Journal of Chemical Health Risks

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JCHR (2024) 14(6), 2210-2218 | ISSN:2251-6727

Design and Evaluation of Bio-Degradable Cosmetic Wipes with Polyherbal Extracts in the Treatment of Acne in Male Adolescents

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(Received: 16 September 2024 Revised: 11 October 2024 Accepted: 11 December 2024)

KEYWORDS

Polyherbal gel, Biodegradable paper, Acne treatment, Neem extract, Pomegranate peel, Sustained release

ABSTRACT:

Background: The increasing prevalence of acne and associated skin conditions necessitates the development of eco-friendly and effective therapeutic formulations. Herbal extracts, known for their bioactive properties, have gained attention as alternatives to synthetic treatments. Neem leaf extract, pomegranate peel extract, flaxseed oil, and lemon oil possess significant antimicrobial, anti-inflammatory, and antioxidant activities, making them promising candidates for anti-acne formulations. This study aims to formulate and evaluate polyherbal gels using biodegradable components, ensuring enhanced application and sustainability.

Materials and Methods: Two gel formulations were prepared using Carbopol (F1) and carboxymethyl cellulose (CMC, F2) as polymer bases. The herbal extracts were incorporated alongside other excipients to achieve optimal gel consistency. The gels were further spread onto biodegradable paper to create dissolvable sheets. Physicochemical properties, including pH, homogeneity, and spreadability, were evaluated. Drug content was assessed using the Folin-Ciocalteu method, while *in-vitro* diffusion studies were conducted using a Franz diffusion cell. The release kinetics were analyzed using mathematical models, including Zero Order, First Order, Higuchi, and Korsmeyer-Peppas. Antimicrobial activity was tested against *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. Antioxidant properties were determined through DPPH and nitric oxide scavenging assays.

Results: Both formulations exhibited desirable physical properties, uniformity, and drug content. *In-vitro* diffusion studies showed sustained release profiles for F1 and F2, with release mechanisms predominantly governed by diffusion. Antimicrobial testing demonstrated significant inhibition against tested pathogens, and antioxidant assays revealed strong free radical scavenging activity.

Conclusion: The polyherbal gel formulations incorporating biodegradable paper present a novel, eco-friendly, and effective approach for acne treatment. This study underscores the potential of integrating traditional herbal medicine with modern pharmaceutical techniques to develop sustainable therapeutic solutions.

1. Introduction

In recent years, the use of herbal remedies for both the prevention and treatment of various diseases has grown significantly. This rise is largely attributed to the perception of herbal products as safe, effective, and conducive to overall health and wellness. Numerous studies have highlighted the antibacterial properties of natural extracts and active ingredients derived from plants; however, the clinical validation of many such remedies remains limited.[1]

The skin, as the body's outermost layer, serves as a critical barrier against ultraviolet (UV) radiation and

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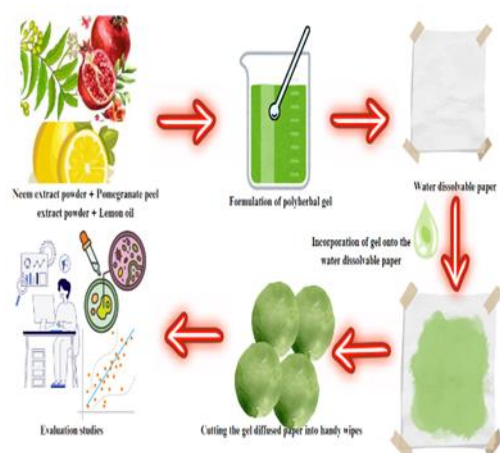
other environmental aggressors. Prolonged UV exposure, particularly on the face, accelerates skin aging. UV radiation is categorized into UVA and UVB. While UVB rays predominantly affect the epidermis and are primarily responsible for sunburn, UVA rays penetrate deeper into the dermis, leading to the production of free radicals. [2] Free radicals are highly reactive molecules with unpaired electrons that can cause oxidative damage to cells and tissues. Antioxidants play a pivotal role in neutralizing reactive oxygen species (ROS) and preventing oxidative damage.[3]



Graphical abstract

Acne vulgaris, a chronic inflammatory condition of the pilosebaceous unit, is one of the most common dermatological issues, particularly affecting adolescents and young adults.[4] Research from the Global Burden of Disease (GBD) study indicates that acne affects approximately 85% of individuals aged 12 to 25 years.[5] Acne is characterized by several factors, including excessive sebum production, follicular hyperkeratinization, oxidative stress, and the release of inflammatory mediators. The condition is further exacerbated by hormonal imbalances, bacterial colonization (primarily *Cutibacterium acnes* and *Staphylococcus epidermidis*), and external factors.[6]

Pathogenesis involves androgen-mediated stimulation of sebaceous gland activity and follicular hyperkeratinization, leading to the obstruction of the pilosebaceous unit.[7] This obstruction facilitates the proliferation of *C. acnes*, triggering an inflammatory cascade. The inflammatory response involves the activation of conventional and unconventional complement pathways, including the release of C5a neutrophil chemotactic factors and hydrolases, which contribute to tissue damage. [8,9] The management of acne often requires addressing these multifaceted pathogenic factors. However, conventional treatments are associated with adverse effects such as dryness, irritation, and photosensitivity, underscoring the need for safer, effective alternatives.

1.1Types of Acne

Acne can be classified based on severity into mild, moderate, and severe forms:

1.1.1. Mild Acne

Mild acne is characterized by the presence of comedones, commonly known as blackheads or whiteheads, which result from blocked skin pores. Blackheads occur when melanin interacts with oxygen, while whiteheads remain closed with a white or yellow tip. Excessive oil production can exacerbate bacterial growth, leading to inflammatory acne.

1.1.2. Moderate Acne

Moderate acne involves a greater number of lesions, including inflamed papules (small raised bumps) and pustules (yellow pus-filled bumps).

1.1.3. Severe Acne

Severe acne is marked by numerous pustules, nodules, and papules, often accompanied by redness, discomfort, and the potential for scarring. The condition is typically observed during puberty, driven by increased androgen production or heightened sensitivity of androgen receptors. [10] These hormonal changes induce follicular hyperkeratinization, enlargement of sebaceous glands, and excessive sebum production, culminating in the formation of comedones and inflammation.[11] When follicular hyperkeratosis hinders the normal flow of sebum to the skin's surface, a microcomedo forms. As sebum accumulates, the microcomedo can develop into a visible comedo. *C. acnes* play a significant role in triggering inflammation in acne, and its prevalence notably increases during puberty [12,13]

Given the multifactorial nature of acne pathogenesis and the limitations of existing therapies, there is a pressing need to explore novel approaches. Bio-degradable cosmetic wipes formulated with polyherbal extracts offer a promising, user-friendly solution for acne management, particularly among male adolescents.

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These formulations aim to integrate the antibacterial, anti-inflammatory, and antioxidant properties of herbal ingredients to address acne comprehensively while minimizing adverse effects.

2.Materials and Methods

2.1. Formulation of gel using polyherbal extract:

2.1.1. Preparation of gel base:

The gel base was formulated using two different polymers: Carbopol (F1) and Carboxymethyl Cellulose (CMC) (F2). For F1, 1 g of Carbopol was dispersed in 30 mL of distilled water using a mixer at 700-800 rpm for 30-45 minutes. Separately, 1 g each of neem leaves extract powder and pomegranate peel extract powder was dissolved in 10 mL of propylene glycol, and the remaining 15 mL of propylene glycol was added to the mixing formulation. To this mixture, 1 mL of flaxseed oil and 3-4 drops of lemon oil were added. Preservatives, including 0.05 g each of propylparaben and methylparaben, were incorporated into the formulation. Triethanolamine was gradually added to adjust the pH of the gel to a neutral range. If necessary, methylene blue was added to impart a pleasant green color.

For F2, the same procedure was followed, substituting Carbopol with CMC. The detailed composition of both formulations is provided in Table 1.

Fig 1: Formulated gel

Table 1: Composition for the formulation of gel using Carbopol and CMC polymers

Ingredients	F1 [Carbopol]	F2 [CMC]
Neem Extract powder (g)	1	1
Pomegranate extract powder(g)	1	1
Lemon Oil(ml)	1	1
Distilled water (ml)	30	30
Propylene Glycol (ml)	25	25
Propyl paraben (g)	0.5	0.5
Methylparaben (g)	0.5	0.5
Flax seed oil (ml)	1	1
Triethanol amine	q.s	q.s

2.1.2. Application of Gel to Paper:

The prepared gel formulations were adjusted to a thin, pourable consistency and evenly spread onto biodegradable, water-dissolvable paper. The gel-coated paper was then air-dried (Fig. 2).

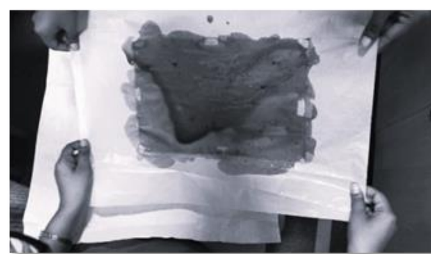

Fig 2: Incorporation of gel onto bio-degradable paper

3.Evaluation Tests for Polyherbal Gel

3.1. Physical Appearance

The formulated anti-acne gel was visually assessed for color, consistency, and overall appearance.

3.2. pH

The pH of the gel was determined by dispersing 5 g of the formulation in 50 mL of distilled water and measuring the pH using a calibrated digital pH meter.

3.3. Homogeneity

The gel formulations were visually inspected to evaluate their homogeneity, ensuring no particulate matter or lumps were present.

3.4. Spreadability:

The spreadability of the gel was evaluated using two glass slides (6 × 2 cm each). The formulation was sandwiched between the slides, and a 100 g weight was applied to ensure uniform spreading. After removing the weight, excess gel was scraped off. A 20 g load was attached to one end of the top slide via a pulley system, while the bottom slide was fixed. The time required for the top slide to travel 6 cm and detach from the bottom

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slide was recorded. The spreadability was calculated using the formula:

$$Spreadability\ (s) = m \times l/t$$

Where, S= Spreadability (gcm/sec), m = weight attached to the top slide l= Glass slide length,t = time (s)

3.5 Drug Content:

To determine the drug content, 1 g of gel was dissolved in 10 mL of methanol in a volumetric flask. A 3 mL aliquot of this stock solution was mixed with 1 mL of Folin-Ciocalteu reagent (diluted 1:10 with distilled water) and 1 mL of sodium carbonate solution (7.5 g/L). The mixture was vortexed for 15 seconds and allowed to stand for 10 minutes for color development. The absorbance was measured spectrophotometrically at 765 nm using an appropriate blank.

3.6. *In – vitro* Diffusion studies:

The in-vitro diffusion study of the formulated gels was conducted using a vertical Franz diffusion cell equipped with a dialysis membrane. Prior to the experiment, the dialysis membrane was soaked in phosphate buffer (pH 7.4) to ensure hydration. The membrane was then securely affixed to one end of the diffusion cell's hollow glass tube. The receptor compartment, a beaker containing 100 mL of phosphate buffer (pH 7.4), was maintained at a constant temperature of 37 ± 0.5 °C using a thermostatic water bath. One gram of each gel formulation was evenly applied to the membrane's surface. Magnetic stirring was employed to ensure uniform mixing in the receptor compartment. At predetermined time intervals, 2 mL aliquots were withdrawn from the receptor compartment and immediately replaced with an equal volume of fresh phosphate buffer to maintain sink conditions. The drug concentration in the withdrawn samples was quantified using a UV-visible spectrophotometer at 250 nm, with appropriate blanks for calibration.

3.7. Release studies:

The release kinetics were analyzed using established mathematical models to understand the mechanism and rate of drug release. The models employed included Zero Order, which examines time-dependent release, First Order, which considers concentration-dependent release, Higuchi, which explores diffusion-based release mechanisms, and Korsmeyer-Peppas, which identifies the nature of the release mechanism (e.g., Fickian or non-Fickian transport). The data obtained from the drug release studies were fitted into these models, and the correlation coefficients (R^2 values) were calculated to determine the most suitable release mechanism for the formulations.

3.8. Antimicrobial Activity for the formulated gel:

The antimicrobial activity of the formulated gel was assessed by evaluating microbial limits against selected bacterial strains, including *Escherichia coli*, *Salmonella spp.*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*. The total bacterial count (TBC) and total fungal count (TFC) were determined as per standard microbiological protocols.

3.9. Anti - Oxidant Assay:

3.9.1. DPPH radical scavenging assay for the formulated gel

The antioxidant potential of the formulated gel was evaluated using the DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging assay. Test solutions of the gel at varying concentrations (100, 200, 400, 800, and 1000 µg/mL) were prepared in distilled water. Standard ascorbic acid solutions were used for comparison. Equal volumes of each test solution and DPPH solution (0.1 mM in methanol) were mixed in labeled tubes. The mixtures were incubated in the dark at room temperature for 30 minutes. The absorbance of each sample was measured at 517 nm using a UV-visible spectrophotometer. The percentage inhibition was calculated using the formula:

$$\%\ Inhibition\ Calculation:$$

$$\frac{(Absorbance\ of\ control - Absorbance\ of\ sample)}{Absorbacne\ of\ control\ X\ 100}$$

3.9.2. Nitric Oxide Scavenging Assay for the formulated gel:

Nitric oxide scavenging activity was assessed using sodium nitroprusside as a nitric oxide donor. Reaction mixtures were prepared by combining sodium nitroprusside (10 mM) with test samples of the gel at concentrations of 100, 200, 400, 800, and 1000 µg/mL in distilled water. Ascorbic acid served as the standard. The mixtures were incubated at 37 °C for 4 hours, after which 0.5 mL of Griess reagent (1% sulfanilamide in 5%

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phosphoric acid and 0.1% N-(1-naphthyl) ethylenediamine dihydrochloride) was added to each reaction mixture. The absorbance was measured at 546 nm using a UV-visible spectrophotometer. The scavenging activity was calculated as described above.

$$\% \, Inhibition \, Calculation: \frac{(Absorbance \, of \, control - Absorbance \, of \, sample)}{Absorbacne \, of \, control \, X \, 100}$$

4. Evaluation test for the gel incorporated paper wipes:

4.1. Physicochemical parameters:

The texture, color, and smell of the prepared papers were assessed to ensure uniformity and aesthetic appeal.

4.2. pH:

The pH of the water-dissolved gel-infused paper solution was measured using a calibrated pH meter to ensure compatibility with skin and to avoid irritation upon application.

4.3 Paper spread-ability:

The spreadability of the product on the surface of the paper was evaluated by spreading a pinch of the product evenly. A smooth and uniform spread was considered an indicator of desirable application properties.

4.4 Anti-Bacterial activity for paper:

The antibacterial activity of the gel-infused paper was evaluated using the agar diffusion method. Nutrient agar medium was prepared, and the following bacterial strains were cultured and used for testing: *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Escherichia coli*, and *Streptococcus mutans*.

The standard antibiotics demonstrated zones of inhibition measuring 25 mm, 20 mm, 23 mm, and 22 mm, respectively. The antibacterial activity of the formulations (F1 and F2) was determined by measuring the zones of inhibition for the gel-induced paper. These zones were compared against the standards to assess the efficacy of the formulations.

5. Results and Discussion

5.1. Evaluation for the formulated gel

5.1.1Physical Appearance:

The gel was in brown colour, which has a characteristic odour and a smooth texture.

5.1.2. pH

The pH of the prepared formulations was determined using a digital pH meter. The pH of the Carbopol-based gel (F1) was found to be 6.6 ± 0.12**,** while the pH of the CMC-based gel (F2) was 6.8 ± 0.18, indicating suitability for topical application.

5.1.3. Homogeneity:

All of the gel formulations were free from lumps or grittiness. (Fig 3)

Fig 3: Homogeneity Test

5.1.4. Spreadability:

The spreadability analysis highlights that CMC-based formulations generally outperform Carbopol-based ones, with higher values across all batches, indicating superior ease of application. Among the Carbopol formulations, Showed the spreadability 19.83 ± 0.03 mm. For CMC, demonstrated the highest spreadability 21.05 ± 0.02 mm. These findings suggest that CMC provides better shear-thinning behavior, making it a preferable gelling agent for formulations requiring enhanced spreadability and uniform application.

5.1.5. Drug content:

All Carbopol formulations had drug contents ranging from 10.07 mg/g to 20.75 mg/g. On the other hand, all CMC formulations had drug contents ranging from 18.65 mg/g to 24.84 mg/g.

5.1.6. ***In – vitro*** **Diffusion studies**

The *in-vitro* drug release study, as depicted in the graph, illustrates a gradual increase in absorbance over time for

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both Carbopol and CMC formulations, indicating sustained drug release profiles. At 60 minutes, the CMC formulation exhibited higher absorbance (0.432 nm) compared to Carbopol (0.454 nm), as shown in the graph (Fig. 4), suggesting slightly faster drug release. The graph highlights that CMC consistently demonstrated better drug diffusion, likely due to its lower viscosity, making it ideal for formulations requiring enhanced release kinetics and rapid therapeutic effects.

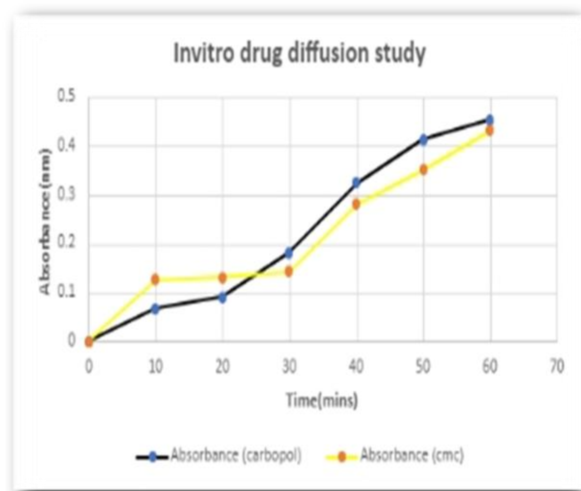

Fig 4: *In-vitro* diffusion studies for Carbopol and CMC gel formulations

5.1.7 Release kinetics

The release kinetics of the CMC formulations, as shown in Graph (Fig 5), were analyzed using Zero Order, First Order, Higuchi, and Korsmeyer-Peppas models. The Zero Order model ($R^2 = 0.9849$) demonstrated a linear drug release over time, suggesting a controlled release mechanism. The Higuchi model ($R^2 = 0.9726$) indicated diffusion-based release. The Korsmeyer-Peppas equation ($R^2 = 0.9641$) further confirmed the diffusion mechanism with a non-Fickian transport pattern. Comparatively, the First Order model ($R^2 = 0.7298$) showed weaker correlation, indicating the release was less dependent on drug concentration. These results highlight sustained and diffusion-driven drug release, favoring therapeutic efficacy.

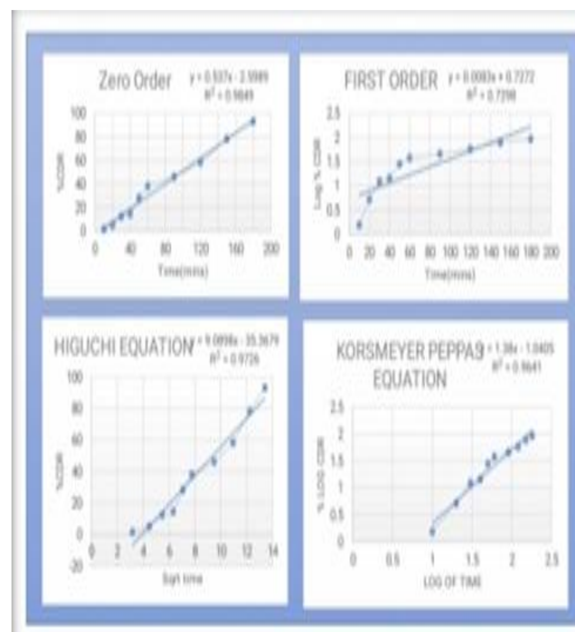

Fig 5: Drug release kinetics of the formulated gel

5.1.8. Anti-Microbial study:

The microbial limit test results, as summarized in Table 2, indicate that the CMC formulation complies with acceptable microbial safety standards except for the presence of *Pseudomonas*. Key pathogenic microorganisms, including *E. coli*, *Salmonella*, and *Staphylococcus*, were absent, ensuring safety against common contaminants. The total bacterial count was within permissible limits at 19 cfu/gm, and yeasts and molds were also absent [Fig 6], highlighting the formulation's fungal safety. However, the presence of *Pseudomonas* necessitates further investigation and potential refinement of the formulation or storage process to ensure complete microbial safety, aligning with pharmaceutical-grade quality standards.

Table 2: Anti-Microbial study of total bacterial count and fungal count for CMC formulation

Test (Microbial Limit)	**Result**
E. coli	Absent
Salmonella	Absent
Pseudomonas	Present
Staphylococcus	Absent
Total bacterial count	19 cfu/gm *
Yeasts and moulds	Absent

*cfu = Colony-forming unit

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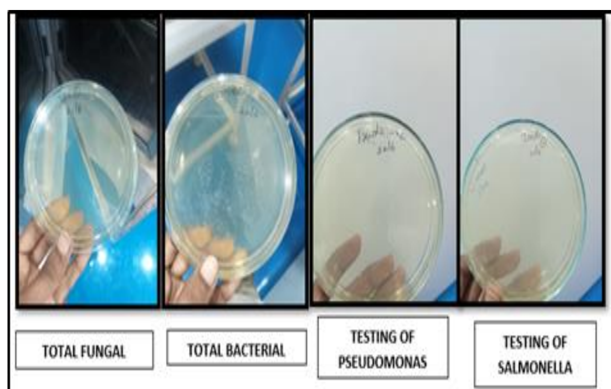

Fig 6: Anti- microbial study for testing of pseudomonas, Salmonella and total fungal, bacterial count

5.1.9. Anti-oxidant study

5.1.9.1. DPPH Assay:

The DPPH radical scavenging assay results, depicted in Fig.7, reveal the antioxidant potential of the formulations. Both CMC and Carbopol formulations exhibited dose-dependent activity, comparable to the standard. At 1000 mg/ml, Carbopol demonstrated the highest inhibition (89.9 ± 0.08%), similar to the standard (89.18 ± 0.05%), while CMC showed slightly lower activity (86.43 ± 0.02%). At lower concentrations, both polymers exhibited significant scavenging activity, with Carbopol consistently outperforming CMC. These results suggest that the formulations, particularly those using Carbopol, possess strong antioxidant properties.

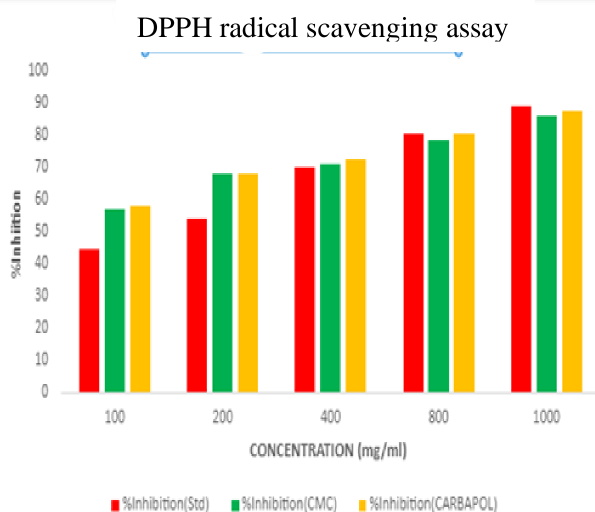

Fig 7: Graph of DPPH radical scavenging Assay

5.1.9.2 Nitric oxide radical scavenging assay:

The nitric oxide radical scavenging assay results, illustrated in Fig. 8, highlight the antioxidant efficacy of the formulations. At a concentration of 100 mg/ml, Carbopol showed the highest inhibition (90.55 ± 0.03%), slightly exceeding both the standard (90.1 ± 0.04%) and CMC (90 ± 0.06%). However, at higher concentrations, the standard maintained stronger inhibition, with 71.4 ± 0.02% at 200 mg/ml compared to CMC (80.65 ± 0.03%) and Carbopol (71.49 ± 0.05%). The trend indicates a decline in activity with increasing concentrations for all groups. These findings underscore Carbopol's strong antioxidant activity at lower concentrations.

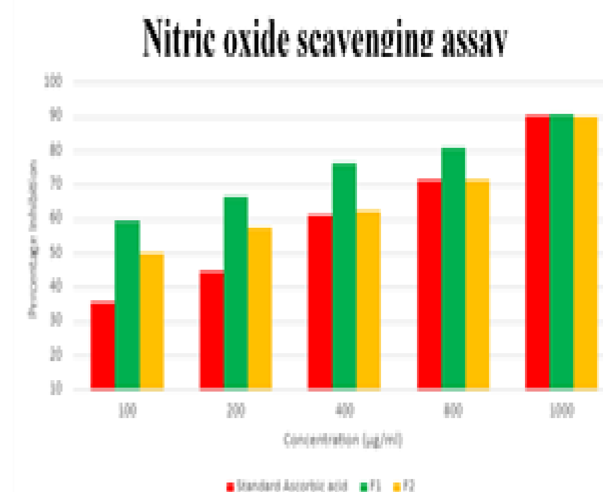

Fig 8: Antioxidant study of formulation and standard by nitric oxide radical scavenging assay

6. Evaluation for the gel incorporated paper wipes

6.1. Physicochemical parameters:

The texture and colour revealed a homogeneous gel integration with consistent paper substrate morphology and the paper exhibited characteristic of gel natural components.

6.2. pH:

The pH of formulated wipe paper was found to be 6.5±0.5 using pH meter

6.3 Paper spread-ability:

Spread-ability tests revealed that the gel-incorporated paper easily allowed product application.

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6.4 Anti-Bacterial activity for paper:

The antibacterial activity results, detailed in Table 3, demonstrate that formulations F1 and F2 effectively inhibit the growth of tested bacterial strains, with zone of inhibition (ZOI) values comparable to standard antibiotics. For *Staphylococcus aureus*, F2 showed a slightly higher ZOI (18 mm) than F1 (17 mm). Against *Klebsiella pneumoniae*, F1 exhibited a higher ZOI (18 mm) than F2 (17 mm). Similarly, *Escherichia coli* and *Streptococcus mutans* showed modest but effective inhibition, with F1 and F2 displaying ZOI values of 15-16 mm and 16-15 mm, respectively. These results suggest F1 and F2 have significant antibacterial potential against diverse pathogens.

Table 3: Anti-bacterial Activity (zone of inhibition)

Bacteria	Antibiotics (mm)	F1[mm]	F2[mm]
Staphylococcus aureus	25mm	17	18
Klebsiella pneumonia	20mm	18	17
Escherichia coli	23mm	15	16
Streptococcus mutans	22mm	16	15

7. Summary and conclusion:

The evaluation of the formulated gel and gel-incorporated paper revealed promising physicochemical, antimicrobial, and antioxidant properties, supporting their potential for therapeutic applications. The gel exhibited a smooth texture, brown color, and a characteristic odor, with a pH range of 6.6±0.12 to 6.8±0.18, indicating compatibility with skin applications. It demonstrated excellent homogeneity without lumps and superior spreadability, particularly in CMC-based formulations. Drug content analysis confirmed uniform distribution, with CMC formulations showing higher drug concentrations compared to Carbopol. *In-vitro* diffusion studies highlighted sustained drug release, with CMC formulations exhibiting faster release kinetics. Release kinetics analysis confirmed a diffusion-driven, non-Fickian mechanism, ensuring controlled and prolonged therapeutic effects. The gel also showed significant antibacterial activity and antioxidant potential, with Carbopol-based formulations outperforming CMC in DPPH and nitric oxide scavenging assays, demonstrating strong free radical inhibition.

The gel-incorporated paper showed excellent physicochemical attributes, maintaining a uniform integration with the gel and optimal pH of 6.5±0.5. Spreadability tests confirmed ease of product application, enhancing usability. Antibacterial studies revealed effective inhibition of pathogens like *Staphylococcus aureus*, *Klebsiella pneumoniae, Escherichia coli*, and *Streptococcus mutans*, with both F1 and F2 formulations showing comparable zones of inhibition to standard antibiotics. These findings suggest that both the gel and paper formulations are well-suited for applications requiring antimicrobial and antioxidant properties, with potential for further development into effective therapeutic and skincare products.

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