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RESEARCH ARTICLE

Studies on Rice Bran Wax as Modified Pharmaceutical Excipient

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ABSTRACT

Waxes have been used in many cosmetic preparations and pharmaceuticals as formulation aids. Rice bran wax is a byproduct of rice bran oil industry. Present investigation has been aimed to explore the possible utility of rice bran wax as ointment base compared to standard base. In the pharmaceutical industries, waxes have been employed for different preparation, such as tablet, ointment, emulsion and even in micro-particles. So study of drug release properties using waxes is far most important. Some waxes like bees wax, carnauba wax, paraffin wax and sugarcane wax etc. are available in the market and is being used by pharmaceutical industries. Present study attempts to find if rice bran wax is useful as ointment base. The oleaginous type ointment bases is prepared by using rice bran wax and evaluated for their clarity, pH, viscosity, spread ability, skin irritation test in vitro diffusion studies and compared with the marketed formulations. The results obtained in the present study indicate, rice bran wax can be used as a good component in ointment base, comparable with white wax.

Keywords: Rice bran wax, ointment, ointment base, waxes

INTRODUCTION

Rice bran wax is an important by product of Rice bran oil industry and belongs to (*Oryza sativa*) Family Graminae and is abundantly available [1]. Rice bran wax is a vegetable wax extracted from rice bran when extract rice oil. It is a treasure biologic wax resource in East Asia where rice is the main food. Rice wax has no odor and bleaches readily, and its impurities are easy to move. Rice bran wax is better as a coating and it's also suitable for cosmetics. Rice bran wax proved to be the best, since it has higher purity and good pharmaceutical function than extracts of sugar cane wax extracts and bee wax extracts. Rice Bran Wax been used as rate retarding polymer. Research has shown that the properties of refined and bleached wax are similar to that of the presently imported carnauba wax. Rice bran wax is better as a drug retardant or sustained release, confectionery and chewing gum than paraffin's or petrochemical waxes [2].Melt granulation method is a simple, efficient, less time and energy consuming process in case of Matrix tablet preparation, no organic solvent or water required, since the molten polymer (wax) can function as thermal binder or retardant.

Ointment of rice bran wax as base acts as better carrier and ointment base for medicaments. The ointment base composition determines not only the extent of penetration but also controls the transfer of medicaments from the base to the body tissue.

In the present study, effort is made to see the utilization and feasibility of rice bran wax in ointment were evaluated for their clarity, pH, viscosity, spreadability, skin irritation test and in vitro diffusion studies using standard procedure.

MATERIALS AND METHODS

Rice bran wax obtained from Triveni Interchem Pvt Ltd., Vapi, and Gujarat, India. Econazole, 5 Fluorouracil and Marketed formulation were procured from the authorized distributor of the company.

Ointment preparation

All the ingredients were weighed according to formula given below. Hard paraffin and cetostearyl alcohol were melted in porcelain dish by keeping on a water bath. Rice Bran Wax and white soft paraffin were added to the above melt and stirred well during melting. Then Econozole was added and triturated well to mix and get smoother texture [3-5].

Formulation development of OE (Ointment of Econazole)

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Table 1: Formulation OE1 to OE4

S. No	Ingredients	Quantity in Gms			
		O_{E1}	C_{E2}	C_{E3}	O_{E4}
1	Econozole	1	1	1	1
2	Rice Bran Wax	5	4	3	5
3	Hard paraffin	4.5	5	5.5	4.5
4	Cetostearyl alcohol	4.5	5	5.5	4.0
5	White soft paraffin	85	85	85	85.5

Table 2: Formulation OE5 to OE9

S. No	Ingredients	Quantity in Gms				
		O_{E5}	O_{E6}	O_{E7}	O_{E8}	O_{E8}
1	Econozole	1	1	1	1	1
2	Rice Bran Wax	4	3	5	4	3
3	Hard paraffin	5.0	5.5	4.0	4.0	4.0
4	Cetostearyl alcohol	4.0	4.0	4.5	5.0	5.5
5	White soft paraffin	86	86.5	85.5	86	86.5

Formulation development of Ointment of 5 Fluorouracil

All the ingredients were weighed according to formula given below. Hard paraffin and cetostearyl alcohol were melted in porcelain dish by keeping on a water bath. Rice Bran Wax and white soft paraffin were added to the above melt and stirred well during melting. Then 5 Fluorouracil was added and triturated well to mix and get smoother texture [3-5].

Characterization of developed formulation

Ointments were evaluated for their clarity, pH, viscosity, spreadability, skin irritation test, in vitro diffusion studies using standard procedure [3-5]. All studies were carried out in triplicate and average values were reported.

Psychorheological characteristic

The Psychorheological characteristic was checked for hair ointment formulations (colour, clogging, homogeneity and texture) and observations [6].

Consistency or hardness of ointment

It was measured by Penetrometer. Three containers were filled carefully and completely, without forming air bubbles and stored at 25+ 0.5 °C for 24 hrs. Three samples were stored at 25+ 0.5 °C and with shear for 5 min. Three samples were melted and carefully and completely filled three containers, without forming air bubbles stored at 25+ 0.5 °C for 24 hrs. Test samples were placed on Penetrometer. Temperature of penetrating object was adjusted at 25+ 0.5 °C and position was also adjusted such that its tip just touches the surface of sample. Penetrating object was released for 5 sec. Depth of penetration was measured. Same was repeated with remaining containers [3-5].

Washability

Formulations were applied on the skin and then ease and extent of washing with water were checked manually and observations [3-5].

Extrudability study

The hair ointment formulations were filled into collapsible metal tubes or aluminum collapsible tubes. The tubes were pressed to extrude the material and the Extrudability of the formulation was checked [3-5].

Spreadability

Two glass slides of standard dimensions (6×2) were selected. The hair ointment formulation whose spreadability had to be determined was placed over one of the slides. The second slide was placed over the slide in such a way that the formulation was sandwiched between them across a length of 6 cms along the slide. 100 grams of weight was placed up on the upper slide so that the hair ointment formulation between the two slides was traced uniformly to form a thin layer.

The weight was removed and the excess of the hair ointment formulation adhering to the slides was scrapped off. The lower slide was fixed on the board of the apparatus and one end of the upper slide was tied to a string to which 20 gram load could be applied 50with the help of a simple pulley. The time taken for the upper slide to travel the distance of 6 cms and separate away from lower slide under the direction of the weight was noted. The experiment was repeated and the average of 6 such determinations was calculated for each hair ointment formulation [3-5].

$$\text{Spreadability} = \frac{m.l}{t}$$

Where, S=Spreadability (gcm/sec)
m = weight tied to the upper slide (20 grams)
l= length of glass slide (6cms).
t = time taken is seconds.

Determination of pH

The pH of the hair ointments were determined by digital pH meter. One gram of ointment was dissolved in 25 ml of distilled water and the electrode was then dipped in to ointment formulation for 30 min until constant reading obtained. And constant reading was noted. The measurements of pH of each formulation were replicated two times [3-5].

Viscosity

The measurement of viscosity of the prepared Ointment was done using Brookfield digital Viscometer. The viscosity was measured using spindle no. 6 at 10 rpm and 25 °C. The sufficient quantity of ointment was filled in appropriate wide mouth container. The ointment was filled in the wide mouth container in such way that it should sufficiently allow to dip the spindle of the Viscometer. Samples of the ointments were allowed to settle over 30 min at the constant temperature (25 ±/1°C) before the measurements [3-5].

Globule diameter

The average globule diameter was calculated with help of microscope [7-9].

***In-vitro* drug release studies using the rehydrated cellophane membrane**

The cellophane membrane approximately 25 cm x 2cm was taken and washed in the running water. It was then soaked in distilled water for 24 hrs, before used for diffusion studies to remove glycerin present on it and was mounted on the diffusion cell for further studies [7-9].

Diffusion studies

The *in-vitro* diffusion of drug from the different ointment preparations were studied using the classical standard cylindrical tube fabricated in the laboratory; a simple modification of the cell is a glass tube of 15 mm internal diameter and 100 mm height. The diffusion cell membrane was applied with one gram of the formulation and was tied securely to one end of the tube, the other end kept open to ambient conditions which acted as donor compartment. The cell was inverted and immersed slightly in 250 ml of beaker containing phosphate buffer, freshly prepared (pH 7.4) as a receptor base and the system was maintained for 2 hrs at 37± 0.5 °C. The media was stirred using magnetic stirrer. Aliquots, each of 5 ml volume were withdrawn periodically at predetermined time interval of 15, 30, 45, 60, 90, 120 min and replaced by an equal volume of the receptor medium. The aliquots were suitably diluted with the receptor medium and analyzed by UV-Vis spectrophotometer at 233.0nm for econazole and 264nm for 5-FU using phosphate buffer as blank [7-9].

Data analysis via drug release kinetics study

The results of *in-vitro* release profile obtained from all the formulations were plotted in kinetic models [7-9] as follows

Zero order release kinetics

Zero order release would be predicted by the following equation,

$Q_t = Q_O + Kt$

Where, Qt is the amount of drug dissolved in time t, Q_0 is the initial amount of drug in the solution (most times, $Q_0=0$) and K is the zero order release constant.

First order release kinetics

First order release would be predicted by the following equation,

$$Q_t = Q_o\, e^{-K_1 t}$$

Where, Qt is the amount of drug released in time t, Q_0 is the initial amount of drug in the solution and K is the first order release constant.

Higuchi kinetics

A plot of the fraction of drug released against root of time will the linear if the release obeys Higuchi Equation. This equation describes drug release as a diffusion process based on the Flick's Law, Square root time dependent.

$Q=Kt^{1/2}$

Q=Amount of drug release per unit area in time t, K=release rate constant

Peppas & korsemeyer equation

The amount of drug released at time t (Mt) with respect to the total amount of drug released (M_∞), can be expressed in terms of an exponential expression as follows:

$M_t / M_\infty = kt^n$

Where, M_t / M_∞ = the fraction of drug released at time t,

K = Constant incorporating the structural and geometrical characteristic of the drug /polymer system.

n = diffusion exponent related to the release

The Peppas model is widely used when the release mechanism is not well known or when more than one type of release phenomenon could be involved. 'n' value could be used to characterize different release mechanism.

Determination of stability studies

Stability conditions

Optimized formulation code OE_3 and OF_3 were prepared and kept in humidity chamber at 25°C ± 2°C/60% RH ± 5% RH for 12 months and samples were withdrawn after every 3 months and evaluated for its Physico-chemical properties such as pH, spreadability, and rheological measurement (as per ICH guideline)

Skin irritation studies of developed formulations

Animals

Wistar rats (150–200 g) were group housed (n= 6) under a standard 12 h light/dark cycle and controlled conditions of temperature and humidity (25±2 °C). Rats received standard rodent chow and water *ad libitum*. Rats were acclimatized to laboratory conditions for 7 days before carrying out the experiments. All the experiments were carried in a noise-free room between 08.00 to 15.00 h. Separate group (n=6) of rats was used for each set of experiments. The animal studies were approved by the Institutional Animal Ethics Committee (IAEC), constituted for the purpose of control and supervision of experimental animals by Ministry of Environment and Forests, Government of India, New Delhi, India.

Skin irritation study

The rats were selected for skin irritation studies of different formulations. The animals were divided into three groups (n = 4) and formulations were topically applied, i.e. the formulations were uniformly applied over the shaven skin of rats. The skin was observed for any visible changes such as erythematic (redness) or edema at 24, 48 and 72 h after the application of various formulations and the primary irritation index was calculated [10]. For each animal, the primary irritation scores were added together for the test formulation for both erythematic and edema at each time specified and divided by the total number of observations. The scores for each animal was added and divided by the total no of animals to give the primary irritation index. The primary irritation index was characterized by number (score) and description (response category).

Group I- Normal

Group II - Standard

Group III- Formulation I (ointment)

Statistical analysis

The values were expressed as mean ± SEM. The statistical significance was assessed using one-way analysis of variance (ANOVA) followed by Tukey's test and $P<0.05$, $P<0.01$, and $P<0.001$ were considered to be statistically significant.

RESULTS AND DISCUSSION

The rice bran wax obtained, purified and its physicochemical characteristics were determined. Ointment base acts as a carrier for medicaments. The ointment base composition determines not only the extent of penetration but also controls the transfer of medicaments from the base to the body tissues. Rice bran wax base was compared with standard base for appearance, spreadability, water number, wash ability and diffusibility.

Many waxes such as white wax, carnauba wax, etc have been tried for cosmetic formulations and have been used as pharmaceutical aids. Compared to these waxes rice bran wax is cheap and obtained from natural source and is abundantly available. It is an important byproduct of rice bran oil industry. Therefore, the present study was carried out to compare its properties and its utility as ointment base. It was the main objective of the present study to investigate whether any ointment base characteristics are associated with rice bran wax or not. It is also hoped that present investigation would provide additional data and information to the cosmetic chemists.

Characterization of ointment formulation

Table 3: Characterization of formulations O_{E1} to O_{E5}

Parameters	Formulation				
	O_{E1}	O_{E2}	O_{E3}	O_{E4}	O_{E5}
Physical Appearance	Translucent, white, smooth on application	Translucent, white, smooth on application	Translucent, white, smooth on application	Translucent, white, smooth on application	Translucent, white, smooth on application
pH	6.36±0.3	6.27±0.1	7.09±0.6	6.76±0.4	6.76±0.4
Viscosity (CP)	23280±7.3	29842±2.8	27514±4.3	33811± 2.2	28554± 2.2
Spreadability (gm.cm/sec)	26.49±0.7	26.31±0.58	32.76±1.2	27.54±1.39	26.54±1.39
% Drug content	96.1±0.46	98.2±0.73	99.7±0.39	96.16±0.2	97.16±0.2
Extrudability	+++	+++	+++	++	++
Consistency	158mm	145mm	162mm	148mm	152mm

Globule diameter	5.48mm	5.47mm	5.42mm	5.41mm	5.42mm

+++ Excellent, ++ Good, + Satisfactory

Table 4: Characterization of formulations O_{E6} to O_{E9} and marketed formulation

Parameters	**Formulation**				
	O_{E6}	**O_{E7}**	**O_{E8}**	**O_{E9}**	**Marketed Formulation**
Physical Appearance	Translucent, white, smooth on application	Translucent, white, smooth on application	Translucent, white, smooth on application	Translucent, white, smooth on application	Translucent, white, smooth on application
pH	6.59±0.2	6.96±0.1	6.98±0.3	6.58±0.3	6.53±0.2
Viscosity (CP)	27515±3.5	32151±3.1	31313±4.8	30154± 1.2	35,426± 4.2
Spreadability (gm.cm/sec)	27.15±0.15	26.59±0.58	27.51±1.8	28.25±1.39	25.54±2.15
% Drug content	96.1±0.46	98.2±0.73	98.7±0.39	95.16±0.2	96.12±0.33
Extrudability	+++	++	++	+++	++
Consistency	150mm	154mm	148mm	149mm	150mm
Globule diameter	5.47mm	5.46mm	5.55mm	5.42mm	5.47mm

+++ Excellent, ++ Good, + Satisfactory

Table 5: Characterization of formulations O_{F1} to O_{F5}

Parameters	**Formulation**				
	O_{F1}	**O_{F2}**	**O_{F3}**	**O_{F4}**	**O_{F5}**
Physical Appearance	Translucent, white, smooth on application	Translucent, white, smooth on application	Translucent, white, smooth on application	Translucent, white, smooth on application	Translucent, white, smooth on application
pH	6.78±0.3	6.98±0.1	6.95±0.6	6.36±0.4	6.91±0.4
Viscosity (CP)	29,840±7.3	33,284±2.8	26,514±4.3	33,456± 2.2	32,542± 2.2
Spreadability (gm.cm/sec)	28.49±0.7	26.31±0.58	33.76±1.2	29.54±1.39	29.54±1.39
% Drug content	97.15±0.25	98.12±0.25	99.8±0.39	97.15±0.22	98.19±0.10
Extrudability	+++	+++	+++	++	++
Consistency	157mm	162mm	162mm	158mm	149mm
Globule diameter	5.42mm	5.43	5.43mm	5.48mm	5.47mm

+++ Excellent, ++ Good, + Satisfactory

Table 6: Characterization of formulations C_{F6} to C_{F9} and marketed formulation

Parameters	**Formulation**				
	O_{F6}	**O_{F7}**	**O_{F8}**	**O_{F9}**	**Marketed Formulation**
Physical Appearance	Translucent, white, smooth on application	Translucent, white, smooth on application	Translucent, white, smooth on application	Translucent, white, smooth on application	Translucent, white, smooth on application
pH	7.02±0.2	7.12±0.5	7.15±0.6	7.10±0.4	6.53±0.3
Viscosity (CP)	31,714±7.2	32,511±2.8	31,278±4.3	30,515± 2.2	35,426± 4.2
Spreadability (gm.cm/sec)	28.49±0.7	26.31±0.58	27.76±1.2	29.54±1.39	25.54±2.15
% Drug content	96.1±0.46	98.2±0.73	98.7±0.39	99.16±0.2	96.12±0.33
Extrudability	++	+++	++	++	++
Consistency	158mm	159mm	158mm	148mm	162mm
Globule diameter	5.36mm	5.38mm	5.40mm	5.38mm	5.35mm

+++ Excellent, ++ Good, + Satisfactory

In-vitro drug release studies of $O_{E1}$to O_{E9} and marketed formulation

Release of drug from oinment base was significantly slower, which confirmed that slight prolonged drug release rate. Incorporation of rice bran wax affected the release rate of the drug. By increasing the amount of wax, the release rate of the drug decreased, which could be related to the increased rigidity of the formulation, followed by its de-creased permeability for the drug.

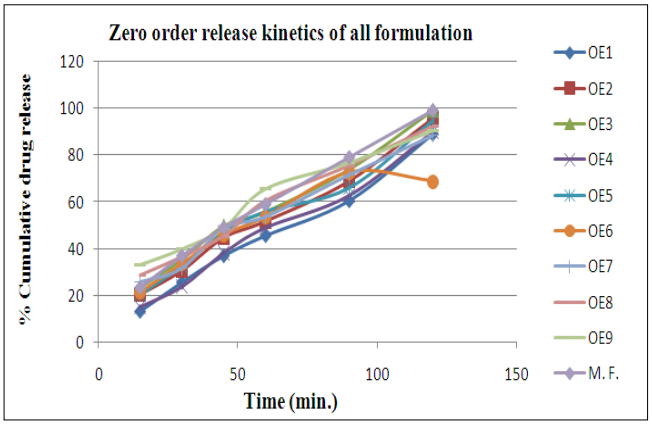


Figure1: Zero order release kinetics of all formulation

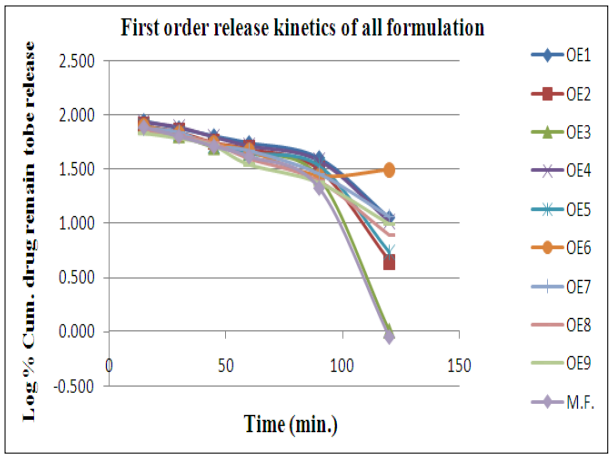


Figure 2: First order release kinetics of all formulation

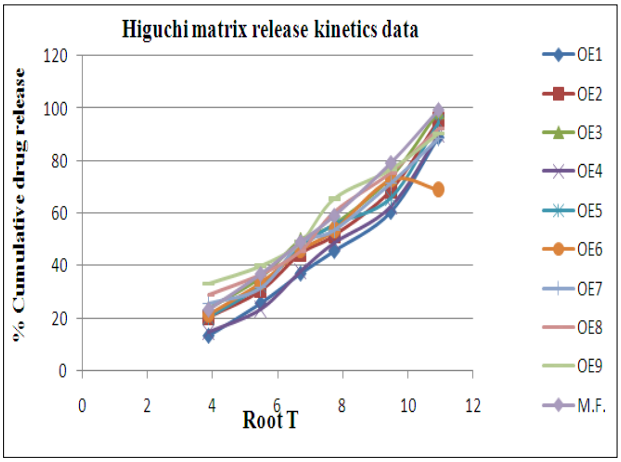


Figure 3: Higuchi matrix release kinetics data

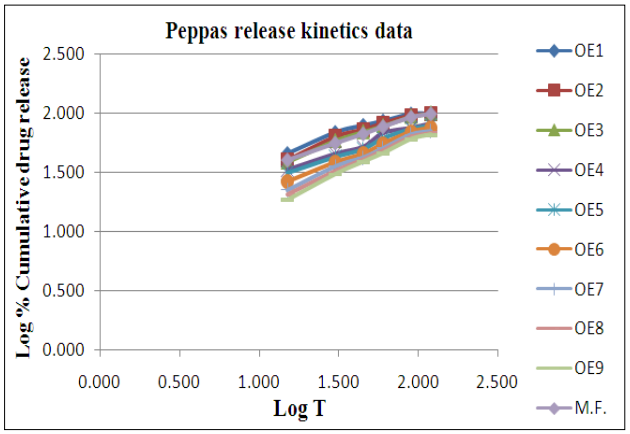


Figure 4: Peppas release kinetics data

Drug release kinetics with model fitting of Econazole ointment

These values of in-vitro release were attempted to fit into various mathematical models, plot of zero order, first order, higuchi matrix and peppas. These values were compared with each other for model fitting equation. Based on the highest regression values (r), the best fit model for all the formulations was zero order release kinetics. Further Korsmeyer and Peppas equation resulted into the values of n > 1, which appears to indicate that the release from the prepared optimized cream formulation (OE3) was, follow peppas release Kinetics.

Table 7: Correlation coefficient of Model fitting (r^2)

Formulation code	Correlation coefficient of Model fitting (R^2)				Best fit model
	Zero order	First order	Higuchi matrix	Peppas kinetics	
OE 1	0.988	0.988	0.967	0.944	Zero
OE 2	0.991	0.991	0.970	0.962	Higuchi
OE 3	0.991	0.991	0.977	0.984	Peppas
OE 4	0.989	0.989	0.970	0.979	Zero
OE 5	0.976	0.976	0.967	0.990	First
OE 6	0.880	0.880	0.940	0.994	Peppas
OE 7	0.987	0.987	0.976	0.991	Peppas
OE 8	0.992	0.992	0.980	0.993	Peppas
OE 9	0.976	0.976	0.977	0.993	Peppas
M.F.	0.996	0.996	0.992	0.995	Zero

In-vitro drug release studies of O_{F1} to O_{F9} and marketed formulation

Release of drug from oinment base was significantly slower, which confirmed that slight prolonged drug release rate. Incorporation of rice bran wax affected the release rate of the drug. By increasing the amount of wax, the release rate of the drug decreased, which could be related to the increased rigidity of the formulation, followed by its de-creased permeability for the drug.

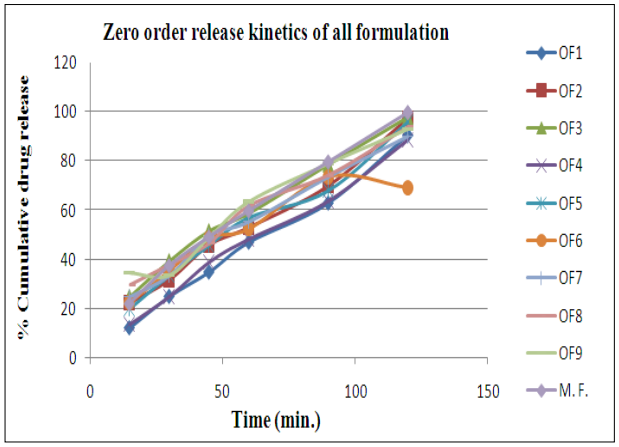


Figure 5: Zero order release kinetics of all formulation

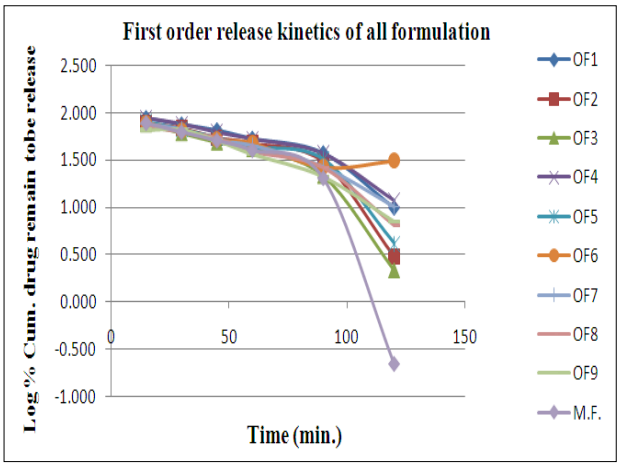


Figure 6: First order release kinetics of all formulation

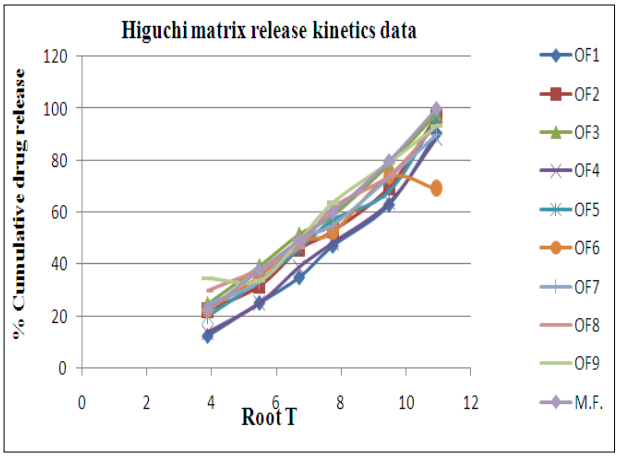


Figure 7: Higuchi matrix release kinetics data

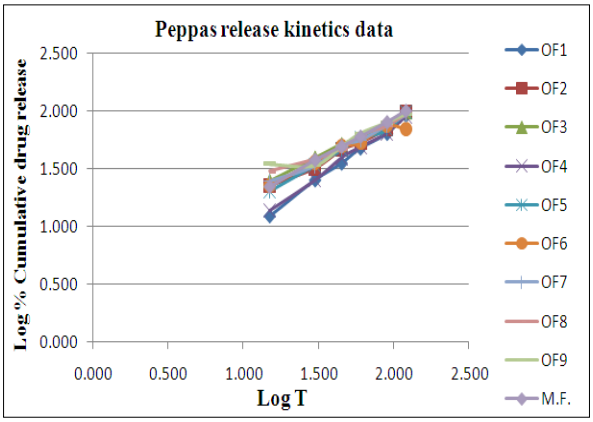


Figure 8: Peppas release kinetics data

Drug release kinetics with model fitting of 5 fluorouracil ointment

These values of *in-vitro* release were attempted to fit into various mathematical models, plot of zero order, first order, higuchi matrix and peppas. These values were compared with each other for model fitting equation. Based on the highest regression values (r), the best fit model for all the formulations was Peppas for optimized formulation O_{F3}.

Table 8: Correlation coefficient of Model fitting (r^2)

Formulation code	Correlation coefficient of Model fitting (R^2)				Best fit model
	Zero order	First order	Higuchi matrix	Peppas kinetics	
OF 1	0.993	0.887	0.973	0.996	Peppas
OF 2	0.991	0.812	0.966	0.985	Higuchi
OF 3	0.993	0.851	0.922	0.997	Peppas
OF 4	0.992	0.914	0.981	0.996	Peppas
OF 5	0.981	0.832	0.975	0.992	Zero
OF 6	0.867	0.868	0.930	0.962	Peppas
OF 7	0.988	0.950	0.988	0.987	Zero
OF 8	0.991	0.905	0.976	0.974	Higuchi
OF 9	0.969	0.944	0.952	0.899	Zero
M.F.	0.994	0.758	0.994	0.999	Peppas

Skin irritation study of developed formulations

Table 9: Effect of formulation on skin irritation activity

S No	Group	Mean skin irritation ± SEM Econazole formulation	Mean skin irritation ± SEM 5 fluorouracil formulation
1	Normal	1.80 ± 0.28	1.75 ± 0.28
2	Standard (M.F.)	0.42 ± 0.08***	0.45 ± 0.08***
3	Formulation I	0.47 ± 0.08***	0.46 ± 0.08***

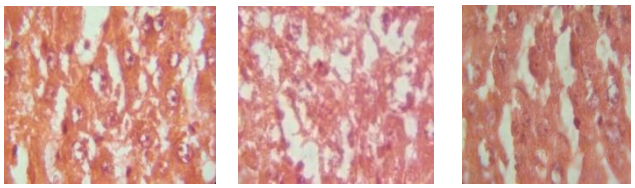
M.F. - Marketed formulation, Formulation I-Ointment

Values expressed as mean ± SEM *P<0.05, **P<0.01, *** P<0.001 as compared to normal

Histopathology

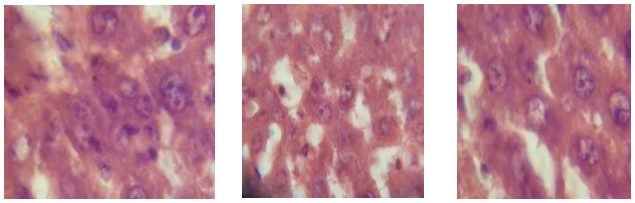
After the induction of skin irritation, animals from each group were sacrificed were excised and fixed in 10% formalin (pH 7.2) and then embedded in paraffin and thick sections were taken to stain

using hematoxylin-eosin dye and mounted in diphenyl xylene and observed for the changes.



Normal **Standard** **Formulation I**

Figure 9: Photo plate 1: Histological changes in econazole formulation observed in the rats



Normal **Standard** **Formulation I**

Figure 10: Photo plate 2: Histological changes in 5 fluorouracil formulation observed in the rats

The prepared topical formulations were tested for skin irritation. The effect of formulations on the rat skin was observed after 24, 48, and 72 h. The skin irritation test revealed negligible irritation scores in the case of all formulations. Hence, the prepared formulations can be considered to be safe for topical application.Ointments are used topically for several purposes like protective, antiseptic, emollient, antipruritic, keratolytic and astringent. The base of an ointment is of prime importance if the finished product is expected to function as any of the above categories. Ointment base acts as a carrier for medicaments. The ointment base composition determines not only the extent of penetration but also controls the transfer of medicaments from the base to the body tissues [11]. The results show that rice bran wax acts as an ointment base as far as its pharmaceutical properties are concerned and it could effectively replace comparatively costlier available ointment bases.

CONCLUSION

Rice bran wax is a natural vegetable wax and is a value added by-product of Rice bran oil refineries. It is hard no tacky wax and contains higher fatty alcohols and esters which make it comparable to Carnauba wax. Waxes (animal and plants) are esters of high molecular weight monohydroxy alcohols and high molecular weight carboxylic acids. They are chemically different from fats and oils, from hydrocarbon or paraffin waxes, and from synthetic polyether waxes such as carbowax. Recent work indicates that rice bran wax is mainly an ester of lignoceric acid and myricyl alcohol. The result shows that there are no physical and chemical changes; therefore rice bran wax can be used in formulations of ointment. To conclude, rice bran wax can be a useful ingredient to formulate ointment base.

REFERENCES

1. Sabale V, Sabale P and. Lakhotiya C. Comparative Evaluation of Rice Bran Wax as an Ointment Base with Standard Base. Indian J Pharm Sci 2003; 71: 77-79.
2. Obaidat A and Obaidat R. Controlled release of tramadol hydrochloride from matrices prepared using glycerol behenate. Eur J Pharm Biopharm 2000; 52: 231-235.
3. Carter SJ. Cooper and Gunn's Dispensing for Pharmaceutical Students: Ointments, Pastes and Jellies. 12th Edition, CBS Publishers and Distributors, India, 1987: 192-210.
4. Bodmier R, Hermann J. Encyclopedia of Pharmaceutical Technology. Vol. 16. In: Swarbrick J, BoylanJC, editors. Waxes. New York: Marcel Deckker, Inc.; 1997: 335-361
5. Lachman L, Liberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy. 3rd ed. Mumbai: Varghese Publishing House; 1987: 534-562.
6. Chakole C.M., Shende M.A., Khadatkar S.N. Formulation and evaluation of novel combined halobetasol propionate and fusidic acid ointment. Int J Chem Tech Res. 2009; 1: 103-116.
7. Sinko PJ. Physical Pharmacy and Pharmaceutical Sciences. 5th ed. Philadelphia: Lippincott Williams and Wilkines; 2006: 301-326.
8. Ansel HC. Introduction to Pharmaceutical Dosage Forms. 4th ed. Philadelphia: Lea and FebigerPublishers; 1985: 291.
9. Jain NK, Sharma SN. A Textbook of Professional Pharmacy. 4th ed. Delhi: VallabhPrakashan; 1998: 237-250.
10. Sabale VP, Sabale PM, Lakhotiya CL. In vitro studies on rice bran wax as skin moisturizer. Indian J Pharm Sci 2007; 69: 215-218.
11. Yun W, Hongsun D, Peide N. Study on refining of rice bran wax. ZhongguoZhong Yao ZaZhi (China) 1998; 5: 23.

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