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Formulation and Evaluation of Herbal Gel Containing *Plumeria Alba Linn.(Apocynaceae)* Leaves Extract

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ABSTRACT

Herbal medicine has become an item of global importance both, medicinal and economical. The present research has been undertaken with the aim to formulate the herbal gel containing *Plumeria alba* extract for skin disease. The gel formulation was designed by using *Plumeria alba*leaves extract & various gelling agents viz: Carbapol 974P, Pectin, Aloe Vera gel, Ocimum Basilicum& Glycerin, propylene glycol, methyl paraben, propyl paraben in required amount of distilled water. The physicochemical Parameters of all formulations were determined. Drug-excipients compatibility studies were confirmed by carrying out FT-IR study. In-vitro drug release in phosphate buffer pH 7.4 and Diffusion study through cellulose membrane, and also Cadaver skin using a Franz diffusion cell, were performed. Stability studies have been carried out as per ICH guidelines for 3 months. It was observed that all the formulations showed good viscosity and Spreadability. *In Vitro* Drug release studies reveal that F5 and F7 formulations show 87.97 % and 84.29 % drug release respectively and permeation studies done with cadaver skin affirmed that F5 and F7 formulation shows 85.32 % and 73.32 drug release respectively. The stability study revealed no significant difference between before and after storage. Overall result indicates that from that the combination of ocimum basilicum seed mucilage gel with natural or synthetic polymer can increase the drug release and stability of gel formulations containing *Plumeria alba* leaves extract.

Keywords: *Plumeri aalba* leaves extract, Pectin, *Aloe Vera* gel, *Ocimum Basilicum* gel.

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INTRODUCTION

Plumeria alba Linn (Apocynaceae) commonly called White Champa, a small laticiferous tree or shrub, nativeof tropical America. It is 4.5m high, occasionally grownin the gardens. The plant is mainly grown for itsornamental and fragrant flowers.The fruit is edible, latex is applied to ulcers,herpes and scabies and seeds possess haemostatic properties. Moreover its bark is bruised and applied as plaster over hard tumours. Whereas the latter taxonomically finds used as purgative, cardiotonic, diuretic and hypotensive. Methanolic extract showed antimicrobial activity against Bacillus anthracis, Pseudomonas aeruginosa. The plant is reported to contain Amyrinacetate, mixture of Amyrins, ß-sitosterol, Scopotetin, the Iriddoids Isoplumericin, Plumieride, Plumieridecoumerate and Plumieride coumerate glucoside. Bioactive richness of these active constituents are present in the plant. However Pharmacognosy information about this plant hasnot been published, particularly the necessity to define quality control procedures of the *P. alba* as raw material. Hence the present investigation deals the Pharmacognostical evaluation of the *Plumeria alba*. Thestudy includes morphological and anatomical determination of physico-chemical constants and the preliminary phytochemical evaluation of the different extracts of *Plumeria alba*[1].The white flowers with a yellow center have an almost waxy feel. After flowering narrowly cylindrical pods borne in pairs attached at the base and filled with winged seeds are sometimes produced[2].

MATERIALS AND METHOD

Plant collection and authentication

The leaves of *Plumeria Alba* linn.(Apocynaceae) was collected from jule solapur area, Solapur and was authenticated by Dr. SP Gaikwad, Life science research laboratory, Department of Botany, Walchand college of Arts and Science, Solapur.

Method of extract preparation

The coarse powder of the leaves (50 gm) was extracted in a soxhlet apparatus with methanol and the solvent was removed by evaporation on a heating mantle by taking care that the temperature did not rise above 60ºC. A semisolid dark viscous crude extract (yield 6.38% w/w)was thus obtained.

Chemicals

Carbopol 974 P(Merck Ltd.), Pectin, Ocimum basilicum seeds, Aloe Vera, Methanol, Formalin, Methyl Paraban (Suprim Chemicals), Propyl Paraben, Glycerin, propylene glycol , Triethanolamine.

Preparation of Gel containing extract

Table 1: Composition of the Batches of Herbal Gels (1% w/w)

Sr.no.	Ingredients-	F1	F2	F3	F4	F5	F6	F7	F8
1	PALE (gm)*	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
2	Pectin	2	-	2	-	-	-	14(ml)	10(ml)
3	Carbopol 974 P	-	0.5	-	0.5	15(ml)	21(ml)	-	-
4	Aloe vera gel (ml)	-	-	15	15	-	-	-	-
5	Ocimumbasilicum gel	-	-	-	-	15	9	6	10
6	Glycerin(ml)	5	5	5	5	5	5	5	5
7	Propylrne glycol(ml)	10	10	10	10	10	10	10	10
8	Methyl parben(gm)	0.015	0.015	0.015	0.015	0.015	0.015	0.015	0.015
9	Propyl paraben(gm)	0.005	0.005	0.005	0.005	0.005	0.005	0.005	0.005
10	Purified water upto	50	50	50	50	50	50	50	50

* *Plumeriaalba* leaves extract

A. Preparation of F1 & F2 Batches –

The PALE (1% w/w) was dissolved in a hot mixture containing propylene glycol and glycerin as moistening agents.

Polyacrylic acid polymer (Carbopol 974 P), polysaccharide polymer (Pectin) gel were prepared by dispersing the calculated amount of polymer in calculated amount of warm water with constant stirring using magnetic stirrer at a moderate speed. Then add the previous mixture containing the extract. The pH of carbopol gel was adjusted using Triethanolamine. Finally methyl and propyl paraben as preservatives were added slowly with continuous stirring & then kept the gel in ice for 5 minute until gel was formed. The prepared gels were packed in wide mouth glass jar covered with screw capped plastic lid after covering the mouth with an aluminum foil and were kept in cool and dark place.

B. Preparation of F3 & F4 Batches

The PALE (1% w/w) was dissolved in a hot mixture containing propylene glycol and glycerin as moistening agents.

Polyacrylic acid polymer (carbopol 974 P), polysaccharide polymer (Pectin) gel were prepared by dispersing the calculated amount of polymer in calculated amount of warm water with constant stirring using magnetic stirrer at a moderate speed. Then 15 ml of the above polymer solution was separated & then added the 15 ml of Aloe Vera gel to each polymer solution respectively. Then add the previous mixture containing the extract. Further procedure followed is same as that of batch no.F1 and F2.

C. Preparation of F5 & F6 Batches

The PALE (1% w/w) was dissolved in a hot mixture containing propylene glycol and glycerin as moistening agents.

Polyacrylic acid polymer (carbopol 974 P) gel was prepared by dispersing the calculated amount of polymer in calculated amount of warm water with constant stirring using magnetic stirrer at a moderate speed.

In F5 batch – The 14 ml of the above polymer solution was separated & then add the 6 ml of Ocimum basilicum gel to polymer solution. (i.e.70:30 ratio)

In F6 batch - The 10 ml of the above polymer solution was separated & then add the 10 ml of Ocimum basilicum gel to polymer solution. (i.e.50:50 ratio)

Then add the previous mixture containing the extract further procedure followed is same as that of batch no.F1 and F2.

D. Preparation of F7 & F8 Batches

The PALE (1% w/w) was dissolved in a hot mixture containing propylene glycol and glycerin as moistening agents.

Polysaccharide polymer (Pectin) gel was prepared by dispersing the calculated amount of polymer in calculated amount of warm water with constant stirring using magnetic stirrer at a moderate speed.

In F7 batch – The 15 ml of the above polymer solution was separated & then addsthe 15 ml of Ocimum basilicum gel to polymer solution. (i.e.50:50 ratio)

In F8 batch - The 21 ml of the above polymer solution was separated & then add the 9 ml of Ocimum basilicum gel to polymer solution. (i.e.70:30 ratio)

Then add the previous mixture containing the extract. The pH of carbopol gel was adjusted using Triethanolamine. Further procedure followed is same as that of batch no.F1 and F2.

EVALUATION OF HERBAL GEL FORMULATIONS

Physical Evaluation[3]

Physical parameters such as color and appearance were evaluated.

Measurement of pH[3]

PH of the gel was measured by using pH meter.

Viscosity[4]

Viscosity of gel was measured by using Brookfield viscometer.

Spreadibility[5]

One of the criteria for a gel to meet the ideal quantities is that it shold possess good spreadability. It is the term expressed to denote the extent of area to which gel readily spreads on application to

skin or affected part. The therapeutic efficacy of a formulation also depends upon its spreading value. spreadability is expressed in terms of time in seconds taken by two slides to slip off from gel and placed in between the slides under the direction of certain load.Lesser the time taken for separation of two slides, better the Spreadability. It is calculated by using the formula:

$$S = M.L / T$$

Where,

M = wt. tied to upper slide

L = length of glass slides

T = time taken to separate the slides.

Extrudability study[6]:

The gel formulations were filled in standard capped collapsible aluminum tubes and sealed by crimping to the end. The weights of the tubes were recorded. The tubes were placed between two glass slides and were clamped. 500gm was placed over the slides and then the cap was removed. The amount of the extruded gel was collected and weighed. The percent of the extruded gel was calculated (>90% extrudability: excellent, >80% extrudability: good, >70%extrudability: fair).

Drug content Determination[5]:

1 g of the prepared gel was mixed with 100ml of Phosphate buffer ph 7.4. Aliquots of different concentration were prepared by suitable dilutions after filtering the stock solution and absorbance was measured. Drug content was calculated using the equation, which was obtained by linear regression analysis of calibration curve.

***In vitro* Drug Release Studies[7]:**

Before the experiment, the cellophane membrane was washed in the running water and then soaked in distilled water for 24 h. The *in vitro* diffusion studies of prepared gels were carried out in Franz type diffusion cell using pre-hydrated cellophane membrane and phosphate buffer pH 7.4 (26 ml) in receptor compartment. 500mgof each of formulation was spread uniformly on the membrane. The donor compartment was kept in contact with a receptor compartment and the temperature was maintained at 37±0.5°C. The solution on the receptor side was stirred on magnetic stirrer. At predetermined time intervals, 2 ml of solution from the receptor compartment was pipetted out periodically at 15, 30, 45, 60, 90, 120, 150, 180, 210, 240 min. and immediately replaced with fresh 2 ml phosphate buffer pH 7.4.The drug concentration on the receptor fluid was determined Spectrophotometrically at 216 nm against appropriate blank.

Diffusion Study by using Cadaver Skin[8]:

Sample of whole adult human skin was obtained from Department of Anatomy, Dinadayal Upadhaya Dental College, Degaon, Solapur. Subcutaneous fat was carefully trimmed and then rinsed with normal saline. Skin was stored in 10% Formalin Solution until used. Diffusion studies were performed as per the procedure mentioned in "In vitro drug release studies".

Stability Study3:

The stability study was performed as per ICH guidelines 6. The formulated gel was filled in the collapsible tubes and stored at different temperatures and humidity conditions, viz. 30^0 C ± 2^0C/ 60% ± 5% RH, 40^0 C ± 2^0C/ 75% ± 5% RH for a period of three months and studied for colour,

RESULTS AND DISCUSSION

The herbal gel was prepared and subjected to evaluation of the various parameters. All the formulations were clear and transparent except pectin gel which was buff, opaque. spreadability of Carbopol containing formulation was good as compared to pectin containing formulations. The pH of all the formulations was in range of 6.29 to 7.28, which lies in the normal pH range of skin. Viscosity of Pectin containing formulations- F1, F3, F7, F8 were found to be more than carbopol containing- F2,F4,F5,F6 formulations.(Results shown in table no.2)Extrudability of all the formulations is higher than 80%. So it can be said that extrudability of all the formulations shows good acceptance properties.(Results shown in table no.3)The F7 batch shows maximum 98.49 % and F3 batch shows minimum 95.26 % drug content.(Results shown in table no.4)The F2 batch shows the highest drug release (91.35 %) which contains the Carbopol as gelling agent. As compared to carbopol which is synthetic polymer, Pectin is natural polymer which also releases 80.72 % (F1) of drug release which is good as compared to carbopol.F5 and F7 formulations shows the 87.97 % and 84.29 % drug release respectively, where F5 batch containing carbopol and Ocimum basillicum (Ratio 50:50) as gelling agents and F7 batch containing pectin and Ocimum basillicum (Ratio 70:30) as gelling agent. (Results shown in table no.5)F5 formulation shows highest 85.32 % drug release and F1 formulation shows the lowest 61.77 % drug release. F2 and F7 formulations shows 73.32 and 63.22 % drug release respectively.(Results shown in table no.6)The optimized batch (F5) was selected for stability study. The formulation was subjected to stability study as per ICH guidelines for the period of three months. by observing that effect of colour, appearance, pH, Spreadability, Drug Content it was confirmed that the developed gel posses good stability. (Results shown in table no.7)

Table 2: Physico chemical evaluation of all formulations

Batches	Colour	Appearance	Viscosity (cps)	Spreadability (gm.cm/sec)	pH
F1	Yellowish	Opaque	2230	12.32	6.72
F2	Brownish	Shiny Transparent	1710	16.10	6.98
F3	Dark Yellow	Transparent	1890	14.10	7.28
F4	Dark Brown	Transparent	1520	17.20	6.84
F5	Slight Brown	Transparent	1830	20.10	7.02
F6	Slight Brown	Transparent	1980	21.22	6.84
F7	Slight Yellow	Transparent	2340	17.42	6.29
F8	Slight Yellow	Transparent	2290	18.48	7.08

Table 3: Extrudabilityof gel formulations

Batches	Weight of gel in tube(gm)	Weight of gel extruded	Extruded amount (%)
F1	9.88	8.63	86.84
F2	9.89	8.26	83.51
F3	9.92	8.32	83.87
F4	9.72	7.88	81.06
F5	9.79	8.12	82.94
F6	9.93	8.46	85.19
F7	10.04	8.40	83.66
F8	9.95	8.80	88.44

Table 4: Drug content of gel formulations

Batches	Drug content (% w/w)
F1	96.27
F2	98.29
F3	95.26
F4	96.39
F5	97.48
F6	96.42
F7	98.49
F8	97.54

Table 5: *In vitro* Drug Release Data Profile for Gel formulations

Time	% Drug release							
(min.)	F1	F2	F3	F4	F5	F6	F7	F8
15	7.374	11.679	3.068	4.254	11.492	0.385	6.812	4.254
30	10.624	13.263	4.677	7.701	12.813	2.162	11.829	7.576
45	15.267	22.638	5.768	12.012	18.41	7.006	15.694	8.883
60	22.266	33.471	8.288	15.426	25.242	22.942	23.595	16.05
90	33.964	38.651	14.591	19.535	32.313	30.767	34.016	20.913
120	38.582	49.917	23.52	28.997	39.235	39.249	41.121	30.057
150	47.371	60.294	28.94	37.028	51.269	51.96	53.899	40.296
180	57.145	70.35	44.199	46.403	63.663	48.409	63.773	45.553
210	70.249	80.08	56.992	59.809	74.641	50.997	72.202	42.276
240	80.723	91.355	43.774	70.029	87.971	53.436	84.294	44.393

n	0.883	0.7873	1.1221	0.9974	0.7764	1.7409	0.9202	0.9242
k	0.5790	1.1723	0.1065	0.2625	1.0770	0.007	0.5278	0.3315
Best fit model	Zero Order	Zero order	Peppas	Peppas	Zero order	First order	Zero order	Peppas

Table 6: Drug Release Data Profile for Gel formulations by using cadaver skin.

Time (min.)	**% Drug release**			
	F1	**F2**	**F5**	**F7**
15	2.382	2.32	10.68	1.945
30	7.182	6.179	13.249	6.275
45	14.522	13.941	21.63	11.114
60	19.389	21.516	29.272	15.415
90	25.798	29.157	38.445	21.046
120	31.472	38.33	46.11	29.024
150	40.069	49.116	58.288	36.57
180	46.798	55.356	69.553	46.981
210	56.096	65.575	79.345	53.768
240	61.77	73.323	85.322	63.22
N	1.1018	1.1231	0.7996	1.1857
k	0.1657	0.1107	1.084	0.1013
Best fit model	Zero order	Zero order	Zero order	Zero Order

Table 7: Stability study of optimized batch (F5)

Month	**Colour**	**Appearance**	**pH**	**Spreadability (gm.cm/sec)**	**Drug Content (% w/w)**
First	Slight brown	Transparent	7.02	20.10	97.48
Second	Slight brown	Transparent	6.98	19.98	96.26
Third	Slight brown	Transparent	6.96	19.92	95.95

CONCLUSION

Drugs of plant origin are more acceptable in the belief that they are safer with fewer side effects than the synthetic ones. Herbal formulations have grown in demand in the world market. All the gel formulations were evaluated for physicochemical parameters and *In Vitro* Drug release studies reveal that F5 and F7 formulations shows the 87.97 % and 84.29 % drug release respectively and permeation studies done with cadaver skin affirmed the F5 and F7 formulation shows 85.32 % and 73.32 drug release respectively. From the above study we found that the combination of Ocimum basilicum seed mucilage gel with natural or synthetic polymer can increase the drug release and stability of gel formulations containing Plumeria alba leaves extract.

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