International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar – Apr 2025, pp: 118-126 www.ijprajournal.com ISSN: 2456-4494

Formulation and Evaluation of Apple and Goldenseal Combine Extract Gel

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Date of Submission: 05-03-2025 Date of Acceptance: 15-03-2025

ABSTRACT:
This study focuses on the formulation and evaluation of gel formulations combining extracts of Apple and Goldenseal, known for their potent phytochemical properties. Various gelling agents including Carbopol 934, Carbopol 940, Hydroxy Propyl Methyl Cellulose (HPMC), and Sodium Carboxy Methyl Cellulose (Na CMC) were employed at varying concentrations to develop stable gels. The formulations were characterized for homogeneity, pH, viscosity, extrudability, and spreadability. The in vitro release profile of the gels was assessed using Franz diffusion cells, and the antioxidant activity was evaluated using DPPH and ABTS assays. Antimicrobial efficacy was tested using the disc diffusion method, while lipid peroxidation inhibition and pyrogallol red bleaching assays were conducted to explore the antioxidant potential of the formulations. Stability studies were performed under accelerated conditions to ensure the preservation of physical and chemical properties over time. The optimized formulations demonstrated promising therapeutic potential, attributed to the bioactive constituents—such as flavonoids, tannins, and alkaloids—present in the extracts. The results suggest that these gels could be effective in dermatological applications, offering antioxidant, antimicrobial, and stability benefits.

I. INTRODUCTION

Topical formulations are widely used in dermatology for treating skin conditions such as acne, infections, inflammation, and wounds. Recently, there has been increasing interest in natural products due to their safety profile and minimal side effects. Apple peel extract, known for its high antioxidant content, and Goldenseal, a medicinal herb rich in antimicrobial alkaloids like berberine, present an interesting combination for skin treatments. This research focuses on developing a topical gel that combines the benefits of both Apple peel and Goldenseal for enhanced skin protection and healing.

The skin acts as a biological barrier, resisting environmental factors like free radicals, which can cause conditions such as edema, inflammation, and skin cancer. Reactive oxygen species (ROS), produced through cellular processes and environmental exposure, can cause oxidative stress, leading to tissue damage and cellular mutations. Antioxidants help mitigate ROS-induced damage, providing protection against oxidative stress and supporting cellular repair.

In certain skin conditions, such as psoriasis and skin cancer, ROS plays a complex role. For example, ROS can disrupt immune responses, affect skin cell growth, and cause DNA damage, which may lead to cancer initiation. Antioxidants are crucial in reducing ROS damage and are being studied for their therapeutic potential in skin diseases.

This study focuses on the formulation of a gel using a combination of Apple and Goldenseal extracts with different gelling agents such as Carbopol 934, Carbopol 940, Hydroxypropylmethylcellulose (HPMC), and Sodium Carboxymethylcellulose (Na CMC). The process involves mixing the extracts with purified water, adding methyl paraben as a preservative, and varying the concentrations of the gelling agents to achieve the desired consistency. The prepared gel formulations are evaluated for homogeneity, pH, viscosity, extrudability, spreadability, in vitro drug release, antimicrobial activity, antioxidant assays (such as DPPH and ABTS), lipid peroxidation inhibition, and stability. The stability of the gels is tested under different temperature conditions to determine the physical and chemical characteristics over time. Semisolid formulations, such as gels, are widely used for external drug applications, allowing for localized drug release across skin layers. These formulations must be chemically and physically stable, non-irritating, user-friendly, and ensure maximum absorption for effective therapy.

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II. MATERIALS AND METHODS

Chemicals and reagents

Gallic acid and berberinwas procured from Yucca enterprises, Carbopol-934 and Carbopol-940, sodium carboxy methyl cellulose were taken from Kemphasol, Mumbai, hydroxyl propyl methyl cellulose was taken from HI media labs, Mumbai, methyl paraben and triethnolamine was obtained from National Chemicals and Reachem labs, Chennai respectively.

Formulation of gels (Jani R, 2010. Goyal S, 2011. Kaur LP, 2010)

Semisolid dosage form like gels are prepared with various types and concentration of gelling agent like Carbopol 940, Carbopol 934, Sodium Carboxy methyl cellulose, hydroxy propyl methyl cellulose. The selection of gelling agent and its concentration is depend on consistency of the finished product.

Gel preparationof combined extract by using Carbopol 934

Tab.No.1 Formulations of combined extract with varying Carbopol 934 concentrations

Contents	Quantity given for 100 grams		
	A7	A8	A9
Extracts	1gm	1gm	1gm
Carbopol-934	0.5%	1%	1.5
Alkali source	q.s.	q.s.	q.s.
Purified water	q.s. to 100gm	q.s.to 100gm	q.s.to 100gm
Methyl paraben	0.2%	0.2%	0.2%

Procedure

Accurately weighed the Apple and Goldenseal extract in equal quantity/combination and dispersed in the same amount of purified water to make the dispersion of this combined extract. Preservative e.g. methyl paraben was added in very less concentration (0.2%) for the stability of finished product. Then after Carbopol 934 as a gelling agent was added in the dispersion till a clear gel was formed. Then stop the addition of gelling agent andmaintain the pH by using alkali, the ready gel was weighted to make up the final volume.

Gel preparationof combined extract by using Carbopol 940

Tab.No.2 Formulationsof combinedextract with varying Carbopol940 concentrations

Contents	Quantity given for 100grams		
	B7	B8	B9
Extracts	1.0	1.0	1.0
Carbopol 940	0.5	1	1.5
Triethanolamine	q.s.	q.s.	q.s.
Purified water	q.s. to 100gm	q.s. to 100gm	q.s. to 100gm
Methyl paraben (preservative)	0.002	0.002	0.002

Procedure

Apple and Berberiesaristata extract were taken in given quantity and the solution is prepared additionalyaccurate quantity of preservative which is methyl paraben was also mix in the process. The purpose of addition of preservative is to keep the final formulation stable. Then in final stage Carbopol 940 which gellingagent is also mixed in the formulation but during addition of carbapol 940 invia continuously stirred. All this procedure was done by keeping the temperature 50^0C.

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Gel preparationof combined extract by using Hydroxy propyl methyl cellulose

Tab.No.3 Formulations of combined extract gelwith varying hydroxy propyl methyl cellulose concentrations

Contents	Quantity for 100 gm			
	C9	C10	C11	C12
Extract	1gm	1 gm	1 gm	1 gm
HPMC	1	1.5	3	4
Triethanolamine	q.s.	q.s.	q.s.	q.s.
Purified water	q.s.	q.s.	q.s.	q.s.
Methyl paraben	0.002 gm	0.002gm	0.002gm	0.002gm

Procedure

Combination of extract was prepared with equal quantity of both extracts. And all the other ingredients were added in the preparation as per the formulation processes which is used for the individual extract formulations. The final volume of the gel was maintained with additional water. In finalsteep methyl paraben preservative was also incorporated in the preparation.

Gel preparationof combined extract by using Sodium Carboxy methyl cellulose

Tab.No.4. Formulations of combined extract gelwith various concentration CMC

Contents	Quantity for 100gms			
	D9(gms)	D10(gms)	D11(gms)	D12(gms)
Extract	1gm	1gm	1gm	1gm
Na CMC	1	1.5	3	4
Triethanolamine	q.s.	q.s.	q.s.	q.s.
Purified water	98	97.5	96	95
Methyl paraben	0.002	0.002	0.002	0.002

Procedure

For preparation of gel in batches D9, D10, D11, D12 different concentration of the Na CMC were used the combined extract was same in quantity in every preparation that is 1.0 gm. In first step mixture of combination extract and purified water was made. Then in secondly remaining ingredients were added to it stepwise. methyl paraben was added for preservation purpose of the formulation.Then neutralise the prepared gel before make up the volume.

Evaluation of formulated gels

Characterization of gel containing combined extracts of Appleand Berberisaristata (Islam MT, 2004.Chowdary KPR, 1996.Devi US, 2002)

Determination of homogeneity of combine extracts gel.

All the formulated gels were verified for homogeneity by visual examination. They were evaluated for their physical appearance without lumps.

PH Measurements of combine extract gel.

pH meter (digital) was used for measurement pH of all formulated gel of

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combinedextract, pH meter was calibrated with the standard buffers before their each use. A defined amount of combinedextractgel was taken and diluted with distilled water (1:10) and mix together. The electrode of digital pH meter was dip in to the prepared combined extract gel for the measurement of pH. pH of gels are taken in triplicates.

etermination of viscosity of combine extracts gel.

The viscometer used for semisolid preparation is the Brookfield Viscometer and Brookfield Viscometer model no RVTP with type RV 7 was rotated at 20 rpm. 100gm combined extract gel was taken in beaker and RV 7 type spindle is dipped in to beaker containing combined extract gel with rotation of selected spindle for 5 minutes & observed the viscosity.

Extrudability of combine extract gel.

Measurement of the extrudability of the combined extract gel/formulated gel is one of the characteristics reflect their acceptability in the form of application. Extrudability is the significant practical consideration for the ability of force required to extrude the gel which was already filled in tubes that collapsible tubes are made up from metallic material which must be compatible to each ingredients used in the gel with tip opening of 5mm diameter then determined extrudability of prepared combine extractgel.

Determination of spreadabilityof combine extracts gel.

Spreadability is the one of the most important evaluation parameter for the acceptability of product in the form of its application. Measurement of spreadability is done by using 1.0 gm of combined extract gel which was placed in between the 10cmX10cm size two glass slides carefully so that the combined extract gel became sandwich amongst glass plates and by applying 2 kg of load at middle of glass plates. After 30 min result was observed in cm and tabulated.

In vitro Drug release pattern of gels (Shah VP, 1993)

The In vitro release of the combined extract gel formulation was studied by Franz diffusion cell. Study will be carried out by using both standards i.e. Gallic acid and berberine which are present in Apple and Goldensealrespectively. Franz diffusion cell having a glass tube with 2.5 cm diameter as withdrawal port for sample. By using artificial skin membrane(cellophane membrane) donar compartment's glass tube is covered which is open end of the glass tube. At moderated speed 1.0 gm of combined extracts gel was placed and continuously stirred in donor compartment during the this experimentation temperature was 37 ± 1^{0}C. Withdraw 5.0ml of sample throughthe sample port and replace with the buffer solute on for regulation of sink condition and dilute the collected sample if required. Samples were taken for observation for their absorbance(by using buffer pH 6.8 as blank) at 255 nm using UV spectrophotometer.

In-vitro antimicrobial study: Disc diffusion method (Shahidi BH, 2004)

Disc method was working to perform an antimicrobial study using filter paper and agar. The diameter of the whatman paper No.1 was 6 mm which was placed in petridishes which were previously dried. The required test sample solutionconcentration was prepared by using DMSO. The concentration applied onto the disc were ranging from of 20 mg/mL to 100 mg/mL, this application was done with the help of micropipette. The whole process was conductedin aseptic condition. by transferring a loopful of micro-organism the study was carried out and it was spread on to the sterile agar medium plate. The loopful of organism was in a suspension form of about 1/10 ml suspension of suitable organism, which was put over the plate by disc diffusion method.

Anti-oxidant assays of combined extracts gels

DPPH radical scavenging assay (GrzegorzBartosz, 2010)

Gel of combined extract for the free radical (DPPH) activity was conducted by the method described below.

DPPH radical was used to determine the scavenging action of free radical with combined extract gel, by consideringradical scavenging and hydrogen donating activity. 1.0mL of DPPH solution in methanol (0.1nM) was added to 3.0mL of test solutions of compounds at various concentrations. After 30minutes, absorbance of solutions was measured at 517nm.

Calculation of antioxidant assay of combined extract gel for IC50 value

Every conc. of withselected test compounds with itsoptical density and butyrated Hydroxyl Toluene was plotted, by plotting this graph 50%inhibition and IC50 was calculated.

% radical scavenging activity = [(Ac–At)/ Ac] X 100.

Ac is the absorbance of (control) sample,

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At is the absorbance of (test) sample.

ABTS Assay

Reaction between the sample and the stable ABTS+• radical cation measured the antioxidant activity of the test samples.

The decrease in the absorbance is due to reduction of ABTS+•chromophore (blue/green) by the antioxidant which is produced from thepotassium persulfate& ABTS free radical response. 7mM the free radical solution (ABTS) solution was prepared using distilledwater. The reaction between ABTS and potassium persulfate (2.45nM) yielded ABTS radical cation (ABTS+•) and this reactant productpermittedin darkness for more than 12 hours. to not less than 16 hours. At 734 nm absorbance was 0.8 ±0.014, the dilution of prepared solution takes place with the use of a phosphate buffer (2 mM, PH 7.4.). ABTS+• solution was mixed to test sample solutions and then after 1minute absorbance was recorded in UV-Vis spectrophotometer at 734nm. Taken blank solution was the phosphate buffer. The percent of radical scavenging activity of sample was measured using below formula:

$$\% \text{ scavenging activity of radical} = (\text{Astd} - \text{Atest})/\text{Astd} \times 100$$

Where, Astd is the absorbance of the control sample,
Atest is the absorbance of the test sample.

Calculation of ABTS assay of combined extract gel for 50 % inhibition concentration (IC50) By selecting C6H8O2 as the referencesampleremaining tests were carried out thrice and the results were reported in average and standard deviation form.

Lipid peroxidation inhibition assay of combined extract gel

The sample (0.5 mL) was prepared using double distilled water (0.5 mL). The sample was mixed and later TBA-TCA-HCl reagent (2.0mL) was added. After for 15minutes the reaction mix was kept dipped in hot water bath. Once the mixture become cool down the tubes was put for centrifuging for 10minutes at 1000rpm and the supernatant solution was expected. The standard solutions of 2 – 10nM concentrations were reacted in similar way& Analyse for their absorbance of chromophore at 535nm using UV-spectrophotometer with a blank.

Effect of combined gel for bleaching of Pyrogallol Red by Peroxynitrite

Peroxynitrite was formed by reacting with the solution hydrogen peroxide, Nitric acid, and sodium nitrite (2M each) and by addition of 4 M sodium hydroxide in frozen conditions (at -70^0 C). Pyrogallol red solution (100µm) was made using 100mM selected buffer solution with pH 7.4. Peroxynitrite solution was then reacted throughvarious concentration of extract and fractions sample solution and Pyrogallol solution with immediate vortexing up to quarter of hour. Spectral analysis was done at 540 nm.

Stability studies of the combined extract gel formulation (Dantas MG, 2016)

When the combinedextract gel is having better stability for their physical chemical & therapeutic characteristics then the combined extract gel is remains their all characteristics for longer period time. The accelerated stability test (AST) is the practice for measurement of stability of gel at condition of high temperature. When increase in temp. of preparation, melting of producttakesplace.& this condition is not suitable for quality gel. It is not suitable for their physical & chemical stability and hence prepared gel stored in temp. of 4-5^0C& room temperature condition depending on regional atmosphere.Finally prepared was observed at each month for next three months also. Number of parameters restrained for analysis are shown below.

Stability Study of combined extract gel
Physical evaluation of gels

The physical parameters of combined extract gelswere examined. Natural preservative are mainly on the basis on their quality for preparation of combined extract gel. Selection of preservatives in the formulation of combined extract for there stability depend on the characteristics of gelling agent.

Due to required stability of the combined extract gel, physicochemical characterization of active drug and all additives/excipients are to be considered. Present discussion will deal with formulation, evaluation and simultaneous estimation of berberine and gallic acid.

Phytochemicals are considered as secondary metabolites of plant. Quality and quantity of phytochemicals differ from varieties. Phytochemical belongs to group alkaloid, flavonoid and terpenoids have promising agent in human health care through modulation of biological activities.Apple peel contains flavonoids,

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Volume 10, Issue 2 Mar – Apr 2025, pp: 118-126 www.ijprajournal.com ISSN: 2456-4494

ellagitannins along with proanthocyanidincompounds which almost 60% around the fruit.

Pomegranate fruit arils contain additionally, flavonoids are leader polyphenols of fruit, dense tannins and hydrolysable tannins. Hydrolysable tannins including ellagitannins and gallotannins consist of the common constituents present in pomegranate, and punicalagin is the major hydrolysable tannin present in pomegranates.

Apple which included gallocatechins, delphinidin, cyanidin, Gallic acid and sitosterol which had therapeutic properties

Physical Evaluation of combined extract gel

Tab.No.5: Physical evaluation of combined extract gel (A8)

Name of test		R.T.(25^{0}C)	37^{0}C	4^{0}C to 5^{0}C
Inspection	Before	Crystal clear	Crystal clear	Crystal clear
	Final	Crystal clear	Crystal clear	Crystal clear
pH of A8 gel	Before	7.0	6.9	6.9
	Final	7.0	7.0	6.9
Viscosity	Before	43550	43500	43000
	Final	43000	43500	42800
Extrudability	Before	+++	+++	+++
	Final	+++	+++	+++
Spreadability	Before	8.1	7.9	7.9
	Final	8.0	7.9	7.6
Separation of phases		Not seen	Not seen	Not seen
Leakage for A8 gel		absent	absent	absent
Appearance of gel	Before	Soft	Soft	Soft
	Final	Soft	Soft	Soft

Tab.No.6: Physical evaluation of combined extract gel (B8)

Name of test		R.T.(25^{0}C)	37^{0}C	4^{0}C to 5^{0}C
Inspection	Before	Crystal clear	Crystal clear	Crystal clear
	Final	Crystal clear	Crystal clear	Crystal clear
pH of B8 gel	Before	7.1	7.1	6.9
	Final	7.0	7	6.8
Viscosity	Before	41000	41000	41000
	Final	41000	40900	39800
Extrudability	Before	+++	+++	+++
	Final	+++	+++	+++

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Spreadability	Before	7.8	7.7	7.7
	Final	7.7	7.7	7.4
Separation of phases		Not seen	Not seen	Not seen
Leakage for B8 gel		absent	absent	absent
Appereance of gel	Before	Soft	Soft	Soft
	Final	Soft	Soft	Soft

Tab.No.4.35: Physical evaluation of combined extract gel (C10)

Name of test		R.T.(25^{0}C)	37^{0}C	4^{0}C to 5^{0}C
Inspection	Before	Crystal clear	Crystal clear	Crystal clear
	Final	Crystal clear	Crystal clear	Crystal clear
pH of C10 gel	Before	6.9	6.9	6.9
	Final	7.1	7	6.9
Viscosity	Before	40200	40100	40000
	Final	40000	40100	39100
Extrudability	Before	++	+++	++
	Final	++	++	++
Spreadability	Before	7.4	7.4	7.3
	Final	7.3	7.4	7.0
Separation of phases		Not seen	Not seen	Not seen
Leakage forC10 gel		absent	absent	absent
Appereance of gel	Before	Soft	Soft	Soft
	Final	Soft	Soft	Soft

Tab.No.7: Physical evaluation of combined extract gel (D10)

Name of test		R.T.(25^{0}C)	37^{0}C	4^{0}C to 5^{0}C
Inspection	Before	Crystal clear	Crystal clear	Crystal clear
	Final	Crystal clear	Crystal clear	Crystal clear
pH of D10 gel	Before	7.0	6.9	6.9
	Final	7.0	7	6.8
Viscosity	Before	39000	39000	39000
	Final	39000	38800	37800

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Extrudability	Before	++	++	++
	Final	++	++	++
Spreadability	Before	6.9	6.9	6.8
	Final	6.9	6.8	6.4
Separation of phases		Not seen	Not seen	Not seen
Leakage for D10 gel		absent	absent	absent
Appereance of gel	Before	Soft	Soft	Soft
	Final	Soft	Soft	Soft

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