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Formulation evaluation and *in-vitro* drug release characteristics of aloe vera herbal suppositories

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ABSTRACT

To achieve successful delivery of drug locally as well as systematically, rectal route has proved its potential. The main objective of this research work was to formulate and evaluate herbal extract Aloe Vera suppositories. Suppositories are inserted directly into the rectum to distribute their herbal powder to internal areas. Aloe Vera contains aloin, which is an anthraquinones glycoside. Aloin has been used as a laxative for constipation. It showed laxative action. Extract of Aloe Vera was done by soxhlet using methanol as solvent. Heat molding method was used for the preparation of suppositories, which were evaluated for their physicochemical properties and in-vitro release characteristics. Suppositories of polyethylene glycol (PEG) 4000 and surfactant showed better permeation of drug and laxative action.

Keywords: Aloe Vera leaf extract, polyethylene glycol (PEG) 4000, Tween 80, Methanol, Herbal suppositories.

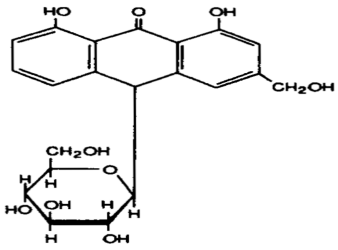
INTRODUCTION

Suppositories are designed for insertion into body cavities where they melt, soften or dissolve and exert local or systemic effects. The suppositories serve as an alternate where oral administration of drug is not suitable as in infants or patients suffering from nausea, vomiting and gastrointestinal disturbances. They provide the advantage that biotransformation of drugs in liver, pH conditions and gastrointestinal enzymes are avoided. [1]

The suppository base play vital role in the release of medicament they hold the drug. The important property of suppository base is that it should remain solid at room temperature but soften, melt or dissolve readily at body temperature so that the drug is released after its administration. [2]

Medicinal plant has specific property and specific use knowing to their biological group of compounds. Several species of the genus aloe has been in use under the common name of aloe *viz*. Aloe Vera. Aloe barbadensis, Aloe ferox, Aloe chinensis, Aloe indica, etc. Amongst these Aloe Vera Linn syn. Aloe barbadensis Miller are accepted as the correct biological source of aloe Vera. Aloe Vera is member of lily (Lillaceae) family is spiky, succulent, and native to warm regions. [3]

Aloin



Herbal Suppositories of Aloe Vera can be used in patients suffering from nausea, gastric ulcers, comatose patients, geriatrics where administration is difficult or not possible through oral route. Studies have showed that the release characteristic of suppositories depends on the physicochemical properties of the drug, its carrier (suppository base) and surfactants. The particle size of drug and chemical composition increase or decrease the rate of release.

MATERIALS AND METHODS

Materials

Method of isolation

Aloe Vera leaves were collected from college botanical garden. The leaves washed with water and rinds were removed. The inner gel scrapped and cut into pieces, solar dried (30-40^{0}C for 2 weeks) and dry gel particles were collected. The dry gel particles were screened using sieves. Solvents used for the extraction and high performance liquid chromatography (HPLC) analysis were of AR and HPLC grade. [4]

Soxhlet extraction- The maximum recoverable aloin was estimated by Soxhlet extraction using methanol. 5 % (w/w) of aloe Vera powder were taken in Soxhlet with 200 ml methanol. Extraction was carried out for 24 hours. Samples free from dry gel were collected at the end, stored in a freezer, and analyzed using HPLC to determine the concentration of aloin in each extract. [5]

Preparation of suppositories

The suppositories bases were accurately weighed and melted on water bath. Finely divided drug powder was thoroughly incorporated in the melted base with continuous stirring. The melted mass was poured in the appropriate suppository mould. Suppositories were kept in refrigerator, at 4^{0}C to avoid the development of cracks and the exposure to room temperature was limited to less than 24h before use in *in- vitro* release studies. [8,9]

Table 1: Code and composition of formulations

Sr.no.	Ingredients	Quantity taken (%)	Use
1	Aloe vera leaf extract	12	Laxative
2	PEG 4000	75.2	Base
3	Tween 80	10	Solubilizing agent
4	Methyl paraben	1.4	Preservative
5	Propyl paraben	1.4	Preservative

Evaluation of Suppositories

Visual characterization

Twenty suppositories from each batch were randomly selected, longitudinally cut and examined through naked eyes for the assessment of physical characters like absence of fissuring, pitting, fat blooming, exudation and migration of active ingredients.[6]

Table no. 2: Visual characterization of the formulation.

Parameters	F1	F2	F3	F4	F5
Fissuring	No	No	No	No	No
Pitting	No	No	No	No	No
Fat blooming	No	No	No	No	No
Exudation	No	No	No	No	No
Migration of active Ingredient	No	No	No	No	No

Length and width: Twenty suppositories were selected randomly from each batch, their length and width was measured using vernier calipers.

Weight variation: Twenty suppositories were weighed and average weight was calculated. Each suppository was weighed individually on electronic balance (Shimadzu make). No suppositories should deviate from average weight by more than 5% except two which may deviate not more than 7.5 %

Friability: Friability testing was performed using Roche friabilator. Twenty suppositories of each formulation were accurately weighed. These suppositories were placed in the rotating drum of the friabilator. Drum was operated for the 100 revolutions at the speed of 25rpm/min. The suppositories were removed and reweighed. Percentage weight loss was calculated using following formula.

$$\% F = \text{Loss in weight} / \text{Initial weight} \times 100$$

Melting point: Macro melting range test was performed with the whole suppository. Suppository from each formulation was placed in a test tube with phosphate buffer pH 7.2 maintained at constant temperature 37± 0.5℃. The time required by the whole suppository to melt or disperse in the media was noted. The melting time plays a crucial role in the release of active ingredient.

Liquefaction*:* Liquefaction time was measured using a burette having a broad opening on one side and a narrow opening on the other; suppository was pushed inside form the broad end side to reach to the narrow end. 5ml of phosphate buffer pH 7.2 was placed inside the burette, maintained at 37± 0.5℃. A thin glass rod was placed on the top of the suppository and the time at which the glass rod just inserts into the suppository was recorded as liquefaction time. This indicates the time taken by the formulation to liquefy under similar pressures found in rectum. [7]

Disintegration test: The disintegration time of the suppositories was performed by using disintegration test apparatus. The time taken for the disintegration of entire suppository was recorded. Phosphate buffer pH 7.2 maintained at 37±0.5℃ was used for this testing.

Drug Content: Drug Content was determined spectrophotometrically. One suppository in 200ml of phosphate buffer pH 7.2 maintained at 37± 0.5^0C till it melted. 1 ml sample was withdrawn and diluted to 100ml with phosphate buffer pH 7.2. The content of aloin was determined by using UV-Visible spectrophotometer (JASCO model-V630) by measuring absorbance of the diluted sample at 262.5nm.

In- vitro Dissolution study:
The study was carried out using dissolution apparatus USP Type II (Paddle)
Dissolution medium: Phosphate buffer, pH 7.2.
Speed of paddle: 100 rpm.
Temperature of medium: 37 ± 0.5°C

The release rate of Aloin was determined using USP Dissolution Testing Apparatus II (Paddle type). The dissolution test was performed using 900 ml of Phosphate buffer pH 7.2, at 37 ± 0.5°C. Aliquot (5 ml) of the solution was collected from the dissolution apparatus and were replaced with fresh dissolution medium. The aliquots were filtered through whatmann filter paper no. 41. Absorbance of these solutions was recorded at 262.5 nm and drug content in dissolution sample was determined by software (PCP disso v3) version.

RESULTS AND DISCUSSION

Table no. 3: Physicochemical Evaluation of Aloin:

Sr. No.	Characteristics	Result
1	Identification	Lower Ammonical layer shows red color
2	Color	Yellowish brown color
3	Taste	Bitter
4	Solubility	Soluble in Methanol(90%), ethanol, acetone, water

5	Melting point	146-148^{0}C
6	TLC Ethyl acetate: Methanol: water (100:13.5:10)	Rf value: 0.7

Isolation of aloin:

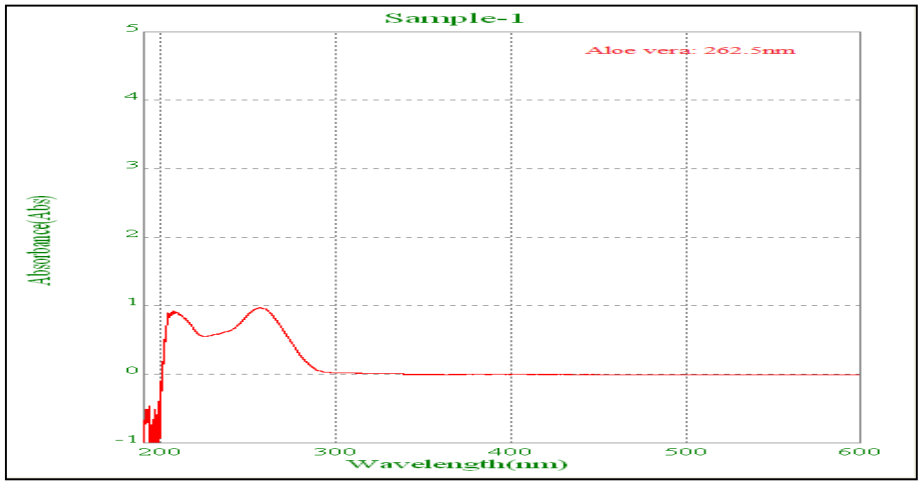


Fig.1: UV spectrum of Aloin

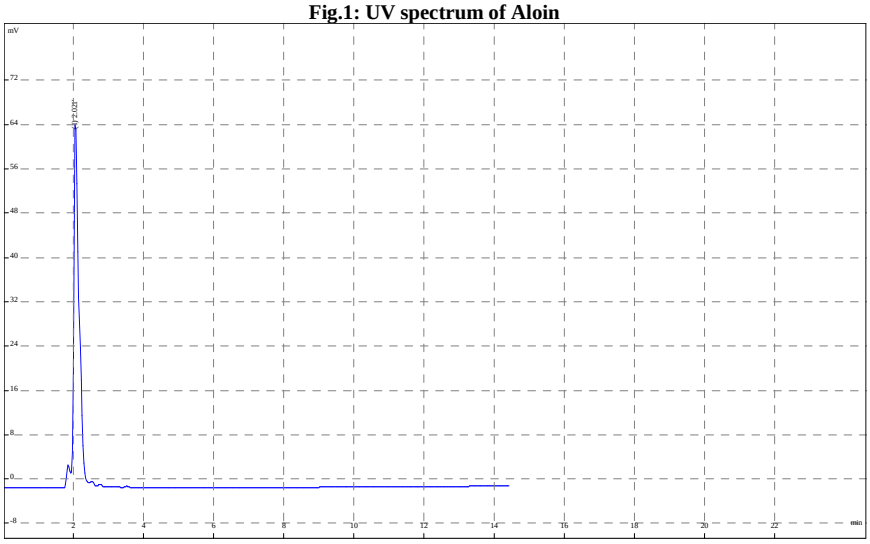


Fig.2: HPLC chromatogram of Aloin

Wavelength: 270nm, Mobile Phase: Methanol 100%, Sample volume: 20µl, Flow rate: 0.9ml/min, Run time: 14.43min**.**

Standard calibration curve of Aloin:

10 mg of Aloe Vera extract was dissolved in 100ml of methanol to get a concentration of 100mcg/ml. from this solution 0.5, 1.0, 1.5, 2.0, 2.5 and 3ml were diluted to 10 ml of methanol to get aliquots of 5, 10, 15, 20, 25 and 30 mcg/ml concentration and were subjected for UV analysis at 262.5nm.

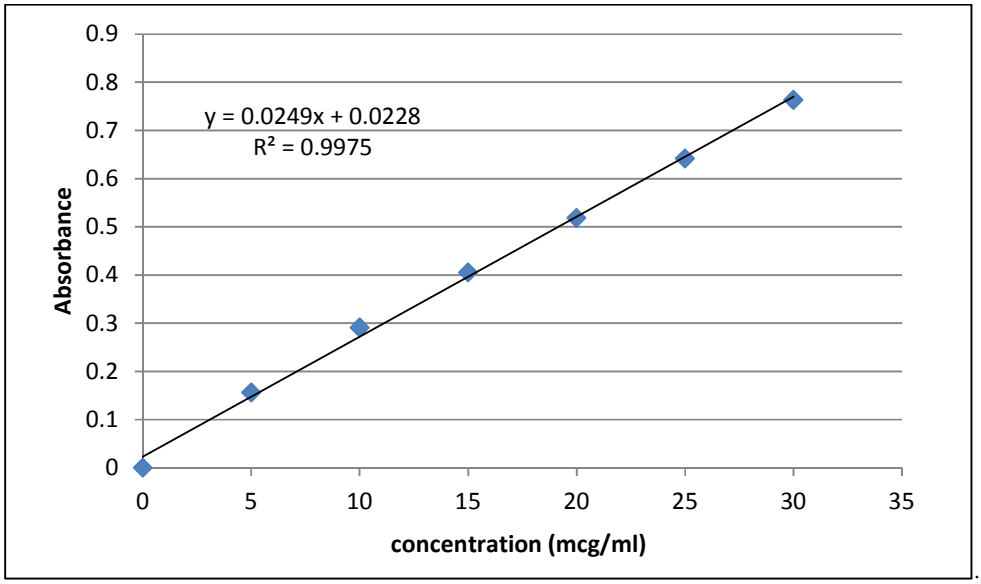


Fig.3: Standard calibration curve of Aloin

Herbal suppositories of Aloe Vera were prepared by Heat molding method using base like PEG 4000. Table 4 and 5 shows the data for the suppositories were evaluated for the properties such as appearance ,length, width, weight variation, melting time, hardness, Friability, Disintegration test, percent drug content.

Table no. 4: Physicochemical characterization of the formulation

Formulation code	Length (cm)	Width (cm)	Weight variation (gm)	Melting		Friability (%)
				Temp. (^{0}C)	Time (min)	
F1	2.23	1.11	1.810±0.11	37.1	35±0.43	0.37
F2	2.22	1.12	1.992±0.11	38	45.3±0.24	0.43
F3	2.26	1.11	1.813±0.12	37	39±0.45	0.38
F4	2.23	1.13	1.910±0.13	38.2	36±0.40	0.37
F5	2.23	1.12	1.984±0.11	37	36±0.25	0.40

Table no. 5: Physicochemical characterization of the formulation

Formulation code	Hardness (Kg/cm^2)	Liquefaction time (min)	Disintegration (min)	Drug Content (%)
F1	2.50±0.14	2.38 ±0.43	9.27±0.03	99.45
F2	3.01±0.11	2.54±0.21	10±0.025	96.24
F3	2.42±0.25	1.45±0.05	9.28±0.031	98.47
F4	2.50±0.24	2.51±0.01	10±0.038	99.08
F5	2.8±0.18	2.47±0.56	9.26±0.024	98.94

Dissolution Profile:

Fig.4: Comparative in-vitro drug release of Aloin from suppositories

The in-vitro drug release profile from different suppositories formulation was shown in fig.4. The dissolution study showed that the suppositories melted in the dissolution medium maintained at 37 ± 5^0C. All five formulations showed more than 50% drug release within 25min. This may be due to the addition of Tween 80 in the formulation. The maximum release of drug in F1, F2, F3, F4, F5 showed 97.78%, 97.00%, 96.65%, 96.66%, 97.57% within 30 min. resp.

The dissolution data for suppositories F1 to F5 was fitted to various drug release kinetic models like Zero order, Matrix, Hix.crow and Korsemeyer Peppas model. The model that gives maximum 'R' value is considered as the best fit model for the release data. It was found that Zero order as best fit model for all the formulations test.

Table 4: Values of rate constants (K) and correlation coefficients (R) for release of Aloin from Suppositories

Batch Code	Zero Order		Matrix		Hix.crow		Korsmeyer Peppas	
	(R)	(K)	(R)	(K)	(R)	(K)	(R)	(K)
F1	0.9351	2.1720	0.8200	10.3929	0.7937	-0.0121	0.9455	2.7240
F2	0.9317	2.1358	0.8130	10.1941	0.7879	-0.0118	0.9440	1.9143
F3	0.9684	2.3064	0.8748	11.1731	0.8414	-0.0123	0.9809	2.3058
F4	0.9823	2.4505	0.9086	11.9820	0.8748	-0.0131	0.9788	2.7175
F5	0.9351	2.1720	0.8200	10.3929	0.7931	-0.0121	0.9455	2.1240

CONCLUSION

Aloe vera herbal suppositories were formulated by heat molding method and were subjected for physical evaluation, weight variation, content uniformity, disintegration, melting point, mechanical strength, and *in-vitro* dissolution studies. All tests shown satisfactory results. All five formulations showed more than 50% drug release within 25min. This is due to the addition of Tween 80 in the formulation. Based on the in- vitro release rate studies, it can be concluded that polyethylene glycol 4000 can be used as a base which were easily soluble in aqueous medium, disperses rapidly and has higher rate of release for immediate release of aloe Vera herbal suppositories.

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