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Research Article

RICE BRAN WAX-A NOVEL EXCEPIENT FOR PHARMACEUTICAL TOPICAL DOSAGE FORMS

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Abstract: The crude rice bran wax was obtained from M/S Bajaj rice mills, Gondia (MS) which was dark brown in color & contains nonwaxy impurities & fixed oil. After purification around 38gm wax obtained which was almost white, light in weight and non-sticky. No instances of skin irritation or sensitization symptoms such as edema / rending of the skin were observed on the skin of Albino rabbits even after 24 hrs. Therefore wax was nontoxic & safe to use in pharmaceutical preparations. In the present study the melting range of rice bran wax was found to be 78–840 which is higher, may reduce the diffusion of drug across the layers of skin. Therefore, in the present study efforts will be made later on to reduce the melting range by addition of low melting point fats like mango kernel fat (M.P. 34.70C). Solubility studies reveal that the wax is soluble in organic solvents like chloroform & petroleum ether showing typical solubility properties of waxes. Refractive index of a compound gives an idea of purity of the compound & the refractive index of the test sample was found to be 1.44 at 700c. Sap value of rice bran wax is 68 – 72. The acid value of rice bran wax is 12 – 14. The iodine value of rice bran wax is 9 – 11. From the above data the physicochemical properties of rice bran wax was found to be within the range of other waxes used in topical preparations. Therefore rice bran wax may be utilized as a base in topical preparations. Different topical formulations such as ointments (oleaginous, modified hydrophilic ointment and modified bellers ointment base) were formulated with purified rice bran wax and compared with simple ointment (control) and marketed formulation. All these formulations contain 2% diclofenac sodium. All the formulations were evaluated for p H rheological studies like apparent viscosity, spread ability and diclofenac sodium content. P H of all formulations was found to be 5.98 – 7.30, thus indicating the suitability for application on the skin. Diclofenac sodium content of all the formulations was found to be above 95% indicating the suitability of the method adopted for preparing the formulations. Shelf life and release of diclofenac sodium content in vivo study will be made further.

Keywords: Rice bran wax, Topical, Pharmaceutical

INTRODUCTION

Many fats and oils contain a number of minor components, which are referred as "nonglycerides" or "waxes". Many of these nonglycerides play an important role in providing pharmaceutical and industrial benefits. In fact the recent trends are directed to explore and establish proper usage of nonglycerides occurring in the natural lipid materials like oils and fats. Such trends are considered extremely important to improve the economy of the lipids and to meet also the newer possibilities of utilization of the nonglycerides and derivatives of oils and fats. Many investigations around the world have already shown newer pathways for utilizing the nonglycerides in some specific fields. R and D efforts are still pursued to find out newer technologies for utilizing the nonglycerides in a diversified manner. Although waxes are abundant in nature, a limited numbers only are commercially used.

During the past few decades a number of non conventional vegetable oils have been accepted as good quality edible oils in India and in other countries. Since India is one of the principle producers of rice in the world enormous stress is laid upon the extraction of oil from rice bran. Rice bran is the brown layer between the rice and outer husk of the paddy. The bran is obtained as the by-product in rice milling. Rice bran contains around 15 – 20% of oil, which can be economically obtained only by solvent extraction process. Rice bran oil is now gaining importance as one of the edible oils in India because of its nutritional property. It contains vitamin E, which is not only has a antioxidant property but also has a antifertility activity.

Crude rice bran wax is dark brown in color and has its own typical physical and chemical composition. The literature survey reveals that rice bran wax has been used in cosmetics and toiletries. Unfortunately the details of this literature are not available. Rice bran wax is also utilized as an ingredient for coating candy and chewing gums. But the utilization of rice bran wax in pharmaceuticals is meager or hardly there is any report inspite of large production. Therefore the rice bran wax utilization in pharmaceuticals is worth investigating. Keeping in view the potential availability of rice, its contents such as oils and wax an attempt is made to utilize rice bran wax as pharmaceutical aid.

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MATERIALS AND METHODS

Procurement of Crude Rice Bran Wax:

The crude rice bran wax was obtained from M/S Bajaj rice mills, Gondia (MS).

Purification and Bleaching Of Crude Rice Bran Wax:

Evaluation of Physicochemical Properties of Bleached Rice Bran Wax (Table.1): Melting range, Solubility, Refractive index, Specific gravity & Skin sensitivity test.

Table.1: Evaluation of physicochemical properties of bleached rice bran wax

S. NO.	PROPERTTIES	RESULT
1	Melting range	78 – 84 °C
2	Solubility	Soluble in chloroform, Petroleum ether, Insoluble in Acetone& Water
3	Refractive index	1.44 at 70°c
4	Specific gravity	0.93
5	Saponificable value	68 – 72
6	Acid value	12 – 14
7	Iodine value	09 – 11
8	Unsaponificable matter	60 - 62

Rice bran wax as an ointment base and its effect in release of Diclofenac sodium

a) Trituration method and fusion method are used in the preparation of ointments. The following oleaginous ingredients are used in the preparation of present ointment

i) Oleaginous Base-

Rice bran wax (bleached)	- 43%
Mango kernel fat	- 30%
Arachis oil	- 25%
Diclofenac sodium	- 02%

The following ingredients used in the present work in fusion method in the preparation of modified hydrophilic ointment base.

ii) Modified hydrophilic ointment base (%w/v)

Rice bran wax	- 20
Stearyl alcohol	- 20
Propylene glycol	- 12
Sod. Lauryl sulphate	- 01
Methyl paraben	- 0.025
Propyl paraben	- 0.015
Sodium metabisulphite	- 0.10
Diclofenac sodium	- 02
Purified water q. s.	- 100

iii) Modified Bellers ointment base (% w/v)

Rice bran wax	- 03
Cetyl alcohol	- 15
Propylene glycol	- 10
Sod. Lauryl sulphate	- 01
Methyl paraben	- 0.025
Propyl paraben	- 0.015
Sodium metabisulphite	- 0.10
Diclofenac sodium	- 02
Purified water q. s.	- 100

Determination of Diclofenac sodium content and Determination of Viscosity and pH of Ointments **(Table.2)**

Table.2: pH, Viscosity, spreadibility and Diclofenac sodium content of different topical preparations containing rice bran wax

Sr. No.	Formulation	P H	Apparent viscosity at 100rpm (cps)	Spreadibility (Sec)	Diclofenac sodium content (%)
1	Simple ointment IP	6.23	32,200	16	96.20
2	Rice bran wax ointment (Oleaginous base)	7.30	22,800	18	95.80
3	Rice bran wax ointment (Modified hydrophilic ointment base)	6.72	285,600	45	97.85
4	Rice bran wax ointment (Modified Bellers ointment base)	5.98	24,250	33	98.04
5	Marketed formulation	6.04	16,200	15	98.20

Release of Diclofenac sodium from rice bran wax ointment **(Table-3, 4, 5, 6, 7, 8: Fig 1- 6)**

Table.3: Cumulative % of Diclofenac sodium released from simple ointment IP (Control) in vitro

Hour	Cumulative % of Diclofenac sodium released *	Std. Dev. (± SD)	Std. Error (± SE)
1	4.81	0.50	0.46
2	8.14	0.30	0.31
3	10.73	0.55	0.42
4	15.54	0.76	0.50
5	19.98	0.74	0.49
6	23.31	0.50	0.40
7	28.12	1.00	0.57
8	30.48	0.57	0.43
9	33.74	1.04	0.58
10	34.92	0.90	0.54

Average of three determinations

Table.4: Cumulative % of Diclofenac sodium released from Rice bran wax ointment (Oleaginous base) in vitro

Hour	Cumulative % of Diclofenac sodium released *	Std. Dev. (± SD)	Std. Error (± SE)
1	4.29	0.05	0.13
2	6.069	0.10	0.18
3	8.95	0.60	0.44
4	11.24	0.30	0.32
5	14.50	0.09	0.17
6	16.42	0.20	0.26
7	19.61	0.60	0.44
8	22.57	0.35	0.34
9	25.97	0.80	0.52
10	29.82	0.35	0.34

* Average of three determinations

Table.5: Cumulative % of Diclofenac sodium released from Rice bran wax ointment (Modified hydrophilic ointment base) in vitro

Hour	Cumulative % of Diclofenac sodium released *	Std. Dev. (± SD)	Std. Error (± SE)
1	6.06	0.05	0.13
2	10.43	0.08	0.16
3	19.68	0.08	0.16
4	22.94	0.13	0.21
5	28.34	0.27	0.30
6	34.18	0.06	0.14
7	39.51	0.05	0.13
8	42.18	0.20	0.26
9	45.73	0.12	0.20
10	48.61	0.07	0.15

* Average of three determinations

Table.6: Cumulative % of Diclofenac sodium released from Rice bran wax ointment (Modified Bellers ointment base) in vitro

Hour	Cumulative % of Diclofenac sodium released *	Std. Dev. (± SD)	Std. Error (± SE)
1	5.77	0.50	0.41
2	11.84	0.58	0.44
3	18.64	1.52	0.71
4	28.12	0.58	0.44
5	31.22	1.02	0.58
6	38.33	1.15	1.73
7	43.06	1.21	1.78
8	46.40	1.15	1.73
9	51.94	1.53	0.50
10	59.94	1.58	0.44

* Average of three determinations

Table.7: Cumulative % of Diclofenac sodium released from Marketed formulation in vitro

Hour	Cumulative % of Diclofenac sodium released *	Std. Dev. (± SD)	Std. Error (± SE)
1	9.69	1.04	0.59
2	17.98	1.15	0.42
3	26.34	1.04	0.59
4	38.33	1.53	0.71
5	45.06	0.52	0.41
6	54.61	1.00	0.58
7	64.38	1.53	0.71
8	71.63	1.00	0.58
9	78.36	1.53	0.71
10	84.50	0.58	0.44

*Average of three determinations

Table.8: Cumulative % of Diclofenac sodium released from different formulations in vitro

Hour	Simple ointment IP (Control)	Rice bran wax ointment (Oleaginous base)	Rice bran wax ointment (Modified hydrophilic ointment base)	Rice bran wax ointment (Modified Bellers ointment base)	Mark formu
1	4.81	4.29	5.77	6.06	9.6
2	8.14	6.06	11.84	10.43	17.(
3	10.73	8.95	18.64	19.68	26.
4	15.54	11.24	28.12	22.94	38.
5	19.98	14.50	31.22	28.34	45.(
6	23.31	16.42	38.33	34.18	54.
7	28.12	19.61	43.06	39.51	64.
8	30.48	22.57	46.40	42.18	71.(
9	33.74	25.97	51.94	45.73	78.
10	34.92	29.82	59.60	48.61	84.

*Average of three determinations

Figure.1- 6: Release of Diclofenac sodium from rice bran wax ointment

Fig - 1 Cumulative % of diclofenac sodium released from simple ointment IP (Control) in vitro

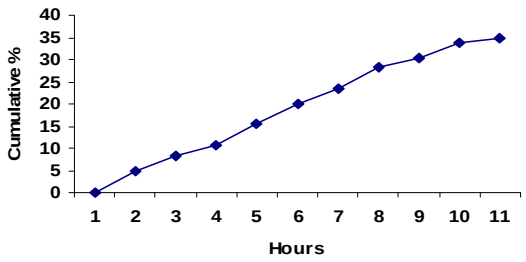


Fig - 2 Cumulative % of diclofenac sodium released from rice bran wax ointment (Oleaginous base) in vitro

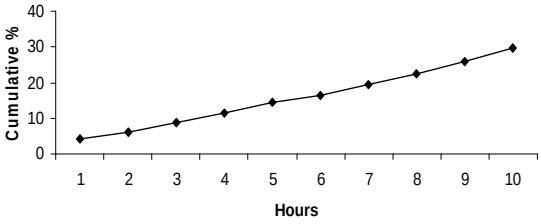


Fig - 3 Cumulative % of diclofenac sodium from rice bran wax ointment (Modified hydrophilic ointment base) in vitro

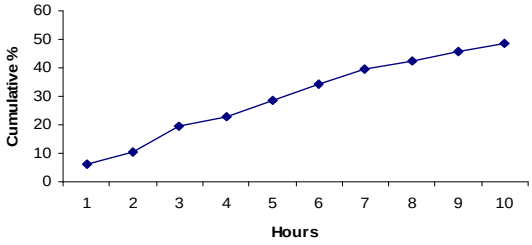


Fig - 4 Cumulative % of diclofenac sodium released from rice bran wax ointment (Modified bellers ointment base) in vitro

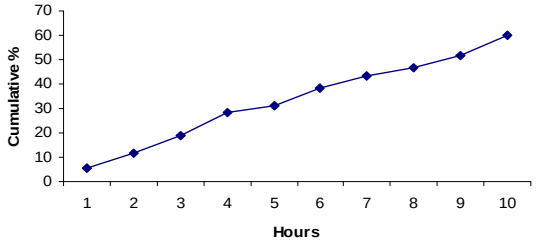


Fig - 5 Cumulative % of diclofenac sodium released from marketed formulation in vitro

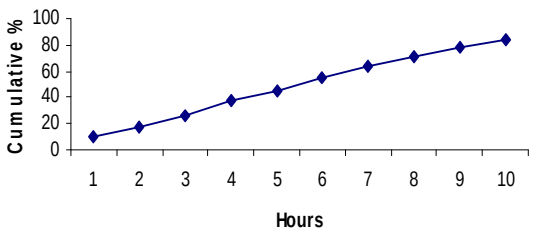
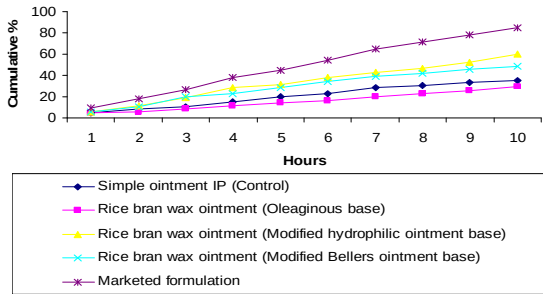


Fig - 6 Cumulative % of diclofenac sodium released from different formulations in vitro



***In vitro* release studies:**

Preparation of skin and estimation of drug: Excised abdominal skin of 15 – 20 weeks old albino mice of either sex was used. The skin on the epidermal side was shaved. While the tissues on the dermal side including blood vessels were removed after which the skin was washed with distilled water and mounted on "Franz diffusion cell" (Franz, 1975). It is a simple glass instrument made of two pieces with an "o" ring of rubber which links both the parts by a clamp. The top portion is for retaining the ointment with a capacity of 3 gm. The receptor phase (phosphate buffer, p H 7.2) constituting the lower part is receptacle of 7.4 ml capacity was completely filled into the cell without air bubbles. It is provided with a sampling part, a temperature jacket and an enlarged portion for the revolving movement of a string lead by a magnetic stirrer. In vitro studies of all rice bran wax formulations were studied up to 10 hrs.

Around 0.5 gm of prepared test ointments was used on the top portion of the Franz diffusion cell and whole assembly was placed on organ bath and the receptor phase was agitated using a magnetic stirrer (100 rpm) and its temperature was regulated at 37°c + 1. Aliquots were (1ml) withdrawn at one hour intervals for 10 hours and were replenished with fresh buffer solution (1ml). This was diluted properly, mixed thoroughly and drug content was determined with a spectrophotometer (Systroniocs, Model 103).

RESULTS AND DISCUSSION

- Procurement of Crude Rice Bran Wax: The crude rice bran wax was obtained from M/S Bajaj rice mills, Gondia (MS) which was dark brown in color and contains non waxy impurities and fixed oil.

- Purification and Bleaching of Crude Rice Bran Wax: Around 38 gm wax was obtained which was almost white, light in weight and non sticky.

- Skin Sensitivity Test (Patch Test) Of Rice Bran Wax: No instances of skin irritation or sensitization symptoms such as edema / rending of the skin were observed on the skin of Albino rabbits even after 24 hrs. Therefore wax was nontoxic and safe to use in pharmaceutical preparations.

In the present study the melting range of rice bran wax was found to be 78–84°c. Kokate *et al.*, (1994) reported the melting range of lanolin (34 – 40°c), yellow bees wax (60 – 65°c) and hard paraffin (50-57°c). Trease and Evans (1983) reported the melting range of lanolin (36 – 42°c) and spermaceti (46-50°c). According to IP (1996) the melting range of lanolin is 34 -44°c. Yellow bee's wax is 61-65°c and yellow soft paraffin is 50- 57°c. From the above comparisons the melting range of rice bran wax was found to be higher, which may reduce the diffusion of drug across the layers of skin. Therefore, in the present study efforts were made to reduce the melting range by addition of low melting point fats like mango kernel fat (M.P. 34.7°C) as reported by Thampi and Schroff (1962). Vegetable oils (William, 1995) like arachis oil in different ratios when added in formulations also reduce melting range.

Solubility studies reveal that the wax is soluble in organic solvents like chloroform and petroleum ether showing typical solubility properties of waxes. Refractive index of a compound gives an idea of purity of the compound and the refractive index of the test sample was found to be 1.44 at 70°c.

Sap value of rice bran wax is 68 – 72 while sap value of other waxes reported by Kokate et al., (1994) is lanolin (92 – 105) and yellow bees wax (90 – 103). As per Wallis (1985) the sap values of lanolin is 90 – 102 and spermaceti is 125 – 136. While IP (1996) gives sap values of lanolin (90 – 105) and yellow bees wax (87 – 104). The acid value of rice bran wax is 12 – 14. Trease and Evans (1983) report the acid value of lanolin (NMT 1) and yellow bees wax (18 – 24). According to Wallis (1985) the acid value of bees wax is 18 – 24 and spermaceti is NMT 1.

The iodine value of rice bran wax is 9 – 11. Trease and Evans (1983) reports the iodine values of lanolin (18 - 32) and yellow bees wax (8 – 11) while according to Wallis (1985) the iodine value of lanolin is 18 – 32 and spermaceti is NMT 1.

From the above data the physicochemical properties of rice bran wax was found to be within the range of other waxes used in topical preparations. Therefore rice bran wax may be utilized as a base in topical preparations.

The literature reports reveals that the rice bran wax has been employed in various external preparations like cosmetics (Buffa, 1976) but no further details could be traced. To evaluate the use of rice bran wax as an ointment base, the studies would be

inconclusive if the report of the skin irritation test is not reported. No instances of skin irritation or sensitization were observed in skin sensitivity test carried out on albino rabbits by the rice bran wax so the wax is harmless to the skin and can be used in topical formulations.

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