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Protective Effect of Waxes on Aspirin Tablets against Moisture

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ABSTRACT

The ability of waxes to protect aspirin tablets from moisture uptake and subsequent hydrolytic degradation was investigated in this study. Aspirin granules were prepared by melt granulation technique. The waxes employed were carnuba wax, goat fat and beeswax each at a concentration ranging from 1 to 10% w/w. Flow properties of the resulting granules was used to select granules with optimum concentration of wax. The granules with adequate flow were compressed to tablets using a single punch machine. Resulting tablets were subjected to moisture sorption tests and the effect of moisture sorption on some tablet properties such as disintegration time (DT), tensile strength (TS), and friability (F) were investigated. Results show that as wax concentration increased, the amount of moisture sorbed by tablets decreased. Tablets containing carnuba wax (5%w/w) had moisture sorption of 5.8% with DT of 4.77 ± 0.48 min and t_{70} (time for 70% release of 30 min) before exposure to moisture. Goat fat (2% w/w) and Beeswax (2% w/w) had moisture sorption of 5.8 and 5.9%, respectively after 5 days exposure. The corresponding moisture sorption for tablets produced by slugging was 12.9% with DT = 12.19 ± 1.22 min and t_{70} = 40 mins) before exposure. After exposure to moisture, the DT, TS and F values of tablets containing carnuba wax (5% w/w) were 4.5±0.4 min, 0.03±0.01MN/m^2 and 0.03 ± 0.01%, respectively. Those of goat fat (at 2% w/w) were 11.0 ± 0.9 min, 0.04 ± 0.00 MN/m^2 and 0.5 ± 0.01% respectively. The DT, TS and F values of aspirin tablets produced by slugging after exposure to moisture were 9.1 ± 0.8 min, 0.01 ± 0.00MNm^2 and 2.7 ± 0.02% respectively. Thus, melt granulation produced tablets with lower moisture sorption properties which disintegrated readily comparable to tablets produced by slugging. The conclusion is that waxes employed in melt granulation at optimal concentrations protected aspirin tablets against moisture uptake and hydrolytic degradation.

KEYWORDS: Aspirin granules, carnuba wax, goat fat, melt granulation, moisture sorption, slugging,

INTRODUCTION

Aspirin (acetyl salicylic acid, ASA) is a very old drug in the management of inflammatory conditions and as an analgesic. Its use has even expanded in terms of current prescription list. It is highly effective with a good safety profile and is still in use after almost a hundred and sixty years, as the most trusted home remedy for pain, worldwide [1]. Besides the primary functions of aspirin, it has been proven in recent times to be used in long term at low doses to help prevent heart attacks, strokes and blood clot formation [2,3]. Recently, some researchers have found evidence that aspirin delays the onset of senile dementia and also protects against bowel and colon cancers [4,5]. It is also very cheap.

Aspirin is hygroscopic. The conventional aspirin tablet easily absorbs moisture from the atmosphere leading to degradation of the drug into acetic acid and salicylic acid [6]. Furthermore, for some drugs, hydrolytic degradation results in toxic products, For example, the antifungal drug flucytosine degrades to fluorouracil, which is cytotoxic [7]. Salicylic acid (product of the hydrolysis of aspirin) is active and has all the pharmacological action of aspirin, but it is known to irritate the bowel much more than aspirin. It is also not as potent as aspirin as an anti-inflammatory agent. Aspirin is too unstable to allow

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the formation of an aqueous aspirin product or even allow for aqueous granulation. For this reason aspirin granules are normally formed by slugging which is a double compression process. In a humid atmosphere, even aspirin produced through double compression process (slugging) can easily degrade when in use from multi-dose container. In order to obviate the drawbacks of degradation caused by moisture in a humid atmosphere, organic solvents are employed for the granulation process. Unfortunately, the use of organic solvents as granulating fluids is expensive and hazardous.

Melt granulation is a technique that involves the trituration of powdered drug in a melted wax followed by screening [8-10]. This technique has been employed to mask the taste of drugs [11], improve drug stability [12,13] and modify drug release properties [14]. Design and applicability of such technique depend on the physicochemical properties of the drug as well as desired properties of the end product [10,14]. Waxes are abundant in nature, only a few have wide pharmaceutical applications. These are widely used as thickeners, release retardant, suspending agents and formulation of beads, implants and microcapsules.

In a previous study, the melt granulation technique was employed as binder to obtain prompt and sustained release tablets of aspirin using different waxes [14]. In this study, the effect of moisture sorption on properties of aspirin tablets produced with locally sourced wax (goat fat) and two other established waxes (carnuba wax and beeswax) was investigated.

MATERIALS AND METHODS

Materials

Acetyl salicylic acid powder used as the test drug was obtained from BDH, Poole, UK. Carnuba wax was obtained from Hale wood Chemicals Ltd, England. Goat fat with melting point of 56-60^{o}C was extracted and purified by the method described by Okor [15]. Beeswax BP is a yellowish white solid with melting point of 62 – 64^{o}C and Maize starch BP, magnesium stereate and talc were obtained from BDH, Poole, UK. All other chemicals used were of reagent grade and were used without further purification

Methods

Melt granulation techniques

The waxes – carnuba wax, goat fat and beeswax - (0.5 g each) were melted in a water bath at a temperature slightly above their melting points. Aspirin powder (50 g) was added to the melted wax and mixed until uniformly blended. This was allowed to cool to room temperature (30-32^{o}C). The mass was forced through a sieve (aperture size 710 µm) and then air dried in an air conditioned room for 4 h and stored in a desiccator for 24 h before characterization and compression to tablet. This procedure was repeated at concentrations ranging from 1 to 10%w/w.

Preparation of aspirin granules and tablets by slugging

Aspirin slugs (wt., 1.6 ± 0.8 g; thickness, 5.24 mm; and diameter, 12 mm) were prepared using a single punch-tableting machine (Manesty, Type F3, Liverpool, UK.). The slugs were compressed at compression loads of 40 indicated as arbitrary units on the load scale of the machine. These slugs were broken down with mortar and pestle and sieved (aperture size 710 µm). The granules were characterized and compressed to tablets using maize starch as disintegrant (5%w/w), magnesium stereate as lubricant (1%w/w) and talc as glidant (1%w/w).

Determination of moisture uptake

The weight of 5 tablets of each batch was determined and the mean weight obtained (M_0). The tablets were stored under relative humidity (RH) of 100 ± 0.5% in a desiccator. RH 100 ± 0.5% was obtained with a vessel of distilled water placed in the glass chamber.

At selected time intervals the samples were removed from the chambers to determine their mean weight (M_t). The percentage moisture uptake (Degree of hydration of the tablets) was computed from the formula in equation 1.

The experiment was done in triplicate and the mean values determined.

$$\frac{M_t - M_0}{M_0} * \frac{100}{1} = \%\ Moisture\ Uptake \quad ---(1)$$

Tablet Friability

Ten (10) tablets were placed in the drum of the friabilator (Erweka, Heusenstamm, Germany) rotating at 50 rpm for 5 min. The % weight lost due to the impact was determined and taken as an index of friability. The test was carried out in triplicate and mean values reported.

Tablet tensile strength (T)

The crushing load of each of 10 tablets was determined with a Monsanto hardness tester (Monsanto Chemical, USA) [16]. Diameters and thicknesses of tablets (10 tablets) were measured using a Gallenkamp micrometer screw guage. The average values of diameter (d), thickness (t) and

crushing load (P) were obtained and used to calculate the tensile strength (T) using Equation 2.

$$T = {}^{2P}/_{\pi dt} \quad ----------(2)$$

Disintegration test

Disintegration test was done using Manesty tablet disintegration machine. Six tablets, from each were placed in six Perspex tubes of the disintegration machine and the motor switched on. The time taken for the tablet to completely disintegrate and pass through the screen into the disintegrating medium was recorded [17].

Statistical analysis

All data were expressed as mean ± SD. The data were statistically analyzed by the Student's t – test. The level of significance was set at $P < 0.05$.

RESULTS AND DISCUSSION

Under high humidity (RH 100%) aspirin granules produced by slugging absorbed more moisture than the ones formulated by melt granulation technique within 5 days of exposure. The surface of the tablet became moist and visible water films were seen. Percentage weight gain after two days of exposure was 12.9% and this value remained constant up to the fifth day (Fig 1). This observation revealed that the degradation occurred as a result of exposure to moisture within the first two days. The percentage amount of moisture absorbed by tablets formulated by melt granulation technique was much lower (by a factor of 2) and this amount decreased with increased wax concentration (Fig 1).

Under ambient temperature and RH 75% and RH 1%, moisture sorption by all types of tablets and granules showed no appreciable measurable value. Thus, indicating that RH 75% and below at ambient temperature is the best storage condition for these tablets.

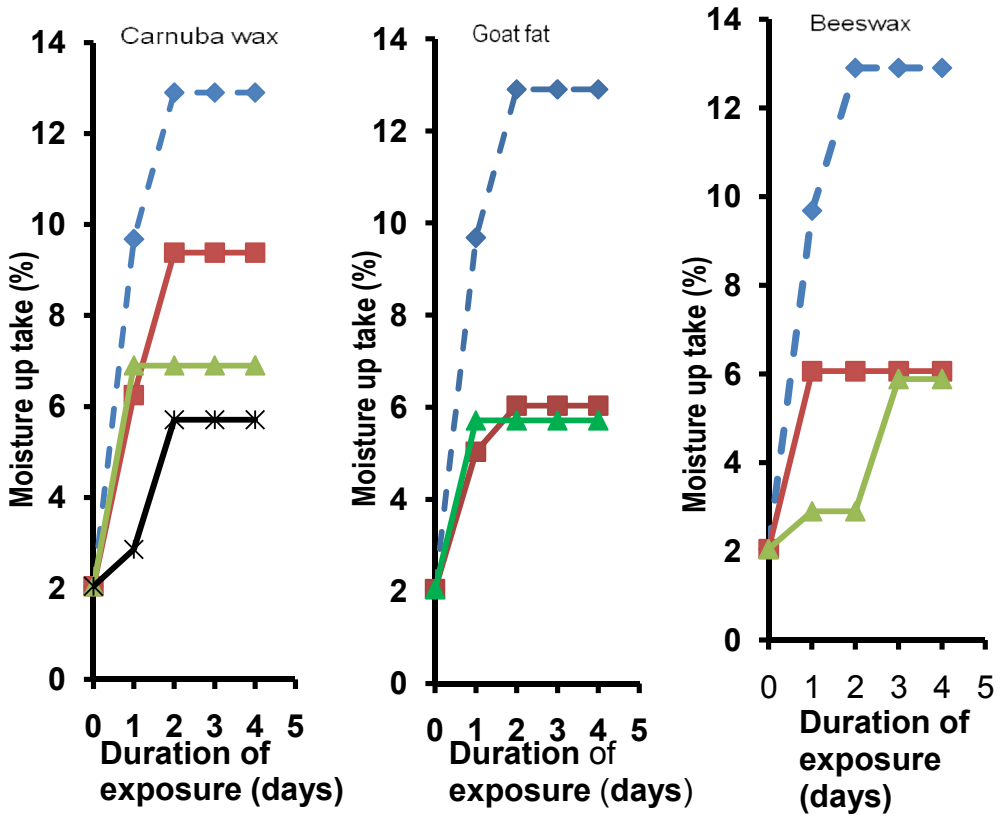

Figure 1: Moisture uptake of aspirin tablets produced by slugging (-♦-), and by melt granulation: different wax contents: 1%w/w (-■-), 2%w/w (-▲ -), 5%w/w (X) at RH 100%.

The tensile strength (TS) of all the tablets was ≤ 0.04 MN/m^2. There was no statistically significant difference between their tensile strength values ($P > 0.05$) before exposure to moisture. However tensile strength values decrease slightly after exposure to moisture. This effect was more pronounced with the conventional tablets than tablets produced by melt granulation (Table 1). The decreased TS values could be due to hydrolytic degradation of aspirin by water. Friability was also affected.

The friability of tablets prepared with carnuba wax decreased with increase in concentration of the carnuba wax. For instance at concentration of 2%w/w, the friability % was 1% while at 5%w/w the friability % was 0.02%. This might be attributed to formation of more cohesive bonds in the tablets at higher wax content, although this was not reflected in their TS - values. The friability of the tablets produced from other waxes (i.e. goat fat and bees wax) was $\geq$ 0.44 %.

On exposure to moisture, the tablets became more friable generally. It must be noted that this effect was more pronounced with the conventional tablets (tablets produced by slugging) than by melt granulation. In addition, the effect was insignificant at higher wax content for all 3 waxes tested (Table 2).

All the tablets made with carnuba wax disintegrated within 8 min while that made from goat fat disintegrated within 12 min before exposure to moisture. The disintegration time for tablets produced from bees wax was 8 min (at 1 %w/w concentration) and 26 min (at 2 %w/w concentration) (Table 3). Tablets produced from conventional granules disintegrated within 12 minutes before exposure to moisture, hence was of similar magnitude with that of melt granulations at low wax contents, i.e. there was no statistically significant difference in disintegration time of aspirin tablets produced by slugging and by melt granulation at low wax content before exposure to moisture. The longer disintegration time observed with goat fat and beeswax at higher wax content compared with that of carnuba wax was due to the fact that the former were more hydrophobic in nature [14].

On exposure to moisture at RH 100 % disintegration time decreased (Table 3). This effect was more with the conventional (slugged) tablets and tablets produced by melt granulation at low wax concentrations (≤ 2% w/w). This was expected as presence of moisture weakened the inter-particulate bonds holding the granules together. This resulted in the tablets crumbling faster during disintegration test (Table 3). This finding is in agreement with previous work [18].

Table1: Tensile strength (TS) before and after exposure to moisture (RH 100%)

Tablet type/ TS (MN/m^2	Wax Concentration (%w/w) and tensile strength (MN/m^2) values of tablets					
	0.0	1.0	2.0	3.0	5.0	7.5
Carnuba wax						
TS_b	-	0.03±0.00	0.03±0.00	0.04±0.01	0.04±0.00	0.04±0.01
TS_a	-	0.02±0.00	0.02±0.01	0.03±0.01	0.03±0.01	0.04±0,01
Goat Fat						
TS_b	-	0.03±0.01	0.04±0.01	-	-	-
TS_a	-	0.02±0.01	0.04±0.00	-	-	-
Beeswax						
TS_b	-	0.03±0.01	0.03±0.00	0.04±0.00	-	-
TS_a	-	0.02±0.00	0.03±0.01	0.04±0.01	-	-
Tablet by slugging						
TS_b						
TS_a	0.03±0.00	-	-	-	-	-
	0.01±0.00	-	-	-	-	-

(-) Means not applicable

TS_b = Tensile strength before; TS_a = Tensile strength after exposure of the tablets to RH 100 % for 48 h

Table 2: Friability % before and after exposure to moisture (RH 100%)

Tablet type / Friability Percentage	Wax Concentration %w/w and friability (%) of tablets					
	0.0	1.0	2.0	3.0	5.0	7.5
Carnuba wax						
F_b	-	1.3±0.02	1.0±0.01	1.0±0.02	0.02±0.01	0.02±0.0
F_a	-	1.5±0.03	1.2±0.02	1.1±0.03	0.03±0.01	0.02±0.1

(-) means not applicable

F_b = Friability % before; F_a = Friability % after exposure of the tablets to RH 100 % for 48 h

Table 3: Disintegration time (DT) of the different tablets before and after exposure to moisture (RH 100 %) for two days

Tablet type / disintegration time (min)	wax concentration (%w/w) and disintegration time (min) of tablets						
	0.0	1.0	2.0	3.0	5.0	7.5	10.0
Carnuba wax							
DT_b	-	5.1±0.7	7.8±1.3	5.5±0.5	4.8±0.5	4.0±0.7	4.7±0.3
DT_a	-	3.1±0.5	4.7±0.9	4.9±0.5	4.5±0.4	4.0±0.6	4.8±0.2
Goat fat							
DT_b	-	4.4±0.1	11.5±0.1	-	-	-	-
DT_a	-	4.0±0.1	11.0±0.9	-	-	-	-
Beeswax							
DT_b	-	7.6±0.3	25.8±0.4	>100	-	-	-
DT_a	-	5.2±0.2	25.0±0.3	>100	-	-	-
Tabs. by slug							
DT_b	12.2±1.2	-	-	-	-	-	-
DT_a	9.1±0.8	-	-	-	-	-	-

(-) means not applicable.

DT_b = Disintegration time before; DT_a = disintegration time after exposure of the tablets to RH 100 % for 48 h

CONCLUSION

Aspirin tablets produced by melt granulation using goat fat, canauba and bees waxes were less susceptible to moisture uptake when compared to tablets produced by slugging. This is an advantage considering that aspirin is hydrolysable. In spite of the hydrophobic nature of the waxes, the test concentrations used did not impair the disintegration and dissolution properties of the tablets made by melt granulation.

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