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FORMULATION AND EVALUATION OF PHYTOSOMAL GEL OF CAMELLIA SINENSIS FOR TREATMENT OF SKIN AGEING

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ABSTRACT

The objective of this research is to focus on phytosomes which are now being used extensively as modern technology in the field of pharmaceuticals as well as neutraceuticals because of its varied therapeutic actions with fewer side effects. Phytosomes possesses excellent pharmacodynamic activity with enhanced bioavailability of many popular herbal extracts like green tea, which can be developed for various uses in cosmeceuticals and neutraceuticals. This research highlights on the unique properties of phytosomes in drug delivery. This paper also contains the preparation of phytosomes, formulation of phytosomal gels its evaluation, advantages and also results and discussion. It also highlights how it is different from marketed formulation, and the future aspects in the field of pharmacy.

INTRODUCTION

Skin Ageing is a very common phenomenon to all living beings. It is signified by progressive deterioration and degeneration of cells and organs. As far as human beings are concerned, aging is a complex phenomenon of physical, psychological, and social changes. According to biologists, aging is a sum of all changes that occur in a living being with the passage of time Sand lead to a decreasing ability to survive stress, to functional impairment, and finally to death.[1,2]

The effect of aging on the world population does have an indirect effect on the worldwide medical care and health scenarios.[3] The United Nations have stated that the number of people worldwide of the age group 60 or above will be rising one in 10 to the current one in five ratios by 2050 and the ratio in developing nations and developed nations are going to double and triple, respectively. These demographic statistics suggest healthcare scenario to be

more careful with the changes associated with aging and to concentrate on more antiaging therapies.[4,5]

Introduction to phytosomes

Phytosome is a patented process developed by Indena, to incorporate phospholipids into standardized extracts and so vastly improve their absorption and utilization. Phytosomes are advanced herbal products produced by binding individual component of herbal extract to phosphatidylcholine resulting in a product that is better absorbed and produces better results than the conventional herbal extracts. Phytosome has an added dimension; the proven health giving activity of the phospholipids themselves. The presence of a surfactant i.e. the phospholipids in the molecule allows obtaining a higher adhesion of the product itself to the surface it comes into contact with and a better interaction of various molecules with cell structure. This aspect is of paramount importance in cosmetics and pharmaceutical formulations.

The phytosome process has been applied to many popular herbal extracts including Ginkgo biloba, grape seed, hawthorn, olive fruits and leaves, milk thistle, green tea, ginseng, kushenin, marsupsin and curcumin. Increased bioavailability of the phytosomes over the simpler, non-complexed plant extract has been demonstrated by pharmacokinetics and activitystudies, conducted in animals as well as human beings. These compounds can be considered novel entities on the basis of their physiochemical and spectroscopic characteristics. Presently phytosomes are used primarily in cosmetics to deliver water soluble substances to the sin. This technology is also useful in pharmaceutical formulations intended for treatment of oral cavity in which the contact times are very short because phospholipid allows a greater adhesion of the product itself to the surface it comes in contact with.[6,7]

Formulation of phytosomes

Phytosomes are prepared by reacting the herbal extract in an aprotic solvent such as methylene chloride, dioxane, and ethyl acetate with the phospholipid such as phosphatidylcholine, phosphatidyl ethanolamine, or phosphatidylserine dissolved in the same solvent. After solubilization has completed, the complex compounds are isolated by removing the solvent under vacuum, by freeze drying or by precipitation with non-solvents such as n-hexane. Thus, the obtained complexes are lipophilic in character and soluble in a polar and aprotic solvent, in which the individual components of the complex are normally insoluble.[8]

Introduction to gels

Gels are defined as semi rigid systems in which the movement of the dispersing medium is restricted by an interlacing three-dimensional network of particles or solvated macromolecules of the dispersed phase. The word ‘‘gel’’ is derived from ‘‘gelatin,’’ and both ‘‘gel’’ and ‘‘jelly’’ can be drawn back to the Latin gelu for ‘‘frost’’ and gel are, meaning ‘‘freeze’’ or ‘‘congeal.’’ This origin indicates the essential idea of a liquid setting to a solid-like material that does not flow, but is elastic and retains some liquid characteristics.[9]

Formulation of phytosomal gel

Phytosomes are prepared by reacting the herbal extract and phospholipid such as soy lecithin in a ratio of 1:1 and dissolving them in an aprotic solvent such as ethyl acetate. After solubilization has completed, the complex compounds are removed by solvent evaporation technique. Thus, phytosomes are obtained. Gel was prepared using carbopol 940 as the gelling agent which was dispersed in a small quantity of distilled water and then stored overnight to ensure complete hydration. The active ingredients such as tender coconut water, A. vera extract, grape seed extract, Vitamin E, and jojoba oil in a suitable solvent such as propylene glycol were added to the dispersion. Then, preservatives such as methylparaben and propylparaben were also added slowly with continuous stirring. Then, the prepared phytosomes were incorporated into the gel, and thus, the phytosomal gel was obtained. This phytosomal gel showed better release of herbal extracts and better penetration to the skin, and as a result, desired antiaging property was obtained.[10]

Advantages of gels[11]

- Gels are used to achieve optimal cutaneous and percutaneous drug delivery.
- They can avoid gastrointestinal drug absorption difficulties caused by gastrointestinal pH.
- Gels are having property to avoid enzymatic activity and drug interaction with food and drinks.
- They can substitute for oral administration of medication when the route is unsuitable.
- They can avoid the first pass effect, that is, the initial pass of drug substance through the human body.
- They avoid systemic and portal circulation following gastrointestinal absorption.
- Gels are not deactivated by liver enzymes because the liver is bypassed.
- They are non-invasive and have patient compliance.
- They are applied over skin for slow and prolonged absorption.

- Gels have also been applied in pharmacy to some viscous suspension for oral use for example Aluminum hydroxide gel.
- They have localized effect with minimum side effects.

Preparation of phytosomal gel

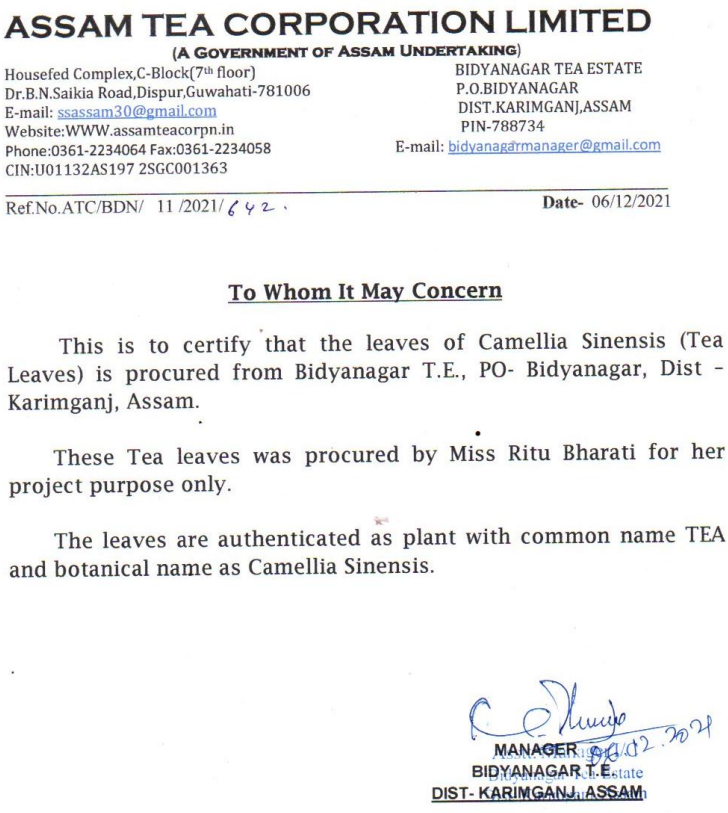
Materials – Carbopol 934, methyl paraben 0.5%, propyl paraben 0.2%, propylene glycol 400 (5%), triethanol amine, aloe vera extract, vit E, green tea extract.

Formulation table

Ingredients	F1	F2	F3	F4
Carbopol 934	1g	1g	1g	1g
Methyl paraben (0.5%)	O.2mL	0.2mL	0.2mL	0.2mL
Propyl Paraben (0.2%)	0.1mL	O.1mL	O.1mL	O.1mL
Propylene glycol 400 (5%)	5mL	5mL	5mL	5mL
Triethanolamine	1.2mL	1.2mL	1.2mL	1.2mL
Aloe Vera	1mL	-	1mL	-
Vit E	0.1mL	-	-	0.1mL

Methods

Procurement of green tea leaves: Firstly, green tea leaves were collected from Bidyanagar tea estate, Assam. The tea leaves were then dried under shady place for around 2 weeks. They were not dried under sunlight as they possess volatile substances.



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To Whom It May Concern

This is to certify that the leaves of Camellia Sinensis (Tea Leaves) is procured from Bidyanagar T.E., PO- Bidyanagar, Dist - Karimganj, Assam.

These Tea leaves was procured by Miss Ritu Bharati for her project purpose only.

The leaves are authenticated as plant with common name TEA and botanical name as Camellia Sinensis.

MANAGER
BIDYANAGAR T.E.
DIST- KARIMGANJ, ASSAM

Extraction and Isolation of green tea extract: The dried tea leaves were then crushed properly and were coarse powder was obtained. 200 gm of tea powder was subjected to soxhlet apparatus using 400 ml of ethanol in an Erlenmeyer flask as solvent. The extraction process was carried out at 60 -70-degree Celsius until the tea powder completely gets saturated. Dark brown color of extract was obtained. Then the saturate was air dried for 24 hrs.

- **Preparation of phytosomes -** Phytosome was prepared using thin-layer hydration method. First, Lipoid P 30 was diluted with dichloromethane, while the green tea leaf extract was diluted with 90% ethanol. Then, both the dissolved phospholipid and green tea leaf extract were poured into the round-bottom flask. The dichloromethane was evaporated using rotary vacuum evaporator at 37o C at gradual speed started in 25 to 150 rpm, and vacuumed until an even and firm thin layer was obtained. Nitrogen gas was flowed into the thin layer, then the layer was stored in the refrigerator up to 24 h. The thin layer was then hydrated with phosphate buffer pH 5, 5 at 40°C. Once the phytosomal suspension was formed, ultrasonication was done for 2 min. Thus, phytosomes are obtained.

- **Formulation of phytosomal gel-** For the preparation of gel 1gm of Carbopol 940 was used as gelling agent which was dispersed in distilled water and kept overnight to make sure complete hydration was obtained. Then 1ml of Aloevera extract along with 0.1ml of Vit E and 0.5 ml of coconut oil were added to propylene glycol and was stirred well until dispersion was achieved. Then, 0.2mL of Methyl paraben and 5Ml Propylene glycol were added as preservatives. Lastly, the prepared phytomosomes obtained from herbal extract of camellia sinensis were incorporated into the gel. As a result, phytosomal gel was obtained.

RESULTS AND DISCUSSION

Compatibility studies

In order to investigate the possible interactions between API's and other polymers and diluents. IR results proved that the drug was found to be compatible with excipients as wave numbers are almost similar to pure drug and also drug excipient mixture. All the samples were scanned at the resolutions of $4cm^{-1}$ over the wave number region $4000\text{-}4000cm^{-1}$ using KBr disk method. Then this mixture was mixed well in a mortar for 3-5mins. A very small amount of this mixture was uniformly speed and sandwich between the pellets and pressed

using KBr pellet press at a pressure of 20,000psi for 1min. the pressure was then released and pellet was placed into the pellet holder and thus scanned in the IR region.

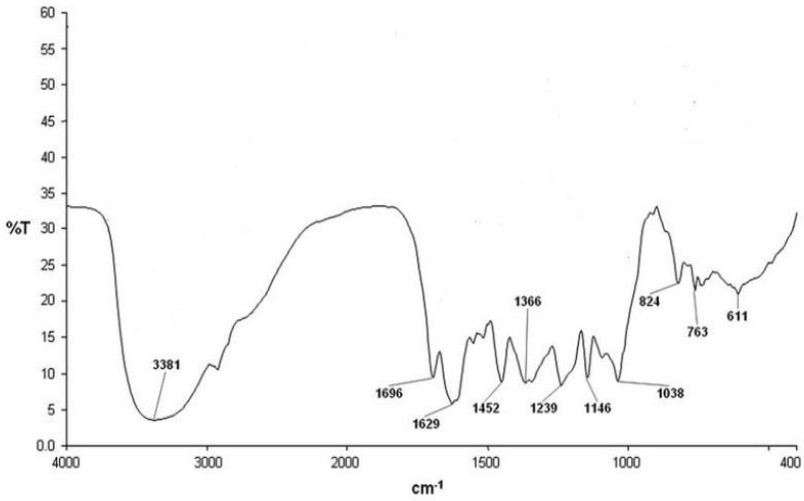

Fig. no. 1: IR of green tea extract.

RESULT AND DISCUSSION

Preformulation

1. Solubility

The colour, odour and taste of the drug were characterized and recorded. The result are shown in table:

Table 1.1: Table of organoleptic properties of drug.

S. No.	Parameters	Observation
1.	Description	Solid
2.	Colour of leaves powder	Light green
3.	Odour	Characteristic
4.	Taste	Pungent

Discussion: From the given data in table 1 it was observed that the organoleptic of test drug matches with the given standard data. This can be used as preliminary identification tool for drug.

2. Solubility studies

The solubility of drug was determined in different solvent system. Sufficient amount of the drug was added to 5ml of each solvent in a volumetric flask and shaken. The sample were kept. In room temperature for 24 hrs. Then the samples were filtered, diluted and examined for the absence or presence of drug particles.

Table no. 2.1: Table of solubility studies of drug in different solvents.

S. No.	Solvent	Solubility
1.	Water	Soluble
2.	Chloroform	Soluble
3.	Methanol	Soluble
4.	Ethanol	Freely Soluble

Discussion: The drug was found to be soluble in water, chloroform and methanol and it was found to be freely oluble in Ethanol.

pH table of different formulations

Table no. 3.1: Table of pH of different formulations.

Formulations	Trial 1	Trial 2	Trail 3	Mean	Standard deviation	Average PH
F1	6.5	6.4	6.6	6.5	0.08	6.5±0.1
F2	6.3	6.4	6.5	6.4	0.08	6.4±0.1
F3	6.5	6.3	6.1	6.3	0.16	6.3±0.16
F4	6	6.2	6.4	6.2	0.16	6.2±0.16

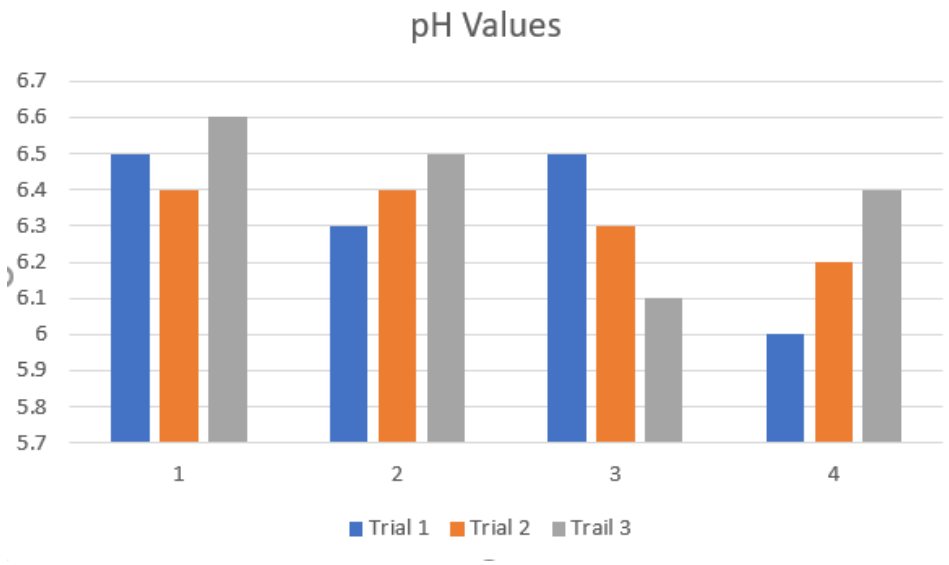

Fig. no. 2: Bar representation of pH of diffeerent formulations.

Discussion: It was previously reported that, for creams and gels to be non-irritant and safe for topical application, their pH has to be fall in the physiologic accepted range for topical preparations, i.e., pH 6–7 units. Table 3 shows that pH of various antiaging cream formulations ranged from 6.2 to 6.5 which lies in the normal physiologic range and thus produces no skin irritation. The pH of the gels was determined using a digital pH meter. pH of various antiaging gel formulations ranged from 6.2 to 6.5 which lies in the normal physiologic range and thus produces no skin irritation.

Viscosity

Formulations	Trial 1	Trial 2	Trial 3	Mean	Standard deviation	AverageViscosity (cps)
F1	2495.74	2486.43	2499.13	2493.767	5.37	2493.76±5.37
F2	2464.21	2461.89	2454.64	2460.247	4.08	2460.247±4.08
F3	2453.88	2460.33	2452.52	2455.577	3.41	2455.57±3.41
F4	2463.19	2480.91	2454.64	2466.247	10.94	2466.24±10.94

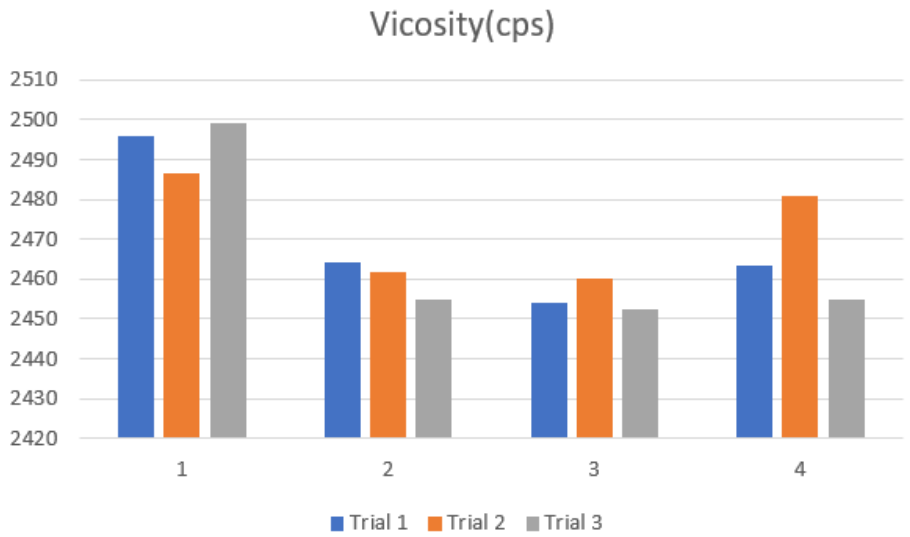

Fig. no. 3: Bar representation of viscosity of diffeerent formulations.

Discussion: The prepared gels were formulated using Carbopol 940. Table 4 shows that the viscosity of various antiaging cream formulations ranged from 2455.577 to 2493.76.

Spreadibility

Formulations	Trial 1	Trial 2	Trail 3	Mean	Standard deviation	Average PH
F1	31.1	31.2	31.3	31.15	0.05	31.15±0.05
F2	35.5	35.7	35.9	35.7	0.16	35.7±0.16
F3	32.2	32.4	32.6	32.4	0.16	32.4±0.16
F4	22.4	23.2	24.6	23.4	0.91	23.4±0.91

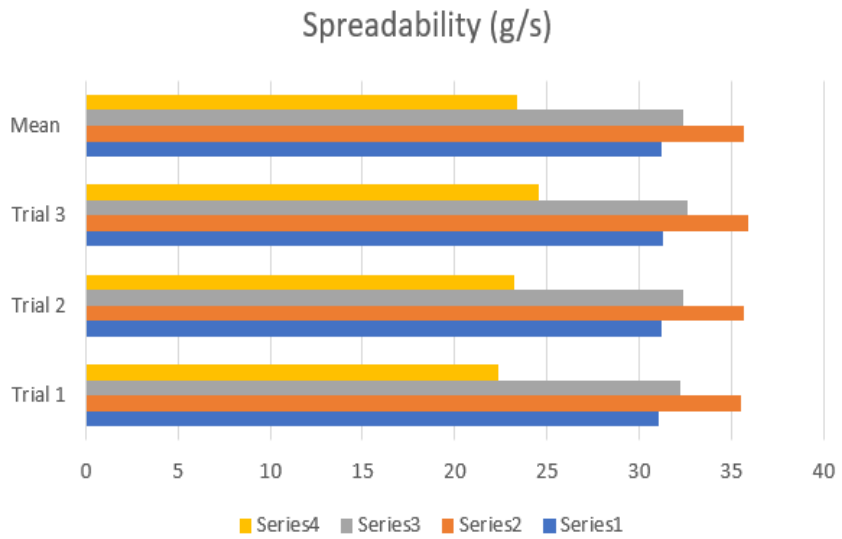

Fig. no. 4: Bar representation of spreadability of diffeerent formulations.

Discussion: The spreadability is an important criterion for uniform and ease of application of topical preparations. It also plays a major role from patient compliance point of view. Application of the formulation to the skin is more comfortable if the base spreads easily, exhibiting maximum "slip" and "drag." Spreadability of creams and gels are measured in terms of average diameter of the spread circle. Table 5 shows that spreadibility of prepared gel lies between a range of 23.4 to 35.7.

Extrudability

Formulations	Trial 1 (gel extruded in gms)	Trial 2 (gel extruded in gms)	Trial 3 (gel extruded in gms)	Trial 1(%)	Trial 2(%)	Trial 3(%)	Mean	Standard deviation	Average PH
F1	41.2	42	40.8	82.4	84	81.6	82.66667	1	82.66±1
F2	43.6	45.9	44.4	87.2	91.8	88.8	89.26667	1.91	89.26±1.91
F3	44.2	43.9	42.21	88.4	87.8	84.42	86.87333	1.75	86.87±1.75
F4	40.5	41.6	43.2	81	83.2	86.4	83.53333	2.22	83.53±2.22

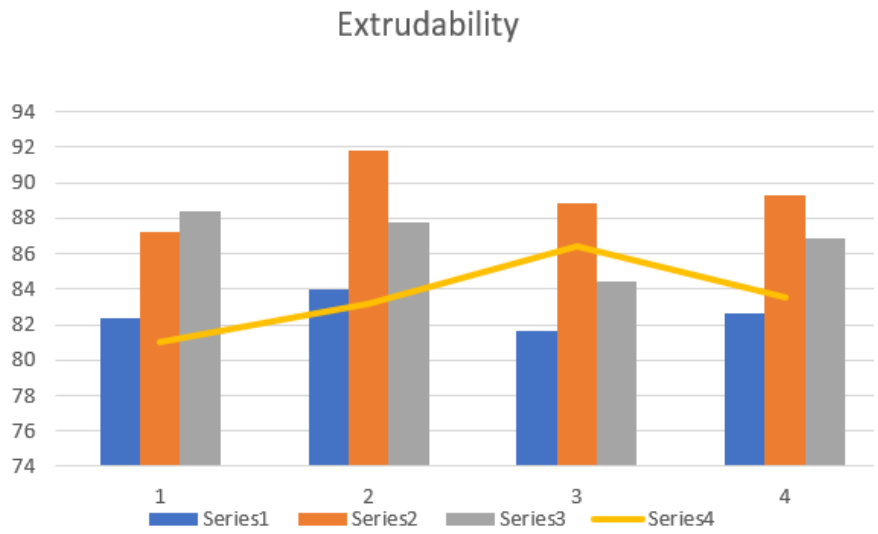

Fig no. 5: Bar representation of extrudability of diffeerent formulations.

Drug release profile

Formulation	Drug release in 3 hr	Drug release in 6 hrs	Drug release in 10 hrs
F1	15.20	25.03	50.93
F2	19.79	30.75	79.22
F3	28.39	35.21	70.69
F4	31.51	47.8	73.44

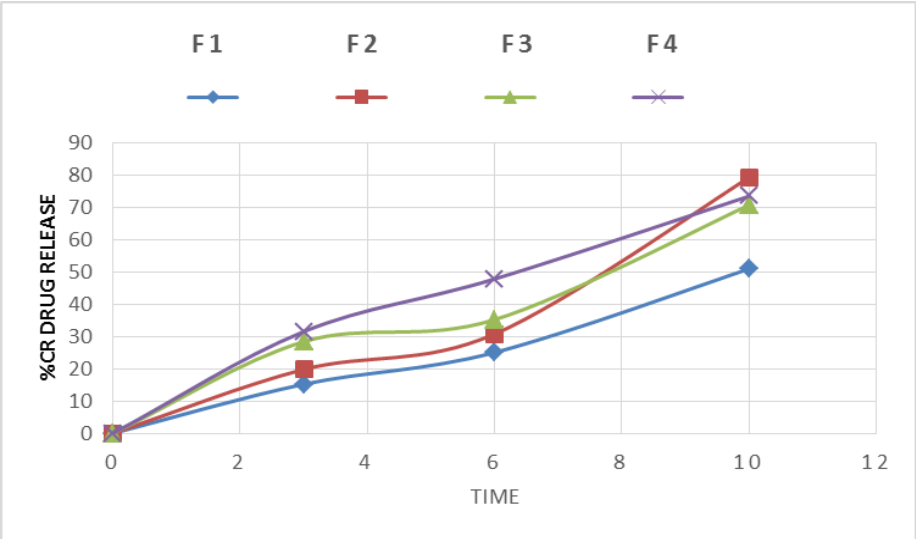

Fig. no. 6: In-vitro Drug release of F1-F4 from green tea extract.

In vitro release kinetic modelling

Formulation code	Zero Order		First Order		Higuchi		Krosmeyer-peper		
	K_0	R^2	K_0	R^2	K_0	R^2	K_0	R^2	n
F1	4.9693	0.9841	-0.0696	0.9541	6.7938	0.9021	1.9866	0.9651	0.9879

F2	7.6659	0.9453	-0.1520	0.8508	8.6576	0.8921	2.0490	0.9157	1.1223
F3	6.6749	0.9625	-0.1169	0.9230	7.8311	0.9090	2.9042	0.8603	0.7319
F4	7.1263	0.9797	-0.1299	0.9847	7.9815	0.9311	3.1814	0.9908	0.6969

CONCLUSION

Nowadays, aging phenomenon has become a severe problem among people as people are very concerned about looking young. Hence, people have started to depend on antiaging cosmetics. However, they few have severe adverse effects, and hence, majority rely on cosmetics containing herbal ingredients as they posses fewer side effects as compared to those with containing chemicals. Antioxidants are the major ingredients present in antiaging cosmetics. The antioxidants chosen for this study were, *A. vera* extract and and Vitamin E. Four different formulations of antiaging phytosomal gel were prepared. Physicochemical parameters such as pH, viscosity, homogeneity, spreadability, and extrudability of prepared antiaging gel were determined and the formula, F2 containing both *A. vera* extract and Vit E was chosen as the optimized formula. *In vitro* antioxidant studies were performed for antiaging phytosomal gel was found to be the formulation having the highest antioxidant activity, and hence, it was the optimized formulation. The optimized formulation was compared with a marketed antiaging gel and it was clear cut that the prepared antiaging phytosomal gel had highest antioxidant activity than the marketed formulation, and hence, it could be used for antiaging treatment.

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