Research Article

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Formulation *in-vitro* evaluation of herbal hydrogel by using "*ricinus communis"* leaf extract

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ABSTRACT

The present study was carried out to formulate "Herbal Hydrogel" by using "Methanolic" and "Petroleum ether" extracts of "*Ricinuscommunis"* leaves, to explore the drug release based on the type and concentration of "Polymers" used in the formulation. Formulation was made by methanolic and petroleum ether extracts of *Ricinuscommunis*and made into gel form. The extract was subjected to preliminary phytochemical screening which indicates the presence of flavanoids, tannins and terpenoids. Isolation of flavonoids was done which consists anti inflammatory activity and by using flavonoids Hydrogel were prepared and the evaluation studies of each formulations were compared.

Keywords: Herbal Hydrogel, Methanolic extract, Petroleum ether extracts, Ricinuscommunis, flavanoids, Polymers, anti inflammatory activity.

INTRODUCTION

Inflammation

Inflammation is a localized protective reaction of cells tissues of the body to allergic or chemical irritation, injury and/or infections. The symptoms of inflammation are characterized by pain, heat, redness, swelling and loss of function that result from dilation of the blood vessels leading to an increased blood supply and from increased intracellular spaces resulting in the movement of leukocytes, protein and fluids into the inflamed regions. This is very necessary to understand the role of chemical mediators of inflammation. These mediators are the substances released as plasma proteins, or that come from cells like mast cells, platelets, neutrophils and monocytes/macrophages. They are triggered by allergic or chemical irritation, injury and infections. These mediators, depending on the duration of injury determine the severity of inflammation and are termed pro-inflammatory fundamental factors. These

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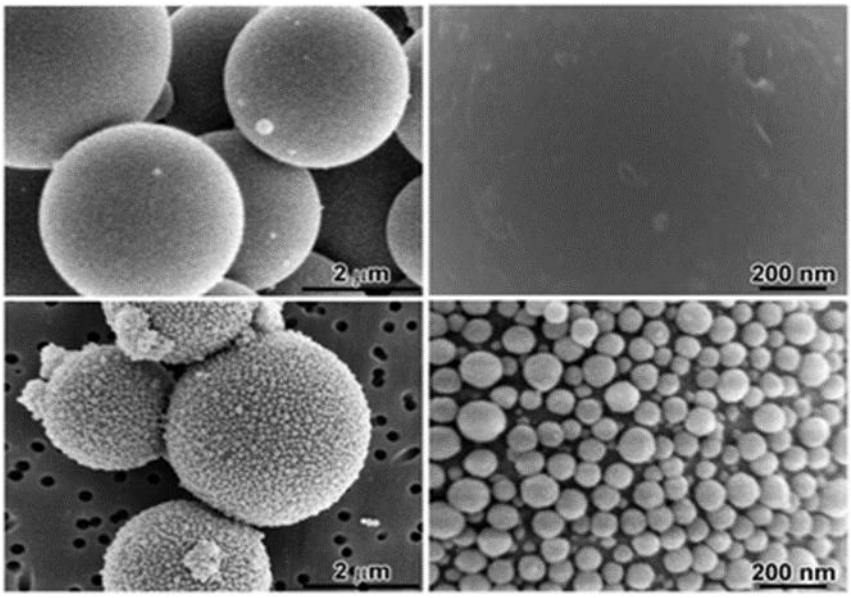
substances bind to specific target receptors on the cells and may increase vascular permeability, promote neutrophil chemotaxis, stimulate smooth muscle contraction, increase direct enzymatic activity, induce pain and/or mediate oxidative damage.5 Examples of chemical mediators include: nitric oxide, prostaglandins, leukotrienes, vasoactive amines (histamine, serotonin), and cytokines. Although some of the cytokines (IL-3 - 4,-5,-6,-10,-13) released are beneficial by acting as anti-inflammatory mediator within the cells.

Hydrogel

A **hydrogel** is a macromolecular polymer gel constructed of a network of cross-linked polymer chains. **Hydrogels** are synthesized from hydrophilic monomers by either chain or step growth, along with a functional crosslinker to promote network formation.

Hydrogel products constitute a group of polymeric materials, the hydrophilic structure of which renders them capable of holding large amounts of water in their three-dimensional networks. Extensive employment of these products in a number of industrial and environmental areas of application is considered to be of prime importance. As expected, natural hydrogels were gradually replaced by synthetic types due to their higher water absorption capacity, long service life, and wide varieties of raw chemical resources. Literature on this subject was found to be expanding, especially in the scientific areas of research. However, a number of publications and technical reports dealing with hydrogel products from the engineering points of view were examined to overview technological aspects covering this growing multidisciplinary field of research. The primary objective of this article is to review the literature concerning classification of hydrogels on different bases, physical and chemical characteristics of these products, and technical feasibility of their utilization. It also involved technologies adopted for hydrogel production together with process design implications, block diagrams, and optimized conditions of the preparation process.



A Typical diagram of Hydrogel

Ricinuscommunis

Botanical Name : Ricinuscommunis
Family : Euphorbiaceae
Synonym : Ricinus oil.

Geographical Distribution

The essential constituent of the seeds of the *Ricinuscommunis* is castor oil. Global castor seed (*Ricinuscommunis*) production is around I million tons per year. Leading producing areas are India (with over 60% of the global yield), China, Brazil,

Eastern Africa and Ethiopia. It is wide spread throughout tropical regions.

Description

Although monotypic, the castor oil plant can vary greatly in its growth habits and appearance depending upon the climatic, Geographical conditions. It is a fast- growing, suckering perennial shrub which can reach the size of a small tree (around 12 meters/39feet).

Ricinuscommunis Leaves

Leaves - glossy leaf is 15-45 centimeters in length, long - stalked, alternate and palmate with 5-12 deep lobes with coarsely toothed segments. Their colour varies from dark green, sometimes with a reddish tinge, to dark reddish purple or bronze. The stems (and the spherical, spiny seed pods) also vary in pigmentation. The pods are more shown than the flowers.

Flowers - The flowers borne in terminal panicle - like inflorescences of green monoecious flowers without petals. The male flowers are yellowish- green with prominent creamy stamens and are carried in ovoid spikes up to 15 centimeters long; the female flowers, born at the tips of the spikes, have prominent red stigmas.

Fruits / seeds- the fruit is a spiny, greenish (to reddish purple) capsule containing large, oval, shiny, bean-like, highly poisonous seed with variable brownish mottling. Castor seeds have a warty appendage called the caruncle, which is a type of elaiosome. The caruncle promotes the dispersal of the seed by ants (myrmecochory).

Historical usage

The use of castor bean oil in India has been documented since 2000 BC for lighting lamps and in local medicine as a laxative, purgative, and cathartic in Unani, Ayurvedic and other ethnomedical systems. Traditional Ayurvedic medicine considers castor oil the king of medicines for curing arthritic diseases.

Uses of “Ricinuscommunis”

Anti- oxidant activity

The DPPH (1,1- diphenyl- 2- picrylhydrazyl) mediated in vitro study reveals that gallic acid, quercetin, gentisic acid, rutin, epicatechin and ellagic acid are the major phenolic compounds responsible for the Anti-oxidant activity of the dry leaves of *Ricinuscommunis*linn.

MATERIALS AND METHODS

- Collection of Leaves
- Powdering
- Extraction.
- Percentage yield.

- Phytochemical screening.
- Isolation of Flavonoids.
- Formulation of herbal Hydrogel.
- Evaluation tests.

Collection of Leaves

Greenish fresh Leaves of *Ricinuscommunis* are collected from local area for our project and the collected leaves are shade dried inorder to evaporate moisture content.

Powdering

The Leaves which are shade dried were powered smoothly.

EXTRACTION

Extract

An extract is a substance made by extracting a part of a raw material, often by using a solvent such as ethanol or water. Extracts may be sold as tinctures or in powder form. The aromatic principles of many spices, nuts, herbs, fruits, etc., and some flowers, are marketed as extracts, among the best known of true extracts being almond, cinnamon, cloves, ginger, lemon, nutmeg, orange, peppermint, pistachio, rose, spearmint, vanilla, violet, and wintergreen.

Soxhlet extractor

A Soxhlet extractor is a piece of laboratory apparatus invented in 1879 by Franz von Soxhlet. It was originally designed for the extraction of a lipid from a solid material. Typically, a Soxhlet extraction is used when the desired compound has a limited solubility in a solvent, and the impurity is insoluble in that solvent. It allows for unmonitored and unmanaged operation while efficiently recycling a small amount of solvent to dissolve a larger amount of material.

The solvent is heated to reflux. The solvent vapour travels up a distillation arm, and floods into the chamber housing the thimble of solid. The condenser ensures that any solvent vapour cools, and drips back down into the chamber housing the solid material. The chamber containing the solid material slowly fills with warm solvent. Some of the desired compound dissolves in the warm solvent. When the Soxhlet chamber is almost full, the chamber is emptied by the siphon. The solvent is returned to the distillation flask. The thimble ensures that the rapid motion of the solvent does not transport any solid material to the still pot. This cycle may be allowed to repeat many times, over hours or days. During each cycle, a portion of the non-volatile compound dissolves in the solvent. After many cycles the desired compound is concentrated in the distillation flask. The advantage of this system is that instead of manyportions of warm solvent being passed through the sample, just one batch of solvent is recycled. After extraction the solvent is removed, typically by means of a rotary evaporator, yielding the extracted compound. The non-soluble portion of the extracted solid remains in the thimble, and is usually discarded.

Percentage yield

The percentage yield (or fractional yield or relative yield), which serves to measure the effectiveness of a synthetic procedure, is calculated by dividing the amount of the desired product obtained by the theoretical yield.

% yield = Actual yield ÷ Theoritical yield ×100

PHYTOCHEMICAL SCREENING

Test for Tannins

1 ml of the extract was added with 5 ml of distilled water and kept for boiling in hot water bath. After boiling, sample was cooled down and to this 0.1% ferric chloride solution was added. Appearance of brownish green or blue black coloration confirms the presence of tannins.

Test for Phlobatanins

1% of HCl was added to the extract (1ml) and boiled in hot water bath. Formation of red precipitate indicates the presence of phlobatannins.

Test for Saponins

1 ml of the extract was taken in a test tube and distilled water (2ml) was added to it. The test tube was then kept in boiling water bath for boiling and was shaken vigorously. Existence of Froth formation persisted for next one hour confirms the presence of saponins.

Test for Flavonoids

1ml of the extract was taken in the test tube and ammonia solution was added (1:5) followed by the addition of conc. sulphuric acid. Appearance of yellow color and its disappearance on standing indicates the positive test for flavonoids.

Test for Terpenoids

5 ml of extract was taken in a test tube and 2 ml of chloroform was added to it followed by the addition of 3 ml of conc. sulfuric acid. Formation of reddish brown layer at the junction of two solutions confirms the presence of terpenoids.

Test for Cardiac Glycosides

5 ml of each extract was added with 2 ml of glacial acetic acid which was followed by the addition of 2 ml of glacial acetic acid, 1 drop of ferric chloride solution and 1 ml of conc. sulphuric acid. Formation of brown ring at interface confirms the presence of cardiac glycosides.

Isolation of Flavonoid

- 1gm of defatted extract taken in a vessel already containing 50ml of aqueous ethanol (70%).
- The Vessel was place into Microwave decomposition system for microwave- assisted extraction.
- The temperature maintained for extraction was 50°C and time for extraction was 9 minutes.
- Then the sample was filtered and volume was made 50ml in a volumetric flask with aqueous ethanol (70%) solvent.

FORMULATION OF HYDROGEL

Herbal "Hydrogel" are prepared by using "Liquid-Liquid suspension polymerization" technique.

Liquid- Liquid suspension polymerization:

The porous Hydrogels are prepared by suspension polymerization method in liquid-liquid systems. In this method the monomers which are immiscible are first dissolved along with active ingredients in a suitable solvent monomer and are then dispersed in the aqueous phases which consist of like surfactant, suspending agent to facilitate formation of suspension. The polymerization is then activated by increasing temperature or irradiation or by addition of catalyst. The polymerization process continues the formation of a reservoir type of system with spherical structure. After the polymerization process the solvent is removed leaving the spherical structured porous microspheres i.e., Hydrogels.

Formulation of Hydrogels through methanolic extract and petroleum ether extract of *Ricinuscommunis*leaves.

Chemicals used in the formulation are:

- Methanolic drug extract
- Petroleum ether drug extract
- Carbapol
- HPMC
- Sodium lauryl sulphate
- Ethanol
- Polyvinylalcohol

Formulation Table

S.NO	Chemicals	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
1	Drug	1.0	1.5	1.0	1.5	1.0	1.5	1.0	1.5
2	Carbapol	2.0	1.5	2.0	1.5	0	0	0	0
3	HPMC	0	0	0	0	2.0	1.5	2.0	1.5
4	Sodium lauryl sulphate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
5	Ethanol	80	80	80	80	80	80	80	80
6	Polyvinyl alcohol	10	10	10	10	10	10	10	10
	Total	94.5	94.5	94.5	94.5	94.5	94.5	94.5	94.5

Where,

F_1 and F_2 = Methanolic drug extract (Carbapol),

F_3 and F_4 = Petroleum ether drug extract (Carbapol),

F_5 and F_6 = Methanolic drug extract (HPMC),

F_7 and F_8 = Petroleum ether drug extract (HPMC).

EVALUATION OF FORMULATED HYDROGELS

- Particle size
- Determination of Production yield
- Determination of pH
- Clarity test
- Spread ability test
- Viscosity

Particle size

Particle size and size shape are evaluated using either an optical microscope or an electronmicroscope. This is an extremely crucial step, as the size of the particles greatly affects the texture of the formulation and its stability. Free-flowing powders with fine aesthetic attributes are possible to obtain by controlling the size of particles during polymerization. Particle size analysis of loaded and unloaded Hydrogels can be performed by laser light diffractometry or any other suitable method. The values (d50) can be expressed for all formulations as mean size range. Particle size is determined by scanning electron microscope (SEM), and each sample is done microscopy for thrice and mean value is taken.

Particle size table

S.NO	Formulation code	Particle size (µm) (mean ± S.D) n = 3
1	F_1	30.8 ± 1.05
2	F_2	29.8 ± 1.00
3	F_3	28.7 ± 1.02
4	F_4	29.7 ± 1.54
5	F_5	37.2 ± 1.32
6	F_6	31.3 ± 1.25
7	F_7	31.9 ± 1.17
8	F_8	33.4 ± 1.23

Determination of Production yield

The production yield of the microparticles can be determined by calculating accurately the initial weight of the raw materials and the last weight of the SPM obtained [8].

The percentage yield obtained by all formulations is compared.

Percentage of Production yield = Production yield ÷ Theoritical yield × 100

F_1 =% Production yield = 92.46 ÷ 94.5 ×100 = 97.8%

F_2 = % Production yield = 93 ÷ 94.5 × 100 = 98.4%

F_3 = % Production yield = 94 ÷ 94.5 × 100 = 99.4%

F_4 = % Production yield = 93 ÷ 94.5 × 100 = 98.4%

Production yield table

S.NO	Formulation code	Production yield
1	F_1	97.8%
2	F_2	98.4%
3	F_3	99.4%
4	F_4	98.4%
5	F_5	84.2%
6	F_6	81.3%
7	F_7	86.3%
8	F_8	87.4%

Determination of pH

The p H is a measure of the acidity or basicity of an aqueous solution. Solutions with a pH less than 7 are said to be acidic and solutions with a pH greater than 7 are basic or alkaline [7].

pH is the negative logarithm of the activity of the (solvated) hydronium ion, more often expressed as the measure of the hydronium ion concentration.

The pH of the prepared gel was measured using pH meter by putting tip of the electrode into the gel and after 2 minutes the result was recorded.

pH Table

S.NO	Formulation code	pH
1	F_1	7.1
2	F_2	7.9
3	F_3	7.4
4	F_4	7.6
5	F_5	6.2
6	F_6	6.9
7	F_7	6.4
8	F_8	6.1

Clarity test

This test is performed to calculate the colour, homogeneity and consistency. This test is performed for semi solid gel preparations to ensure its smoothness. Semi solid smooth gel is obtained by proper mixing of drug and the polymer by a magnetic stirrer [7].

Developed gel was tested for homogeneity by visual inspection after the gel has been set in the container. The gel was tested for its appearance and presence of any aggregates.

All the tests for colour, homogeneity and consistency are done for thrice and the mean values are taken, all the formulations are compared for its smoothness.

Clarity test table

S.NO	Formulation code	Colour	Consistency	Homogeneity
1	F_1	Dark green	Semi solid smooth gel	Low
2	F_2	Dark green	Semi solid smooth gel	High
3	F_3	Blackish green	Semi solid smooth gel	Moderate
4	F_4	Blackish green	Semi solid smooth gel	High
5	F_5	Green	Semi solid smooth gel	Low
6	F_6	Green	Semi solid smooth gel	Moderate
7	F_7	Green	Semi solid smooth gel	Low
8	F_8	Green	Semi solid smooth gel	Moderate

Spread ability test

A sample of 0.1 g of gel was pressed between two slides with 500g weights and left for about 5 min where no more spreading was expected. Diameters of spread circles were measured in cm and were taken as comparative values for spread ability.

For this test each sample is taken thrice and tested for its diameter of spreading capacity and the mean values are calculated for each formulation.

Spread ability test table

S.NO	Formulation code	Spread ability (cm)
1	**F_1**	**3.22**
2	**F_2**	**2.68**
3	**F_3**	**2.98**
4	**F_4**	**2.73**
5	**F_5**	**1.51**
6	**F_6**	**1.65**
7	**F_7**	**1.96**
8	**F_8**	**1.43**

Viscosity

The viscosity of the different gel formulations was determined using a "Brookfield viscometer" with spindle no 7 at 50 rpm. The viscosity of the formulation is due to concentration of polymer and type of the polymer used in each formulation. For the evaluation of viscosity of each formulation is tested thrice and the mean values are compared and seen for the deviation [6].

As it is a topical gel preparation it must be highly viscous.

Viscosity table

S.NO	Formulation code	Viscosity (p) (mean ± SD)
1	F_1	207.91 ± 2.223
2	F_2	206.72 ± 1.14
3	F_3	210.4 ± 1.23
4	F_4	205.27 ± 1.13
5	F_5	189.44 ± 1.22
6	F_6	199.72 ± 2.32
7	F_7	187.91 ± 3.22
8	F_8	199.27 ± 2.22

RESULTS AND DISCUSSION

Percentage yield

Percentage yield can be calculated by using formula.

Percent yield = Actual yield ÷ Theoritical yield × 100

Table of Extraction Percentage

S.NO	Solvent used for extraction	Percentage yield
1	Methanol (Carbapol)	13.33%
2	Petroleum Ether (Carbapol)	8.33%
3	Methanol (HPMC)	12.66%
4	PetroleumEther (HPMC)	7.0%

"*Ricinuscommunis*" leaf constituents are more soluble in the Methanol when compared to Petroleum ether. So, the methanolic extract percentage yield is more when compared to petroleum ether. The solvent methanol is polar in nature, the polar constituents are soluble in this solvent. The solvent petroleum ether is non- polar in nature, the non- polar constituents are soluble in this solvent. The methanolic extract percentage yield is better when compared to petroleum ether extract of "*Ricinuscommunis"*. As the methanol is polar solvent it got more percentage yield.

Phytochemical tests

S.NO	Chemical constituents	Methanolic extract	Petroleum ether extract
1	Tannins	Present	Present
2	Phlobatannins	Absent	Absent
3	Saponins	Present	Absent
4	Flavonoids	Present	Present
5	Terpenoids	Present	Present
6	Cardiac glycosides	Absent	Absent

The Phytochemical tests are done to confirm the chemical constituents present in the leaf. Flavonoids, Tannins and terpenoids are present in both the extracts and flavanoids are essential for the anti-inflammatory activity [4].

Saponins are present in methanolic extract as they are soluble in polar solvent and insoluble in petroleum ether. So, flavanoids are isolated from the extract.

Formulation table

SNO.	Chemicals	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
1	Drug	1.0	1.5	1.0	1.5	1.0	1.5	1.0	1.5
2	Carbapol	2.0	1.5	2.0	1.5	0.0	0.0	0.0	0.0
3	HPMC	0.0	0.0	0.0	0.0	2.0	1.5	2.0	1.5
4	Sodium lauryl sulphate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
5	Ethanol	80	80	80	80	80	80	80	80
6	Poly vinyl alcohol	10	10	10	10	10	10	10	10
	Total	94.5	94.5	94.5	94.5	94.5	94.5	94.5	94.5

In the formulation of Hydrogels, the concentration and type of polymer varies and the concentration of drug is also changed formulation to formulation. In the F_1, F_2, F_3 and F_4 formulations carbapol is used as a polymer and in the F_5, F_6, F_7 and F_8 formulations HPMC is used as a polymer.

Sodium lauryl sulphate, Ethanol, Poly vinyl alcohol are used in the equal quantities and the formulations are prepared.

Sodium lauryl sulphate is used as a foaming agent, ethanol is volatile solvent used for dissolving both drug and polymer and then ethanol evaporates, poly vinyl alcohol acts as external phase which forms pores in the Hydrogel preparation [6].

The concentration of polymer effects on the drug release. The quantity of formulations obtained is about 94.5 ml.

Evaluation table

Formulation code	Production yield	Particle size	Viscosity	pH	Clarity	Spread ability
F_1	97.8%	30.8± 1.05	207.91± 2.223	7.1	Dark green	3.22
F_2	98.4%	29.8 ±1.00	206.72± 1.14	7.9	Dark green	2.68
F_3	99.4%	28.7± 1.02	210.4± 1.23	7.4	Blackish green	2.98
F_4	98.4%	29.7±1.54	205.27± 1.13	7.6	Blackish green	2.73
F_5	84.2%	37.2± 1.32	189.44± 1.22	6.2	Green	1.51
F_6	81.3%	31.3± 1.25	199.72± 2.32	6.9	Green	1.65
F_7	86.3%	31.9± 1.17	187.91± 3.22	6.4	Green	1.96
F_8	87.4%	33.4± 1.23	199.27± 2.22	6.1	Green	1.43

In the above mentioned table the production yield, particle size, viscosity, pH, clarity and spread ability of different formulations from F_1 to F_8 are compared.

The formulation F_3 has better production yield, particle size, viscosity, pH, clarityand spread ability when compared to other formulations.

The formulation F_3 shows

S.NO	Evaluation test	Result
1	Production yield	99.4%
2	Particle size	28.7± 1.02 µm
3	Viscosity	210.4± 1.23
4	pH	7.4
5	Clarity	Blackish green
6	Spread ability	2.98 cm

The particle size, viscosity, clarity and spread ability are based on the type and concentration of the polymer used i.e., carbapol. Production yield and p H is depends up on solvent used for extraction as well as internal and external phases in the Hydrogel [4].

It shows that the carbapol polymer gives better results when compared to the HPMC polymer.

Particle size of F_3 Hydrogels formulation at different sizes of lens

Spherical Hydrogel by carbapol at 232x

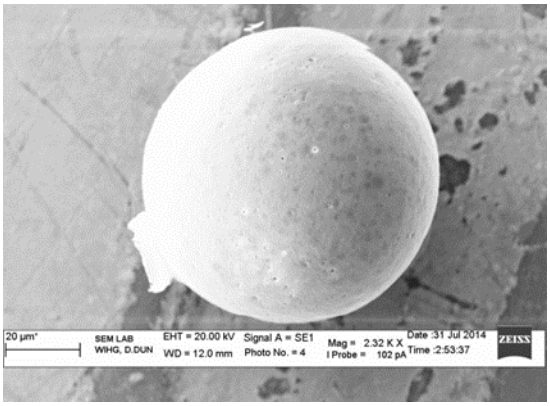


Image showing clusters of Hydrogel at 714x

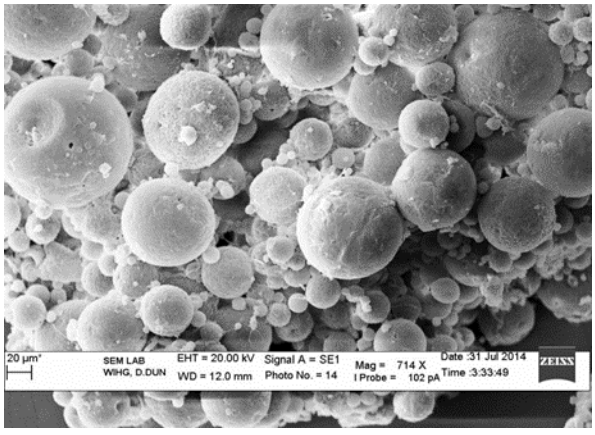
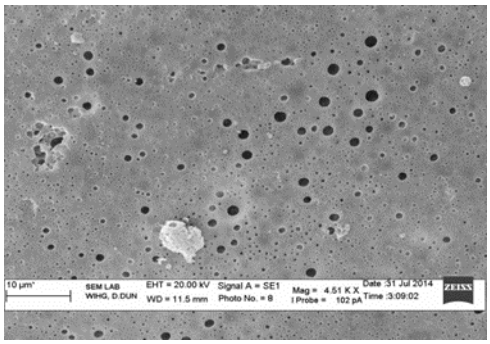


Image showing high porosity of the Hydrogel at 451 KX



CONCLUSION

The present study was to design, formulate and evaluate kaempferol-3-o-beta rutinoside and kaempferol-3-o-beta-d- xylopyrinoid loaded Hydrogel gel for topical suspended drug delivery. Hydrogels were prepared by liquid- liquid suspension polymerization method using carbapol and poly vinyl alcohol in F_1 to F_4 formulations and using HPMC and poly vinyl alcohol in F_5 to F_8 formulations.Ethanol is the internal phase suitable for the preparation of Hydrogel and the external phase was found to be water. Mixture of Carbapol and drug in ethanol served as internal phase in F_1 to F_4 formulations and the mixture of HPMC and drug in ethanol served as internal phase in F_5 to F_8 formulations.Solution of poly vinyl alcohol in water served as external phase. When compared with all the eight formulations it was found that the F_3 formulation has better production yield, particle size, viscosity, pH, clarityand spread ability. This is due to the type and concentration of polymer used in the formulation. The presented work demonstrates the literature concerning classification of hydrogels on different bases, physical and chemical characteristics of these products and technical feasibility of their utilization.

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