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Pharmaceutical assessment and pharmacological evaluation of Dexibuprofen-Aloe vera trans emulgel

Thiruppathi M, Lavakumar V, Natarajan P and Sowmiya C

Abstract
The aim of the research was to prepare dexibuprofen emulsion for incorporation in *Aloe vera* gel base to formulate 'Dexibuprofen – *Aloe vera* trans emulgel' (DAE) and to carryout *in-vitro* pharmaceutical assessment and *in-vivo* analgesic and anti-inflammatory studies of the product. Dexibuprofen is a racemic enantiomer of ibuprofen and its more pharmacologically effective than ibuprofen. The drug loading capacity of transdermal gels is low for hydrophobic drugs such as dexibuprofen. Dexibuprofen can be effectively incorporated into emulgels (a combination of emulsion and gel). *Aloe vera* has a mild anti-inflammatory effect and in the present study *Aloe vera* gel was formulated and used as a gel base to prepare DAE. The prepared emulgels were evaluated for pharmaceutical parameters like viscosity, pH, *in-vitro* permeation, stability and skin irritation test. *In-vivo* anti-inflammatory studies were performed using fresh egg white albumin induced hind paw edema method and analgesic studies were performed by using tail flick method in Wistar rats. The results were compared with that of diclofenac gel. When applying the gel on skin leads no skin irritation. Stability studies proved the integrity of the formulation. The percentage of inhibition of edema was highest for the prepared DAE (60.94% inhibition after 180 min) compared to standard diclofenac gel (49.6%). From our results, it was concluded that the *Aloe vera* gel acts as an effective gel base to prepare dexibuprofen emulgel with high drug loading capacity (78% drug content) with significant anti-inflammatory effect.

Keywords: Inflammation, stability, *in vitro* permeation, drug diffusion, plethysmograph

Introduction
Dexibuprofen is the S (+) (dextrorotatory) enantiomer of ibuprofen and accounts for analgesic, anti-inflammatory, antipyretic activities of the recemic compound. It is employed to treat inflammation, rheumatoid arthritis, osteoarthritis and dysmenorrhea [1]. The anti-inflammatory effects are believed to be due to inhibition of both COX-1 and COX-2, which leads to the inhibition of prostaglandin synthesis [2]. Dexibuprofen acts on hypothalamus, which produce an antipyretic effects due to the increased peripheral blood flow, vasodilatation and subsequent heat reduce [3]. The advantages of dexibuprofen include greater clinical efficacy, ease in dose optimization, less variability in therapeutic effects, all of these half the dose of ibuprofen. Greater peak analgesia was also seen with dexibuprofen. It is indicated for the relief of sign and symptoms of osteoarthritis, rheumatoid disorders such as osseous rheumatism, ankylosing sodalities, juvenile arthritis, muscular rheumatism and degenerative joint disease. It is used for the acute symptomatic treatment of painful menstruation, symptomatic treatment muscle pain, head ache and dental pain [4].

Aloe vera is a stemless, drought resisting, stemless, succulent plant and has been used ancient times for medicinal purposes. Family – *Liliaceae*. It has stiff grey to bright green lance-shaped leaves containing gel-like substances in a central mucilaginous pulp. Recent research has shown that the pharmacologically active agent is used for the psoriasis treatment [5]. The active agents have shown considerable palliative, antipruritic, wound healing and anti-inflammatory properties, thus mitigating consideration of aloe vera as an effective remedy for the treatment of psoriasis [6]. It is also used for wound healing, burn, sunburn, etc. Aloe contains Bradykinase, magnesium and salicylic acid or some of the compounds that help with wound healing and help reduce redness, swelling and inflammation. *Aloe vera* has been used in various commercial products because of these therapeutic properties. It was claimed that the acetylated mannan present in the central parenchymal portion of *Aloe vera* is responsible for the anti-inflammatory effects [7]. It was reported that anti-inflammatory effect of *Aloe vera* gel is similar to that of indomethacin and dexamethasone in carrageenan-induced paw edema in rats [8]. In addition, as aqueous gel base, *Aloe vera* offers antimicrobial, antifungal, UV

protection and wound healing characteristics. In the present research work, the central parenchymal portion of *Aloe vera* was formulated into gel using sodium alginate.

Materials and Methods

Materials

Dexibuprofen was obtained as a gift sample from Zuventus healthcare ltd. Bangalore, India. *Aloe barbedensis* Miller leaves were collected locally. Sodium alginate, Methyl paraben and Carrageenan were obtained from HiMedia Labs Pvt. Ltd., Mumbai.

Animals used

Selection of animals

Male wister albino rats are weighing about 180 – 230 g were used for the study. Animals are placed in polypropylene cages and maintained under standard laboratory conditions. They were acclimatize to laboratory conditions for 10 days before commencing the experiment. The study was approved by the Institutional Ethical Committee, which follows the CPSCEA guidelines.
(XXXIII/IAEC/509/01/C/CPCSEA/AKCP015/Mar 2017)

Methodology

Collection *of Aloe vera Pulp*

A fresh *Aloe vera* leaves were obtained from the plant and washed with water repeatedly to remove solid mud particles on the leaves. The leaves were then kept inverted for 30 minutes to allow the yellow sap to drain out. The leaves were then treated with water to completely wash out the yellow sap. For each leaf, the spikes placed along their margins were removed before longitudinal slicing to separate the epidermis from parenchyma [9]. The central parenchymatous portion (pulp) was removed by peeling the outer skin and pericarp. Care was taken not to avoid tearing the green rind, which can contaminate the pulp. The central parenchymatous pulp was scooped out carefully. As *Aloe vera* pulp is highly acidic due to acidic compounds like acetyl mannan, the pulp was subjected to repeated washing with water and finally treated with 0.1 N NaOH solution to maintain neutral pH conditions.

Preparation of Aloe vera Gel

The treated pulp was blended to obtain the juice. The obtained juice was filtered through a cotton bed to remove the leftover rind particles. Following this, the juice was subjected to vacuum filtration repeatedly until a clear liquid was obtained. To the clear liquid juice obtained, 1% w/w sodium alginate and 0.5%w/w methylparaben was added and dispersed uniformly until no lumps were left. As sodium alginate gellifies under alkaline conditions, 0.5 N NaOH solution was added drop-wise until a gel was formed. This gel of *Aloe vera* was stored in air tight containers to prevent oxidation.

Preparation of Dexibuprofen- Aloe vera Transemulgel

The oil phase of the emulsion was prepared by dissolving 0.5 ml of Span 20 in 4.5 ml of light liquid paraffin and 0.5% w/w dexibuprofen was dissolved in the oil phase. The aqueous phase was prepared by dissolving 0.5% Tween 20 in purified water. Both the oil and aqueous phases were separately heated to 70º- 80 ºC. Following this the oily phase was added to the aqueous phase with continuous stirring until the product cooled to room temperature resulting in the formation of a dexibuprofen o/w emulsion. The dexibuprofen o/w emulsion was added while continuously stirring, to the prepared *Aloe vera* gel in 1:1 weight ratio to produce homogenous DAE. The emulgel was treated with 0.5 N NaOH to obtain consistency in the product. The prepared emulgel was stored in an airtight container. An *Aloe vera gel* without drug was also prepared for further comparative studies. The prepared transemulgel was observed visually for colour, appearance and consistency.

In vitro Pharmaceutical Evaluation

1. Physical examination

The prepared formulations were examined by visually for their colour, appearance and consistency [10]

2. pH Measurement

The pH of the prepared emulgel formulation was measured by using digital pH meter (Elico LI 120 model).

3. Viscosity Measurement

The flow behaviour of the prepared formulations was studied in a Brookfield Viscometer (LVDV-E) using spindle # 61.The assembly was connected to a thermostatically controlled circulating water bath maintained at 25 °C. The formulation whose viscosity was to be determined was added to a beaker covered with a thermostatic jacket. The spindle was allowed to move freely into the emulgel and the viscosity was noted [11].

4. Analytical Method development

Preparation of standard and test solutions

i) Dexibuprofen standard stock solution I

Accurately weighed 10 mg of Dexibuprofen was dissolved in 10 ml methanol and transferred to a 10 ml volumetric flask sonicate it for 5 min, finally, volume was made up to the mark with methanol to make 1000µg/ml stock solution.

ii) Dexibuprofen standard stock solution II

1ml of Dexibuprofen stock solution I was taken and transferred into 10ml of volumetric flask and add 5ml of phosphate buffer pH 7.4 and wait for 5mins in a sonicator, then finally make up with of phosphate buffer pH 7.4 to make 100µg/ml.

5. Determination of and absorption maxima of dexibuprofen: The stock solutions of dexibuprofen (I&II) were diluted further with phosphate buffer pH7.4 to get working standard solution of 5, 10, 50 µg/ml of dexibuprofen. These standard solutions were analysed by by using UV spectrophotometer (Shimadzu 1700). The diluted solutions were scanned in the spectrum mode over the range of 200-600 nm against as phosphate buffer pH 7.4 as blank runs. The UV spectra of the dexibuprofen were conducted and being recorded.

6. Procedure for calibration curve: The standard solutions were prepared by the suitable dilution of the stock solution I with methanol and stock solution II with phosphate buffer pH 7.4 to obtain working standard (5,10,20,30,40,50&60µg/ml). All the measurements were performed at room temperature. The absorbance of the solutions containing Dexibuprofen was determined at 287nm using a phosphate buffer pH 7.4 as blank. For linearity study, dilutions were made for Dexibuprofen in the range of 5 to 60 µg/ml. These concentrations were prepared by diluting the stock solution with phosphate buffer pH 7.4. The calibration curve was

reputable at this wavelength by plotting graph between absorbance and concentration. The standard calibration curve was as shown in the figure no 2.

7. Drug Content Determination: Dexibuprofen content in DAE was measured by dissolving a known quantity of both the formulations in phosphate buffer pH 7.4. Absorbance was measured after suitable dissolutions at 287 nm in UV-Visible Spectrophotometer (Shimadzu UV1700). Percentage of drug content was calculated with the help of standard graph.

8. *In vitro* drug diffusion Studies: The diffusion studies were performed in a vertical Franz diffusion cell using egg membrane as a barrier layer. The transemulgel was applied on the membrane placed between donor and acceptor compartment. Phosphate buffer pH 7.4 was used as a dissolution medium. The stirring and temperature were maintained by parking the set up on a magnetic stirrer with temperature control. The temperature was controlled at 37±1 ºC. The samples were obtained at 0, 30 60, 90, 120 and 150 min. The receptor compartment was maintained for sink condition using phosphate buffer pH 7.4. The flux (J) was determined as the angular coefficient of curve obtained by plotting the accumulative quantity of the penetrated drug versus time. The permeability coefficient (Kp) of dexibuprofen was calculated using the following equation [12]. In all the data listed in the table no 3 and the drug release profiles are
shown in fig no 3.

$$Kp = \frac{J}{c}$$

Where, C is the initial concentration of drug in the formulation applied to the membrane.

9. Accelerated stability testing
The stability study of transemulgel was conducted as per ICH guidelines by employing different environmental conditions. The emulgel about 10 g was firmly packed in aluminium collapsible tubes. The emulgels were stored in a stability chamber at three different storage conditions of 25 °C/ 60% RH, 40 °C/ 60% RH and 55 °C/ 75% RH. The emulgels were evaluated for their appearance, viscosity, pH, drug content and in-vitro drug diffusion when forty five days. These all the data are listed
the table no 4.

Characterization of Dexibuprofen - Aloe vera transemulgel using FTIR spectroscopy
FT-IR stands for Fourier remodel below Red, the preferred method of infrared spectroscopy. In infrared spectroscopy, the radiation is passed through a sample. Some of the infrared emission is absorbed by the sample and a few of it's passed through (transmitted) the sample. The resulting spectrum represents the molecular absorption and transmission at different wave number creating a molecular fingerprint of the sample.
Drug and excipients separately, as well as their mixture, were analyzed by FTIR.
Sample 1: Dexibuprofen
Sample 2: placebo (aloe vera + sodium alginate)
Sample 3: Mixture of dexibuprofen and excipients

Pharmacological Evaluation
Skin irritation test (patch test)
Guidelines of the institutional animal commission were followed for this experiment. The hair on the dorsal facet of Wistar anomaly rats was removed by clipping 1 day before this portion of the experiments. A set of 4 rats was used in the study. The prepared emulgel was applied on the properly shaved skin of rats and observed for undesirable skin changes like change in colour, redness of the skin, change in skin morphology for a period of 24hr. [13] The results are shown in figure no.8.

1. *In vivo* anti-inflammatory activity
Egg white albumin inducing paw edema model
Animals were divided into four groups, each consisting of six rats per group and were treated as follows,
Group I**:** a control group which received 0.1 ml of fresh egg albumin
Group II**:** Aloe vera gel and 0.1 ml of fresh egg albumin
Group III**:** Dexibuprofen–*Aloe vera* transemulgel (DAE) and 0.1ml of egg albumin
Group IV**:** Standard drug diclofenac emulgel and 0.1 ml of fresh egg albumin

Thirty minutes post-treatment, Inflammation was induced in the rat by the injection of egg albumin (0.1 mL, 1% in normal saline) into the subplantar tissue of the left hind paw. The linear circumference of the injected paw was measured before and 0, 30, 60, 120, 180 and 240 mins after the administration of the egg albumin administration by mercury displacement method using a plethysmometer. [14] The percentage inhibition of paw edema was compared with fresh egg albumin control group and calculated using the formula, [15]

$$\%\text{Inhibition} = \frac{Vc - Vt}{Vc}$$

Where, Vc is the increase in paw volume in control group and Vt is the increase in paw volume in treated groups.

2. Analgesic activity
Tail flick method
Animals were divided into four groups, each consisting of four rats per group and were treated as follows,

Group I **:** Control group;no topical treatment was given
Group II**:** Aloe vera gel
Group III**:** Dexibuprofen –*Aloe vera* transemulgel (DAE)
Group IV**:** Standard drug diclofenac emulgel

The analgesic activity was carried out using analgesiometer. The tail flick test was carried out by focusing radiant heat on the dorsal surface of the tail. Latency, or the time it took the rats to withdraw their tails from a noxious thermal stimulus, was measured using an analgesiometer. To minimize tissue injury, a maximum latency of 30 sec was imposed. For each set of experiments, dexibuprofen emulgel formulations (containing 50mg/kg). Each rat was then tested before and 0, 30, 60, 90, 120, 150, and 180 min after the topical administration of each formulation (n = 6 for each group) [16-18].

4.7 Statistical Analysis
Statistical analysis was performed using a one-way analysis of

variance (ANOVA) to test the difference between the means of dexibuprofen emulgel formulation with control and positive control group. The mean and standard error mean (SEM) of n = 6 was calculated. The resulting data were considered statistically significant at $P < 0.05$. For the *in vivo* studies, differences between drug treated and control groups were also evaluated using Dunnett‟s, t‟ test. The mean and SEM of n = 6 were calculated. A chance level of $P < 0.05$ was considered statistically significant.

Results and Discussion

Pharmaceutical evaluation

1. Physical appearance: The prepared Dexibuprofen - Aloe vera transemulgels (DAE) were colourless and transparent with a homogenous texture and glossy in appearance which indicates the consistency of gels towards topical applications.

2. pH Measurement: *Aloe vera* is highly acidic due to the presence of acidic constituent acetyl mannan. The pH of *Aloe* pulp was found to be 2.34. The pH of transdermal formulations should not be acidic as it causes the skin irritation. Hence the *Aloe* pulp was treated with 0.1N NaOH to maintain neutral pH. The pH values are shown in Table no 1. The pH of the blended A*loe vera* juice was maintained at alkaline conditions using 0.5 N NaOH to favour the gelling of sodium alginate and the pH was found at 8.52 for *Aloe vera* gel. The pH of *Aloe vera gel* was 8.23. As dexibuprofen is acidic, the pH of DAE was further reduced to 7.56 which is a suitable pH for transdermal application. The pH values of all developed formulations were brought around to normal pH, which are which are considerably accepted. Hence, the consistencies of developed gel formulations containing Dexibuprofen alovera emulgel were better as compared with marketed gel with smooth and homogeneous appearance.

3. Viscosity Measurement: Viscosity is an important parameter since it affects spreadability and devotion of transdermal preparations to the skin surface. The values of viscosity for the prepared formulations are shown in Table no 1. From the results, it was observed that the viscosity was found to be higher for *Aloe vera* gel. The prepared emulgels showed a decrease in viscosity compared to *Aloe* gel because of the liquid consistency of the emulsions added to emulgels. The viscosity was unaffected by the presence of dexibuprofen. Hence, the consistencies of developed gel formulations containing dexibrufen were better as compared with marketed gel. The marketed gel and prepared gel formulations were shared a smooth and homogeneous appearance.

Table 1: Pharmaceutical evaluations of Dexibuprofen Aloe vera transemulgel

Formulation	pH	Viscosity (CPs)	% drug content	Flux (µg cm-2 h-1)	Permeability coefficient (Kp) (cm h-1)
Aloe vera pulp	2.34±0.28	-	-	-	-
Aloe vera gel	8.52±1.04	140±0.76	-	-	-
Aloe vera with sodium alginate gel	8.23±0.67	130±0.48	-	-	-
DAE	7.56±0.79	112±0.99	89.4±2.8	0.624	$15.3x10^{-4}$

Analytical Method

Dexibuprofen showed the absorption maxima at 287 nm and it obeys the beer lamberts law from 10 to 60 mcg/ml. The line equation and r2 values are shown in the figure no.2.

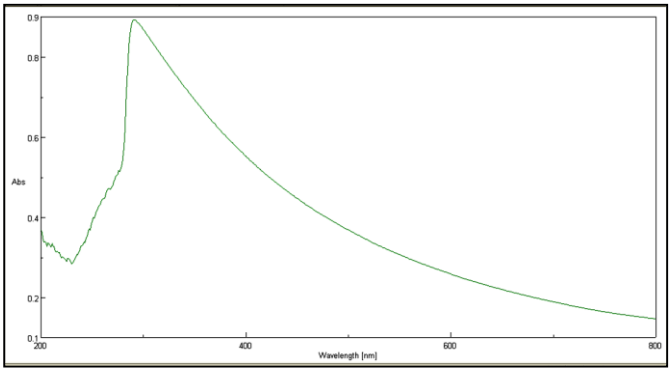


Fig 1: Determination of absorption maxima (λ max) of Dexibuprofen

Table 2: Construction of standard graph of Dexibuprofen:

Conc(mcg/ml)	Absorbance
0	0
10	0.15
20	0.3
30	0.38
40	0.59
50	0.8
60	0.98

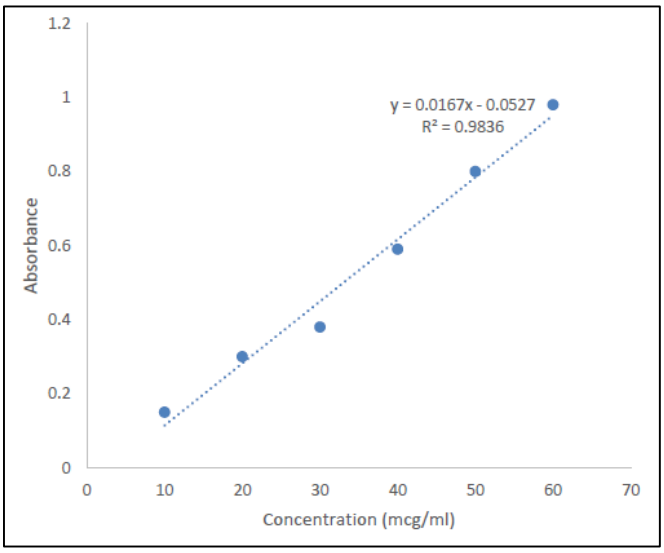


Fig 2: Standard calibration curve for analysis of Dexibuprofen at 287 nm

Drug content

Drug content was determined and given in the table no 3. From the results it was observed that the percentage drug content is high with DAE indicated that the drug loading capacity for the prepared emulgel is high

In vitro Drug diffusion studies

The study showed the release of the drugs from its emulsified gel formulation. The table no 3.showed the amounts of drug

release from the prepared dexibuprofen transemulgel formulation. A 62% of the drug is released from the prepared transemulgel in 30 min which indicates the drug release is more with transgels. The hydrophobic dexibuprofen was effectively incorporated into aloe vera trans gel. The drug release profiles are shown in fig no 3. The flux and the permeability coefficient of prepared transemulgel are calculated and shown in table no.1. The flux and permeability coefficient is high with the prepared transgels because of the higher penetrating power of aloe vera gel.

Table 3: *In vitro* drug diffusion studies on dexibuprofen Aloe vera transemulgel

Time (min)	DAE	
	Cum.amt. of drug release (mcg/cm2)	% drug release
30	53.22 ± 1.22	62
60	62.1 ± 2.0	71
90	62.99 ± 2.1	72
120	63.1 ± 2.3	73
150	68.0 ±3.5	78

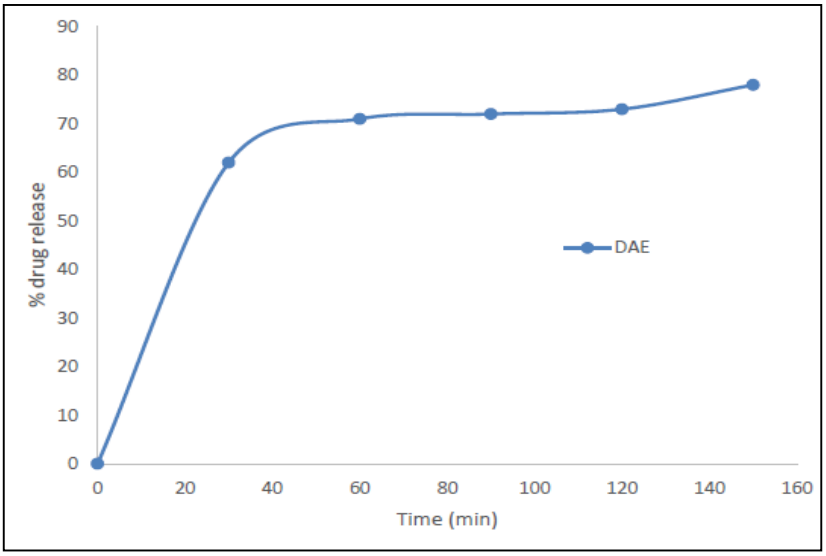


Fig 3: *in vitro* drug diffusion of dexibuprofen Aloe vera transemulgel

Accelerated stability studies

The stability studies on prepared emulgel were conducted as per ICH guidelines. The results were shown in table no. 4. and it is indicated that the prepared emulgels are stable and does not show much change in storage for 45 days at various temperatures and humidity. However, the formulation stored on 550C/ 75% RH showed a slight reduction in drug content and a slight change in physical appearance. There is no significant change in the drug release profiles. (Table 4) which indicates the prepared formulation are more stable.

Table 4: Stability studies of dexibuprofen – Aloe vera transemulgel (DAE)

Storage Conditions	Appearance		Viscosity (Cps)		pH		Drug content (%)	
	Before	After	Before	After	Before	After	Before	After
25^0C/60% RH	Colorless	Colorless	112	110	7.56	7.56	89.4	89.0
40^0C/ 60% RH	Colorless	Colorless	112	108	7.56	7.52	89.4	88.8
55^0C/ 75% RH	Colorless	Milky white	112	102	7.56	7.2	89.4	85.2

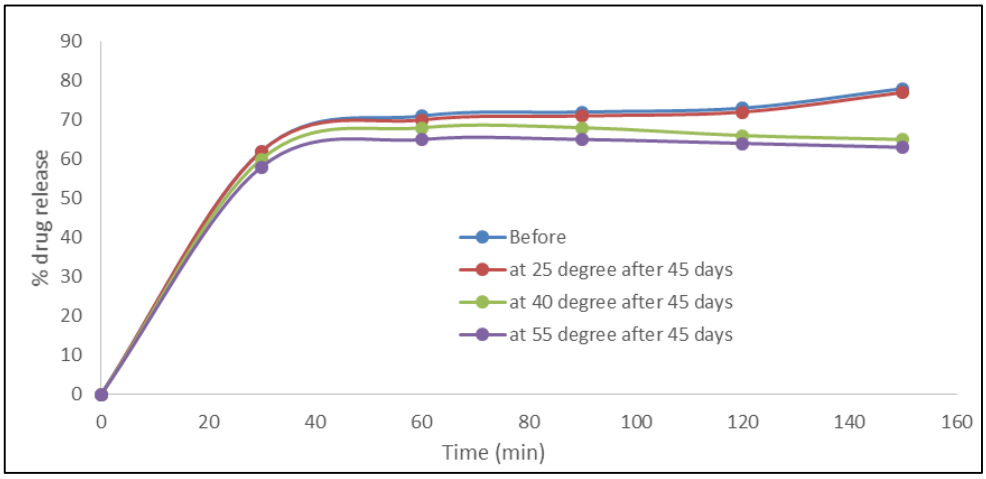


Fig 4: Graphical representation of stability studies of DAE

Ftir Spectroscopy

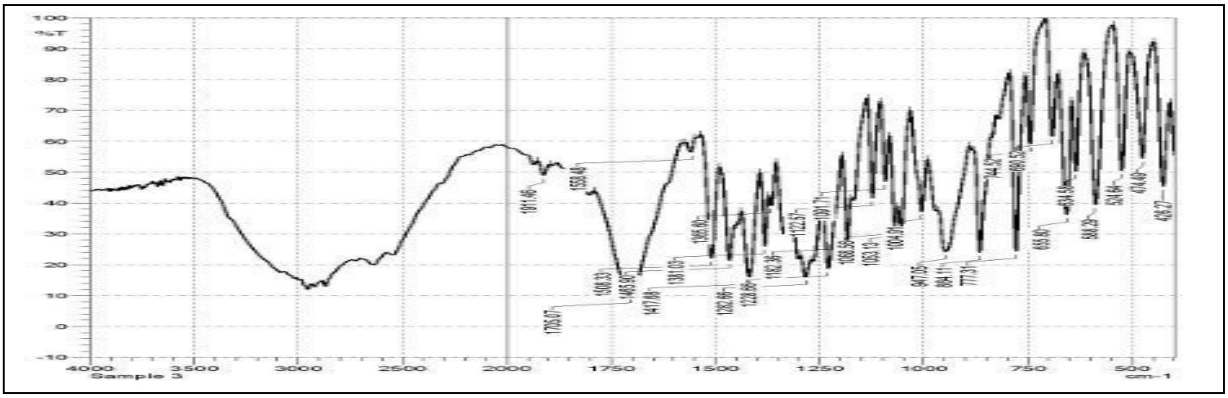


Fig 5: FT-IR Studies on Dexibuprofen

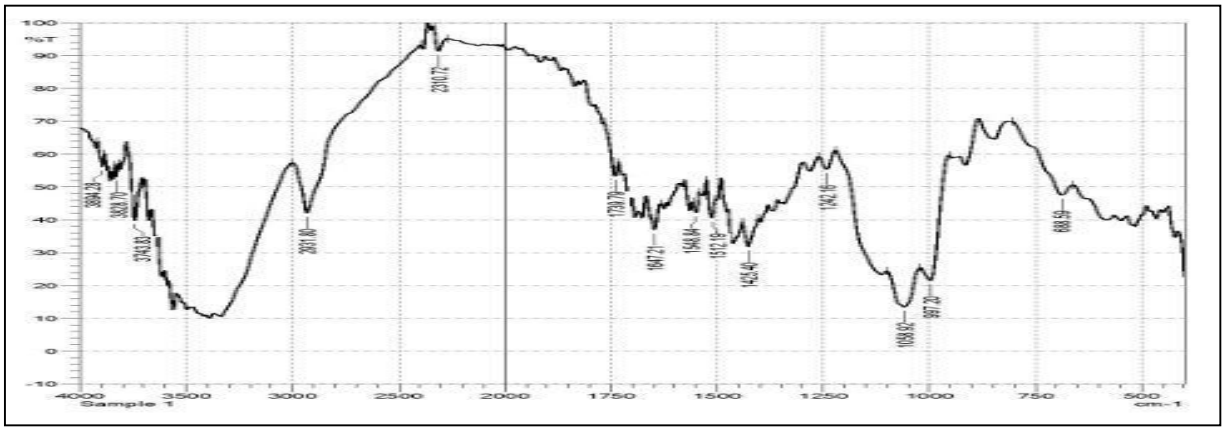


Fig 6: FT-IR Studies on aloe vera gel

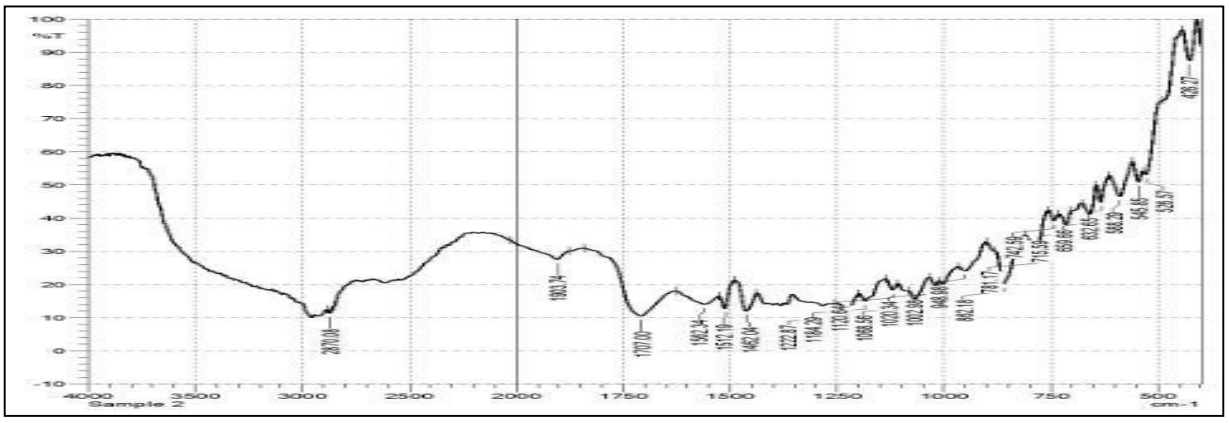


Fig 7: FT-IR Studies on Dexibuprofen incorporated with aloe vera gel

Table 5: Interpretations of FTIR Spectroscopy

Functional groups	(Wave number cm^{-1})		
	Reference	Drug	Drug and Excipient mixture
C=O	1705 - 1725	1705	1707
Aromatic CH_3	700 - 850	744	742
OH	1050 - 1150	1068	1068
C_6H_6	1450 - 1600	1465	1462

Discussion

The FTIR spectra of drug and excipients are shown in Fig 5, 6, & 7. Fig 5 showed that the characteristic C=O peak at 1705 cm-1, aromatic CH3 at 744 cm-1 OH peak at 1068cm-1and C_6H_6 peak at 1465 cm-1. Fig 7. showed that the characteristic C=O peak at 1707 cm-1, aromatic CH3 at 742 cm-1 OH peak at 1068cm-1and C_6H_6 peak at 1462 cm-1. Hence there is no apperence of new peaks and disappearence of existance peaks in the presence of exicipients indicates the drugs and excipient are more compatible.

Pharmacological Evaluation

Skin irritation test

Discussion

There is no variation in skin colour and morphology, as well as redness of the skin, was not observed every 24hrs and the study period it indicates that the gel doesn't cause any irritation to the skin, hence it is safe for application.

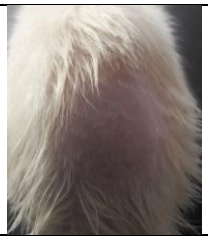
Time	0hrs	3hrs	6hrs	12hrs	24hrs
Results					

Fig 8: Skin irritation test

Anti-Inflammatory Activity
Fresh Egg White Induced Paw Edema Method

Table 5: Effect of anti- Inflammatory Activity of dexibuprofen Aloe vera transemulgel by Fresh Egg White Induced Paw Edema Method

Time after fresh egg albumin administration (min)	Paw volume (mean ± sem)			
	Group I (control)	Group II (Aloe vera gel)	Group III (DAE)	Group IV Diclofenac emulgel(Standard)
0	0.41±0.0075	0.39±0.004	0.36±0.026	0. 38±0.005
30	0.45±0.090	0.42±0.076	0.37±0.079	0.36±0.082
60	0.49±0.066	0.37±0.082	0.34±0.090	0.33±0.073
120	0.54±0.064	0.34±0.090*	0.30±0.108**	0.30±0.104**
180	0.53±0.068	0.29±0.011**	0.26±0.137***	0.27±0.017***
240	0.43±0.098	0.25±0.017***	0.24±0.015***	0.23±0.010***

Results are expressed as mean + SEM,(n=6), * P<0.05, **P<0.01, *** P<0.001 as compared to control by one way ANOVA followed by Dunnet"s t- test

Table 6: Percentage inhibition of Fresh Egg White induced rat paw edema Model

Time after fresh egg albumin administration (min)	Percentage inhibition (%)		
	Group II (Aloe vera gel)	Group III (DAE)	Group IV Diclofenac emulgel (Standard)
0	4.87	12.19	7.31
30	6.66	17.77	20
60	24.48	30.61	32.65
120	37.03	44.44	44.44
180	56.60	50.94	49.05
240	41.86	44.18	46.51

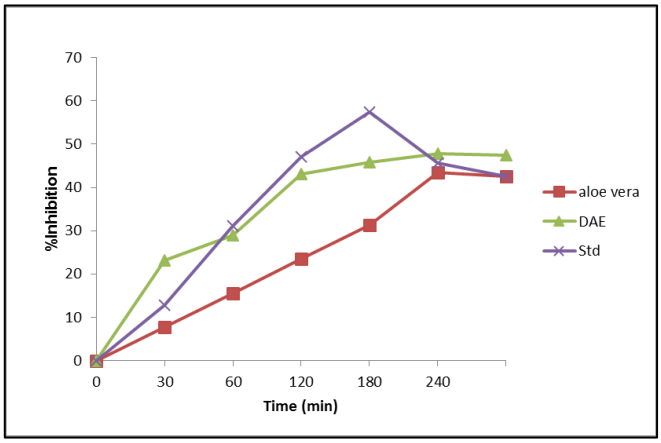


Fig 9: Percentage inhibition plot of fresh egg albumin induced rat paw edema in all the groups. Values are presented as Mean ± S.D (n=4). * p<0.05, ** p<0.01, *** p<0.001 compared to Group I (Control).

Discussion

Paw oedema experiments were carried out as previously described by measuring the paw volume in a plethysmometer at differenttime intervals (30 min, 1–4 h) after 0.05 mL egg white. 24 animals were considered for this study, and the inflammation was measured at left Paw of animals at standard intervals mentioned in the table 5. It is quite interesting to observe that the dexibrufen emulgel reduced the significantly reduced the inflammation in course time duration of 3-4 hrs. At 3-4hrs hrs dose time, it was observed that 56.6-41.86% respectively with alovera emulgel. Where as, 50.94 to 47.5% inhibition was observed in DAE emulgel. From these findings it was interesting to observe that, the prepared formulation was more significant when compared with the standard diclofenac.

Analgesic Activity
Analgesic activity of dexibuprofen Aloe vera transemulgel by tail flick method.

Table 7: Effect of analgesic activity of dexibuprofen Aloe vera transemulgel by Tail flick method

Groups	Time of treatment of the gel in minutes (mean ± sem)						
	Basal reaction time	30	60	90	120	150	180
Group I (Control)	4.43± 0.18	4.21±0.09	4.14±0.16	4.04±0.08	3.973±0.058	3.85±0.043	3.39±0.032
Group II (Aloe vera gel)	4.37± 0.18	4.91±0.27	5.93±0.26*	5.93±0.25*	6.97±0.06**	6.90±0.24**	6.35±0.32
Group III (DAE)	3.66±0.248	3.98±0.06	4.215±0.02*	6.19±0.18*	7.37±0.14*	8.95±0.18**	8.847±0.21
Group IV (standard)	3.918±0.17	6.94±0.08	7.56±0.15**	8.98±0.07**	8.735±0.19**	8.55±0.09	8.29±0.25

Results are expressed as mean + SEM, (n=6), * P<0.05, **P<0.01, ***P<0.001 as compared to control by one way ANOVA followed by Dunnet"s t- test.

Discussion

In our present study, analgesic activity was observed by the time between placing the tail of the rat on the radiant heat source and sharp withdrawal of the tail was recorded as "reaction time". Cut off time of ten seconds was imposed in all sets of experiments taken as maximum latency so as to rule out thermal injury while noting down the reaction time. Table no.7. represents, analgesic activity seems to be significantly increased during the course time intervals of 30 – 120 min, latter seems to be decreased. It was found that the analgesic activity for DAE at 30, 60, 90 and 120 min were 4.91±0.27, 5.93±0.26, 5.93±0.25 and 6.97±0.06. The above finding seems to be significant when compared with the standard. This was evident that pain threshold increased significantly during the period of observation in all the four goups and seems to reduced after treatment with DAE due to its analgesia through a peripheral action

Conclusion

In the coming years, topical drug delivery would be used extensively to ensure better patient compliance. Since gels are helpful in enhancing spreadability, adhesion, viscosity, and extrusion; this novel drug delivery has become popular. Moreover, these gels are suitable for loading hydrophobic drugs in water soluble gel bases for better drug diffusion profiles. The DAE showed promising results using sodium alginate as gelling agent. DAE was formulated in Aloe vera gel base and subjected to physicochemical studies, that is, rheological studies, pH measurement, *in vitro* release studies From the *in vitro* studies, DAE showed significantly better release than aloveral emulgel. *In vivo* study was also performed by egg white induced paw edema to reveal the anti-inflammatory potentials of DAE. Also, the prepared formulation was proven better for analgesic activity. These results supported by already published reports. Hence, Aloe vera has a synergistic anti-inflammatory effect along with dexibuprofen in emulgel formulation.

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