed for an experiment.

5. Extraction process for Tulsi leaves :^[60]

The collected leaves were cleaned with water to eliminate dusts and material that were present on the surface of the tulsi leaves from its habitats. The clean dust free tulsi leaves were shade dried at room temperature. After a period of 4-5 days to get the extract, the tulsi leaves were grind to fine powder using a grinding machine than the powder material. The fine powder of tulsi was placed in a clean container in order to be prepared for extraction. Aqueous extract preparation of *Ocimum sanctum* (leaves)- The leaves extract of *Ocimum sanctum* was taken in adequate quantities using distilled water. The procedure involved a step where 20g of powdered *Ocimum sanctum* leaves were placed in 200ml beaker, and then 100ml of distilled water was added to the beaker. The mixture was left to sit in the room temperature (approximately 22hrs) for proper mixing and also proper mixing and also proper elucidation of

the extract to dissolve in the solvent. The extract was then filtered using muslin cloth and then whatman no.1 filter paper to get a green coloured filtrate, which was used in the experiment.



Figure 12 : Extraction process

Figure 13 : Filtration

3.2 Formulation Of Gel:

A herbal gel for the purpose of blood coagulation involves incorporating *Blumea* leaf extract, *Moringa* seed extract, Alum solution, Neem leaf extract and Tulsi leaf extract in an appropriate gel base to create the required product. This formula would be beneficial for the purpose of blood coagulation at the required sites by accelerating the hemostatic activity with its antimicrobial activity coupled with anti-inflammatory activity benefits. The appropriate gel base for the preparation is made using the right gelling agents to achieve the desired nature, i.e., fluidity with appropriate spreadability for application sites for the required conditions. The appropriate selection of the right excipients would enable the formulation to exhibit required efficacy, stability and application for the described use of the product with requirements for wounds, etc.

Formulation Table:



Table 2 : Formulation table

INGREDIENT NAME	BATCH		
	I	II	III
Blumea leaf extract	1 ml	3 ml	4 ml
Moringa seed extract	2 ml	3 ml	4 ml
Alum extract	0.78 ml	1 ml	1.25 ml
Neem leaf extract	2 ml	3 ml	3 ml
Tulsi leaf extract	1.5 ml	2 ml	3 ml
Carbopol 940	2 gm	2 gm	2 gm
Propylene glycol	7.5 ml	7.5 ml	7.5 ml
Glycerin	3.5 ml	3.5 ml	3.5 ml
Methyl paraben	1 ml	1 ml	1 ml
Triethanolamine	q.s.	q.s.	q.s.
Distilled Water	q.s.	q.s.	q.s.

Role of Ingredients:**Table 3 : Role of Ingredients**

Sr. No.	NAME OF INGREDIENTS	ROLE
1	Blumea leaf extract	As blood coagulating agent
2	Moringa seed extract	Helps in blood coagulation
3	Alum extract	As Astringent
4	Neem leaf extract	Anti Oxidant agent
5	Tulsi leaf extract	Anti Septic agent
6	Carbopol 940	Gelling agent
7	Triethanolamine	As stabilizer
8	Methyl Paraben	As preservative
9	Distilled water	As solvent

3.3 PROCEDURE TO PREPARE GEL:**Preparation of gel base :**

Weight required quantity of Carbopol 940 in three different beakers and add sufficient quantity of distilled water in each beaker. Stir it constantly for properly disperse carbopol in distilled water. Allow it to swell for 30 minutes or more as require. Add Glycerin and Propylene glycol in this base as per given quantity in each beaker.

Addition of Active ingredients/extracts :

Add all extracts in different ratio in different beaker. Stir well for proper mixing of all extract with gel base. Using this process, Three herbal gel was prepared which having different concentration of all extracts in each gel.

Addition of other agents :

Add required amount of preservatives in gel. Stir well for proper mixing.

Adjusting the pH of gel :

Check the pH of all gel and adjust it as same as skin pH 5.5 to 6.5 . Slowly add Triethanolamine to adjust



the pH to the desired range because it neutralize the carbopol 940. Stirr it well for proper neutralization and homogeneity.

Ensure homogeneity of all three gels and smoothness with no lumps or air bubbles. Evaluate all physical properties of gel.

Final mixing :



Figure 14 : Preparation of Batch I, Batch II and Batch III of herbal gel

3.4 Evaluation Parameters Of Gel:

1. Physical Evaluation :

Color : The formulations colors were examined in daylight.

Consistency : Skin application was used to test it.

Greasiness : application on the skin was used to assess greasiness.

Odor : the gels' odor was assessed by smelling them.

2. Homogeneity :^[61]

Once the gels were inside the container, each was visually observed. For the presence of aggregates, they were observed.

3. Grittiness :^[62-67]

To test for the presence of particulate matter, the properties of all the compositions are checked under the microscope.

4. PH measurement :^[62-67]

To measure the PH of various gel composition preparations, a digital PH meter will be used. A gram

of the gel will be added after introducing 100ml of fresh distilled water and this will keep a side for 2 hours. The PH level of each composition is to be measured 3 times before computation.

5. Consistency :

To ensure consistency and stiffness, Apply a small amount of gel to the skin to see if the gel flows smoothly or breaks.

6. Moisture content :

Weight 2 gm of herbal gel, dry it in a hot air oven at 105 degrees celsius for 30-60 minutes, then weight the remaining gel to determine the quantity of moisture lost.

$$\text{Moisture \%} = \frac{\text{wet gel weight} - \text{dry gel weight}}{\text{wet gel weight}} * 100$$

7. Total solid content :

Determine the percentage of total solid by weighing a specified amount of herbal gel and evaporating the solvent at 105 degrees celsius until the weight remain constant.

$$\text{Total solid content} = 100 - \text{Moisture \%}$$

8. Spreadability :^[68,69]



It shows the size of the area where gel easily spreads after being applied to the skin or affected area. Spreading value also affects the therapeutic potency. Spreadability is defined as the amount of time, measured in seconds, that two slides take to separate from gel that is positioned between them under a specific stress. Better spreadability is achieved when two slides are separated in less time. The spreadability is calculated,

$$S = M * L / T$$

Where, M = weight attached to the higher slides.

L = Glass slides length.

T = amount of time needed to divided the slides.

9. The drug content :^[62-67]

Quantity of solvent containing the drug is taken, and volume is 100ml. The drug is then mixed and shaken with some measured quality of gel, 1 gm. The absorbance is recorded from UV-spectrophotometer after some dilution of the drug content.

10. Washability :-

After applying the formulation to the skin, washability, i.e., washability when water is introduced, was evaluated following application of the formulate the skin.

3.5 Marketed Formulation:





**Figure 15 : Marketed Formulation of gel
Hemostatic activity**

4. RESULT AND DISCUSSION:

4.1 Phytochemical Analysis :-^[70]

1. For Blumea balsamifera :

It contains chemical constituents like Alkaloids, Flavonoids, Tannins etc.

Table 4 : Result of Phytochemical analysis of Blumea balsamifera

CHEMICAL CONSTITUENT	TEST	OBSERVATION	INFERENCE
Alkaloids	Mayer's test: Few ml of extract + 1-2 drops of Mayer's reagent along the sides of test tube	A creamy white precipitate	Alkaloids are present. (positive result)
Flavonoids	Alkaline reagent test: 1 ml of extract + 2 ml of 2% NaOH solution (+ few drops dil. HCl)	An intense yellow colour observe (this becomes colourless on addition of diluted acid)	Flavonoids are present. (positive result)
Tannins and Phenolics	Ferric chloride test: Aqueous solution of extract + few drops 5% ferric chloride solution	Dark green colour solution	Tannins and Phenolics are present. (positive result)
Terpenoids	5ml of plant extract + 2 ml of chloroform + 3 ml of conc. H ₂ SO ₄	Reddish brown interface	Terpenoids are present. (positive result)
Glycosides (cardiac glycosides)	Keller - Killani test: 1 ml extract + 1.5 ml glacial acetic acid + 1 drop of 5% ferric chloride + conc. H ₂ SO ₄ (from the side of test tube)	Brown ring at layer	Cardiac glycoside is present. (positive result)
Steroids	Libermann Burchard test: 50 gm extract is dissolved in 2 ml acetic anhydride + 1-2 drops of conc. H ₂ SO ₄ from the side of test tube	Bluish - Green colour	Steroids are present. (positive result)

2. For Moringa extract :

It contains chemical constituents like Alkaloids, Tannins, Glycosides etc.

Table 5 : Result of Phytochemical analysis of Moringa extract

CHEMICAL CONSTITUENT	TEST	OBSERVATION	INFERENCE
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Alkaloids	Mayer's test: Few ml of extract + 1-2 drops of Mayer's reagent along the sides of test tube	A creamy white precipitate	Alkaloids are present. (positive result)
Tannins	Gelatin test: Plant extract is dissolved in 5 ml distilled water + 1% gelatin solution + 10% NaCl	A white precipitate	Tannins are present. (positive result)
Saponins	Foam test: 0.5 gm extract + 2ml of Water shake well	Persistent foam	Saponins are present. (positive result)
Glycosides (cardiac glycosides)	Keller - Killani test: 1 ml extract + 1.5 ml glacial acetic acid + 1 drop of 5% ferric chloride + conc. H_2SO_4 (from the side of test tube)	Brown ring at layer	Cardiac glycoside is present. (positive result)
carbohydrate	Molisch's test: 2 ml extract + 2 drops of Molisch's reagent + 1 ml conc. H_2SO_4 from the side of test tube	Violet ring at interphase between two layers	Carbohydrate is present. (positive result)

3. For Alum :

It contains chemical constituents like Sulfate, Aluminium etc.

Table 6 : Result of chemical analysis of Alum

CHEMICAL CONSTITUENT / TEST NAME	TEST	OBSERVATION	INFERENCE
Sulfate Test	Test solution + Few drops of $BaCl_2$ + Dil. HCl	A White precipitate	Sulfate group is present. (positive result)
Aluminium Test	Test solution + Ammonium hydroxide or Sodium hydroxide dropwise	White gelatinous precipitates	Aluminium is present. (positive result)
Solubility Test	Dissolves Alum in water	A Clear, Colourless solution	Indicate purity and solubility of Alum. (positive result)
pH Test	Use pH meter or pH paper	Slightly acidic	Indicate acidic nature.

4. For Neem :

It contains chemical constituents like Alkaloids, Flavonoids, Saponins etc.

Table 7 : Result of Phytochemical analysis of Neem

CHEMICAL CONSTITUENT	TEST	OBSERVATION	INFERENCE
Alkaloids	Wagner's Test: Few ml of extract + 1-2 drops of Wagner's reagent (from side of test tube)	A Brown / Reddish precipitates	Alkaloids are present. (positive result)
Flavonoids	Lead acetate Test: 1 ml plant extract + few drops of 10% lead acetate solution	A Yellow precipitates	Flavonoids are present. (positive result)
Saponins	Foam Test: 0.5 gm extract + 2ml of Water shake well	Persistent foam	Saponins are present. (positive result)
Tannins and Phenolics	Ferric chloride Test: Aqueous solution of extract + few drops 5% ferric chloride solution	Dark green colour solution	Tannins and Phenolics are present. (positive result)
Terpenoids	Salkowski's Test: Extract + few drops of conc. H ₂ SO ₄ (shaken well and allowed to stand)	Golden yellow layer at bottom	Triterpinoids are present. (positive result)

5. For Tulsi :

It contains chemical constituents like Alkaloids, Flavonoids, Saponins etc.

Table 8 : Result of Phytochemical analysis of Tulsi

CHEMICAL CONSTITUENT	TEST	OBSERVATION	INFERENCE
Alkaloids	Wagner's Test: Few ml of extract + 1-2 drops of Wagner's reagent (from side of test tube)	A Brown / Reddish precipitates	Alkaloids are present. (positive result)
Flavonoids	Alkaline reagent test: 1 ml of extract + 2 ml of 2% NaOH solution (+ few drops dil. HCl)	An intense yellow colour observe (this becomes colourless on addition of diluted acid)	Flavonoids are present. (positive result)
Saponins	Foam Test: 0.5 gm extract + 2ml of Water shake well	Persistent foam	Saponins are present. (positive result)



Tannins and Phenolics	Ferric chloride Test: Aqueous solution of extract + few drops 5% ferric chloride solution	Dark green colour solution	Tannins and Phenolics are present. (positive result)
Proteins	Xanthoproteic Test: Plant extract + few drops of conc. Nitric acid	Yellow colour solution	Proteins are present. (positive result)
carbohydrate	Molisch's test: 2 ml extract + 2 drops of Molisch's reagent + 1 ml conc. H ₂ SO ₄ from the side of test tube	Violet ring at interphase between two layers	Carbohydrate is present. (positive result)

4.2 Result Of Chemical Analysis :-



Figure 16 : Result of Phytochemical test of *Blumea balsamifera*

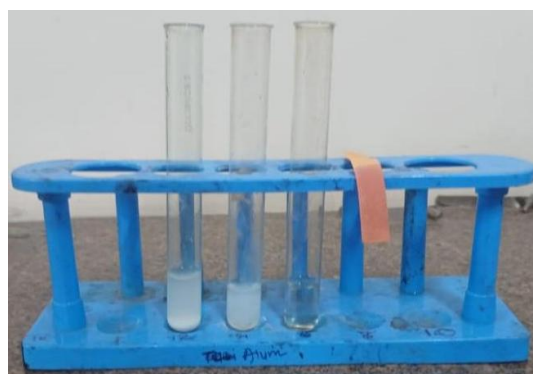


Figure 18 : Result of chemical test of Alum



Figure 17 : Result of Phytochemical test of Moringa extract



Figure 19 : Result of Phytochemical test of Neem



Figure 20 : Result of Phytochemical test of Tulsi

4.2 Result Of Evaluation Parameters:

Table 9 : Result of physical appearance

Colour	Brown
Texture	Smooth Semi-solid gel
Odour	Pleasant

Table 10 : Result of Homogeneity

FORMULATION NUMBER	HOMOGENICITY
Batch 1	Homogeneous
Batch 2	Homogeneous
Batch 3	Homogeneous

Table 11 : Result of Grittiness

FORMULATION NUMBER	GRITTIENESS
Batch 1	Free from Grittiness
Batch 2	Free from Grittiness
Batch 3	Free from Grittiness

Table 12 : Result of pH

FORMULATION NUMBER	pH RANGE
Batch 1	5.95
Batch 2	6.14
Batch 3	6.48

Table 13 : Result of Consistency

FORMULATION NUMBER	CONSISTENCY
Batch 1	Transparant Semisolid

Batch 2	Transparant Semisolid
Batch 3	Transparant Semisolid

Table 14 : Result of Moisture content

FORMULATION NUMBER	% MOISTURE CONTENT
Batch 1	0.95 %
Batch 2	1.05 %
Batch 3	1.13 %

Table 15 : Result of Total solid content

FORMULATION NUMBER	% TOTAL SOLID CONTENT
Batch 1	99.05 %
Batch 2	98.95 %
Batch 3	98.87 %

Table 16 : Result of Spreadability

FORMULATION NUMBER	SPREADABILITY
Batch 1	0.8 gm.cm/sec.
Batch 2	1.00 gm.cm/sec.
Batch 3	1.33 gm.cm/sec.

Table 17 : Result of Washability

FORMULATION NUMBER	WASHABILITY
Batch 1	Easily washable
Batch 2	Easily washable
Batch 3	Easily washable

CONCLUSION:

The creation of a poly-herbal haemostatic gel that was robust, stable and aesthetically pleasing made the study successful in the end. By combining ultramodern pharmaceutical wisdom with traditional ethanobotany, the study fulfilled important mileposts. *Blumea balsamifera* and *Moringa* seeds produce a binary medium of action that efficiently activates the foreign pathway of the coagulation waterfall, causing a “thrombin burst”. The stylish base forcing that the active constituents remain at the point of injury and maintain the cooling goods and pathogen resistant edge is Carbopol 940.



Superior physical profile includes all phrasings passed variable rigorous evaluation for washability, unity and grit, which ensures high case compliance and ease of use, indeed under exigency and clinical conditions. Unlike the precious synthetic sealants, which may provoke vexation in the skin, the herbal gel is made up of biocompatible constituents which are not only bring effectiveness but also environment friendly. In conclusion, this herbal gel formula has moved the conception of topical crack care forward in hops and bounds, furnishing an effective and accessible remedy for rapid-fire blood coagulation and infection control.

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