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MOISTURE BARRIER APPLICATION OF SELECTED COMMERCIAL COATING SYSTEMS

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ABSTRACT

Moisture absorbed during manufacturing process and storage specially causes degradation of moisture sensitive drug and its dosage form. Application of moisture barrier system prevents such deleterious effects. Various commercial coating systems are available for protection of moisture sensitive drugs. To evaluate moisture barrier application of three selected commercial coating systems i.e. Aquarius® MG, Kollicoat® protect and Opadry® AMB. Compressed tablets of three moisture sensitive model drugs i.e. Ranitidine hydrochloride and Aspirin were coated with Aquarius® MG, Kollicoat® Protect and Opadry® AMB. Coating process was performed at parameters recommended by manufacturers of selected systems in a controlled coating process. After coating, both coated and uncoated tablets kept on stress study at 25 ± 2°C / 75 ± 5% RH and 40 ± 2°C / 75 ± 5% RH open condition for 7 days. Both coated and uncoated tablets were evaluated for change in physical properties like appearance and Chemical properties like content of free salicylic acid content. Study showed least physical and chemical change was observed when tablet of moisture sensitive drugs was coated with Opadry® AMB as compared to other selected commercial coating systems.Different coatings system effectively decreased the rate of moisture absorption but not the extent of water uptake during open storage at room temperature and 75 ± 5% RH. Ranitidine hydrochloride tablets coated with Opadry® AMB showed minimum physical change. Also aspirin tablets showed improved stability as free salicylic acid content was significantly reduced after coating with Opadry® AMB.

KEYWORDS : *Aqueous, Commercial, Coating system, Moisture protection, Stress study.*

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INTRODUCTION

Moisture plays remarkable negative role in pharmaceutical product, particularly for dosage forms containing moisture sensitive drugs because physical and chemical stability of these drugs are affected by moisture. Moisture can be absorbed by dosage forms during manufacturing process as well as during storage. Absorbed moisture may cause alteration in rate of decomposition, agglomeration and dissolution of drugs and ultimately performance of final product[1]. Presence of moisture possesses a critical challenge on drug stability because it accelerate the hydrolysis of drug as well as facilitates reaction with other excipients, thereby affecting stability and shelf life of the final product. The effect of moisture absorption on physical properties, tablet performance, disintegration time, and shelf life of coated tablets has been already reported in literature[2].

The rate and extent of moisture absorption influence the selection of packaging materials. The relationship between moisture absorption with dissolution profile in different packing condition was recorded previously[3]. Manufacturing under controlled condition, packaging in moisture resistant material can reduce the moisture effect to some extent but to avoid such undesirable changes application of moisture barrier system i.e. moisture barrier coating becomes necessary and may provide the direct protection to the dosage form.

Selection of type of coating systems: Drugs prone to degradation in presence of moisture can be protected by use of appropriate packaging material[8, 9], protective polymer coatings[14] and the composition of the formulation[16]. Coating with non aqueous polymeric coating deals with regulatory restrictions, cumbersome procedures, pollution etc whereas sugar coating have disadvantage of long processing time and high water influx during coating. Hence it was decided to select aqueous moisture barrier film coating systems for the current study. In this study commercial aqueous coating systems were selected and were evaluated for moisture barrier applications. Out of various available systems, Aquarius® MG by Hercules Aqualon, Kollicoat® protect by BASF, Opadry® AMB by Colorcon.

It has been proved that factors affecting the water vapour permeation are film composition[11], additives in the film[20, 21, 22] and solvent used to dissolved or disperse the polymer[19]. Aquarius® MG contains Hypromellose, Titanium dioxide, Natural wax, Triacetin as key ingredients. Kollicoat® Protect is a coating based on Kollicoat® IR (polyvinyl alcohol-polyethylene glycol graft copolymer), it contains PVA-PEG graft copolymer (55%-65%), PVA (35%-45%), Silicon dioxide (0.1%-0.3%). Opadry® AMB contains PVA- partly hydrolyzed (25-55%), Titanium dioxide, Talc, Lecithin (Soya), xanthan gum as key ingredients. Due to these major differences in composition and additives, these systems were selected for current evaluation.

Selection of model drugs: The three selected model drugs, Ranitidine hydrochloride and Aspirin show following changes due to exposure to moisture.

A. **Ranitidine hydrochloride:** Ranitidine is extensively used as anti-ulcerant. It is a very hygroscopic drug and changes colour from white or pale yellow to brown and which evaluative parameter for current study [5, 6] was.
B. **Aspirin[33]:** It is a part of group of medications called as non steroidal anti inflammatory (NSAIDs). It is also known as acetylsalicylic acid often used as an analgesic to relieve minor aches and pains, as a antipyretic to reduce fever. Aspirin can be hydrolyzed to form free salicylic acid hence for evaluation of moisture barrier application determination of free salicylic acid content is an evaluative parameter. Hydrolysis reaction of aspirin is shown below in figure 1.

The aim of the present study was to evaluate the moisture barrier property of selected commercially available coating systems by exposing the tablets of selected model drugs to high percent relative humidity and high temperature conditions.

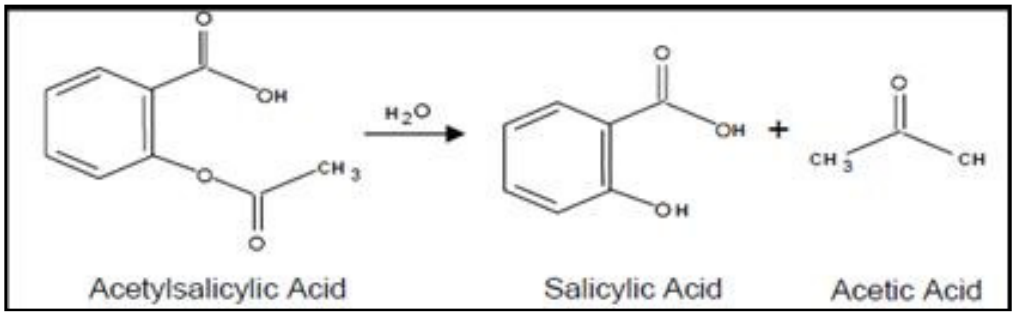

Figure 1 : Hydrolysis reaction of aspirin

MATERIALS AND METHODS:

Materials

Ranitidine hydrochloride (USP) and Aspirin (USP) were obtained as gift sample from Orchev Pharma, Microcrystalline cellulose (Avicel PH-102), Lactose anhydrous (Supertab 11 SD), Copovidone (Kollidon VA 64), Pregelatinized starch (Starch 1500), Colloidal silicon dioxide (Aerosil 200 Pharma), Titanium dioxide, Talc, Iron oxide red and Magnesium stearate were also obtained as generous gift from FMC Bio-polymer, DMV Fonterra, BASF, Colorcon, FMC Biopolymer, Evonik, Kronos international, Luzenac Pharma, BASF and Ferro respectively. The selected commercial coating systems i.e. Aquarius® MG, Kollicoat® Protect and Partially Opadry® AMB were supplied by Aqualon, BASF and Colorcon respectively.

Methods

Preparation of core tablets

Different formulations of core tablets were prepared according to table 1. Tablets were prepared using a direct compression method of manufacturing (batch size ~ 3 kg). Disintegrant, binder (if any) and filler were passed through 40-mesh screen along with model drug and blended in drum hoop blender. Lubricant and glidant (if any), were passed through 60-mesh screen and blended with the prepared drug-excipient blend. The lubricated blend was compressed into tablets on a rotary tablet press (Rimek 12 station multi tooling compression machine) using suitable punches with hardness range 50-80 N.

Table 1: Composition of core tablet

	Tablet Composition (mg/unit)	
Ingredients	**Ranitidine hydrochloride**	**Aspirin**
Ranitidine hydrochloride USP equivalent to 150 mg of Ranitidine	167.00	-
Aspirin USP	-	100.00
Microcrystalline cellulose	70.75	85.00
Lactose anhydrous	-	62.50
Copovidone	-	25.00
Pregelatinized starch	60.00	-
Colloidal silicon dioxide	1.50	-
Magesium stearate	0.75	2.50
Total	300	275
Punches (Standard concave shape)	9.5 mm	9 mm

Preparation of coating dispersion

All the selected systems were prepared as per information provided in technical brochure of their suppliers. The composition of the each coating system is given in the table 2.

Table 2: Composition of Coating dispersion

Ingredients	**Coating composition (% w/w)**		
	Aquarius® MG	**Kollicoat® Protect**	**Opadry® AMB**

Ingredients	Coating composition (% w/w)		
	Aquarius® MG	Kollicoat® Protect	Opadry® AMB
Aquarius® MG	20	-	-
Kollicoat® Protect	-	12	-
Opadry® AMB	-	-	19.5
Titanium dioxide	-	2.5	-
Talc	-	5.0	-
Iron oxide red	-	0.5	0.5
Purified Water	80	80	80
Total	100	100	100

Preparation of Aquarius® MG coating dispersion

Aquarius® MG was dispersed in purified water using conventional overhead stirrer. Stirring was done for 45 minutes and then resultant dispersion was passed through 100-mesh screen.

Preparation of Kollicoat® Protect coating dispersion

Kollicoat® Protect was dissolved in approximate 60 % w/w purified water of total composition using over head stirrer. Titanium dioxide, Talc and iron oxide red was dispersed in remaining purified water and homogenized properly. The pigment dispersion was added in the Kollicoat® Protect solution under stirring. Resultant dispersion was passed through 100-mesh screen.

Preparation of Opadry® AMB coating dispersion

Opadry® AMB was dispersed in water using over head stirrer. Iron oxide red was dispersed to it and stirred properly. The prepared dispersion was passed through 100-mesh screen.

Coating of the core tablets

Each coating system contains different polymer hence require different preparation process, the recommended parameters for the coating is mentioned in the table 3. The tablets were coated by using all the four selected coating systems in duplicate using perforated coating pan (Ganscoater). For Aquarius® MG, Kollicoat® Protect and Opadry® AMB coating system 4 % of solid content coating was applied.

Table 3: Recommended parameters for coating of tablets as per the literature of suppliers

Parameters	Aquarius® MG	Kollicoat® Protect	Opadry® AMB
Spray atomization pressure (bars)	2	3	1.7
Fan pressure (bars)	1.75	1.5	1.7
Solid content (%w/w)	20	20	20
Inlet air temperature (°C)	60-80	55-65	60-70
Product temperature (°C)	40-45	30-50	45-55
Spray rate (g/min)	20	25	25
Weight gain (%)	4	4	4

Evaluation of coated and uncoated tablets

In order to carry out comparative evaluation of all coating systems, both coated and uncoated tablets were exposed to stress conditions of high humidity and temperature i.e. 25°C $\pm$ 2 °C /75% $\pm$ 5% RH and 40°C $\pm$ 2 °C /75% $\pm$ 5% RH for 1, 2, 3 and 7 days in open condition in dedicated temperature-humidity controlled chambers. The subjected tablets were evaluated for the parameters mentioned below.

Change in physical appearance

Physical appearance of coated and uncoated tablet of Ranitidine hydrochloride was evaluated over a period of 7 days at predetermined interval of 1, 2, 3 and 7 days. The images of each interval were captured.

Determination of free salicylic acid (FSA) content in aspirin tablets

Aspirin gets hydrolyzed in presence of moisture to form salicylic acid hence free salicylic acid content determination of aspirin was carried out by using HPLC method with certain modifications. The percent increment in free salicylic acid (FSA) content was calculated using the following equation,

% Increment in FSA content = ($FSA_{(Final)}$ – $FSA_{(Initial)}$/ $FSA_{(Initial)}$) X 100

Where, $FSA_{(Final)}$ & $FSA_{(Initial)}$ denotes final and initial free salicylic acid content of tablet respectively.

RESULTS AND DISCUSSION:

Preparation of core tablets

The selected actives were formulated into tablets using direct compression method with active content of 37 % w/w for aspirin and 56% in case of ranitidine hydrochloride. The flow property of the lubricated blend of each selected model drug was found satisfactory and there was no weight variation was observed during the entire compression run. The compressed tablets had hardness in the range of 55-77N with disintegration time of less than 10 minutes. The tablets also had friability of less than 0.2% at 100 rpm and less than 1% at 500 rpm indicating suitability of core for coating purposes. The physical parameters of core tablets of all model drugs are mentioned in the table 4.

Table 4: Physical parameters of core tablets

Properties	Ranitidine hydrochloride	Aspirin
Weight (mg)	298-302	273-276
Thickness (mm)	4.41-4.48	4.04-4.12
Hardness (N)	55-65	68-77
Disintegration time (sec)	240-252	272-290
Friability @ 100 rev (% w/w)	0.15	0.12
Friability @ 500 rev (% w/w)	0.59	0.89

Coating dispersion preparation and Coating of core tablet

Tablets of all the actives were coated using the selected coating systems up to 4% weight gain (Recommended coating level) for evaluating its efficiency of moisture protection in depth and to select appropriate coating level. The processing parameters were reported and are summarized below in table 5 (The range covers coating of all the actives in duplicate trials) however the physical parameters of core tablets of all model drugs are mentioned in the table 6.

Table 5: Coating process parameters for the selected coating system

Parameters	Aquarius® MG	Kollicoat® Protect	Opadry® AMB
Equipment	Ganscoater		
Product load (g)	700		
Spray gun (mm)	0.8		
Spray atomization pressure (bars)	1.2		
Fan pressure (bars)	2		
Solid content (%w/w)	20		
Temperature of inlet air (°C)	58-75	53-65	65-88
Product temperature (°C)	40-46	30-32	45-50
Spray rate (g/min)	3.1-4.0	3.2-3.4	3-3.2
Weight gain (%)	4	4	4

Table 6. Physicochemical properties of both uncoated and coated tablets are given below:

Model drugs	Properties	Uncoated tablets	Aquarius® MG coated tablets	Kollicoat® Protect coated tablets	Opadry® AMB coated tablets
Ranitidine hydrochloride	Weight (mg)	298-302	312-316	312-317	311-316
	Thickness (mm)	4.41-4.48	4.52-4.58	4.51-4.56	4.47-4.54
	Hardness	55-65	91-105	107-113	99-123

Model drugs	Properties	Uncoated tablets	Aquarius® MG coated tablets	Kollicoat® Protect coated tablets	Opadry® AMB coated tablets
	(Newtons)				
	Disintegration Time (seconds)	240-252	420-457	325-370	340-373
Aspirin	Weight (mg)	273-276	282-289	279-285	281-291
	Thickness (mm)	4.04-4.12	4.27-4.29	4.20-4.26	4.26-4.30
	Hardness (Newtons)	68-77	94-101	98-106	116-122
	Disintegration Time (seconds)	272-290	540-632	292-378	299-315

Ranitidine HCl Stress Study:

Change in physical appearance

Ranitidine hydrochloride is a hygroscopic drug and used as anti-ulcerative. As it comes in contact with moisture its colour gets changed. The marketed ranitidine tablet requires special packing for preventing it from moisture. Ranitidine absorbs significant moisture from the atmosphere, hence tablets prepared from it absorbs the moisture significantly. Hence, ranitidine is an ideal model drug for evaluating moisture barrier potency of the coating system as it changes colour when comes in contact with water from the surrounding atmosphere. Ranitidine hydrochloride tablets were evaluated for change in physical appearance. The uncoated tablets could not be evaluated as the tablets crumbled into a wet mass and became difficult to handle. The coated tablets at 40°C ± 2 °C /75% ± 5% RH condition also crumbled into a wet mass and hence not studied further; however the tablets at 25°C ± 2 °C /75% ± 5% RH condition showed very good comparative evaluation as shown below in figure 2 and the physical evaluation of changes in tablets is summarized in the table 7.

Table 7: Physical evaluation of change in tablet after exposure at 25°C ± 2 °C /75% ± 5% RH open condition

S. no.	System	Observation
1.	Aquarius® MG	Bursting due to swelling
2.	Kollicoat® Protect	Swelling and softening
3.	Opadry® AMB	Swelling

(A) Uncoated tablets after 0, 1, 2, 3 and 7 days

(B) Uncoated tablet (extreme left) with 4 % Aquarius® MG coated tablets after 0, 1, 2, 3 & 7 days

(C) Uncoated tablet (extreme left) with 4 % Kollicoat® Protect coated tablets after 0, 1, 2, 3 & 7 days

(D) Uncoated tablet (extreme left) with 4 % Opadry® AMB coated tablets after 1, 2, 3 and 7 days

Figure 2: Change in appearance of uncoated and various coating system coated ranitidine hydrochloride tablets after exposure at 25°C ± 2 °C /75% ± 5% RH open condition (A, B,C and D).

The tablets coated using Aquarius® MG showed breaking of the coat while tablets coated with Kollicoat® protect showed significant swelling. The tablets coated with Opadry® AMB showed comparable swelling but less than that seen in tablets coated using Kollicoat protect.

At 25°C ± 2 °C /75% ± 5% RH condition, Opadry® AMB was found to be comparable for moisture barrier efficiency with the other commercial coating systems used at 4% coating levels.

Aspirin Tablet Stress Study: Free salicylic acid content determination

Aspirin tablets were evaluated for percent increment in FSA content. These data are depicted below in figure 3.

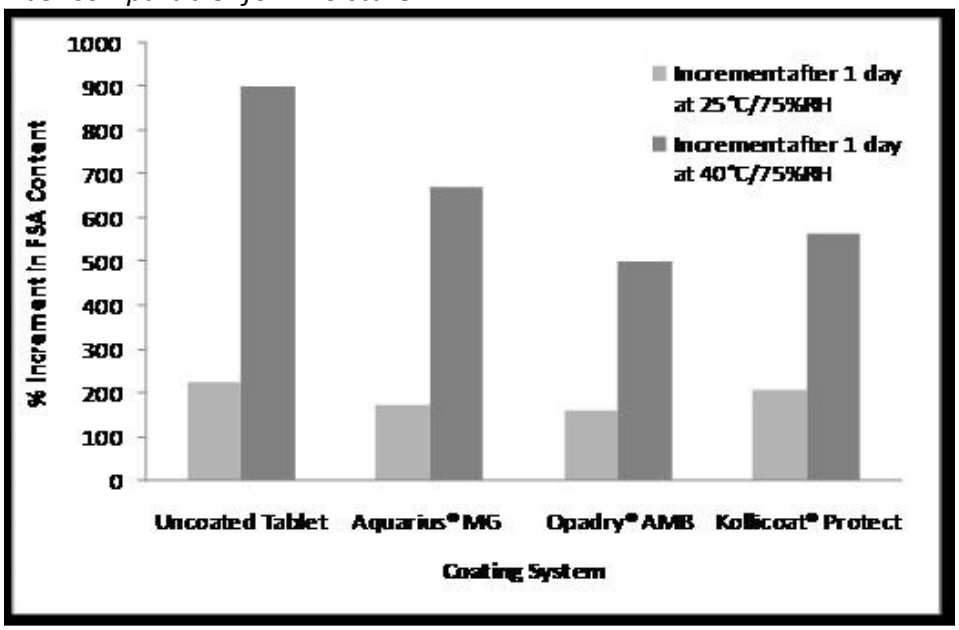

Figure 3: Percent increment in free salicylic acid content in aspirin after stress study at 25°C ± 2 °C /75% ± 5% RH & 40°C ± 2 °C /75% ± 5% RH after 1 day period

The increase in FSA content was marginal at 25°C ± 2 °C /75% ± 5% RH condition while significant at 40°C ± 2 °C /75% ± 5% RH condition for uncoated tablets.

A marginal decrease was observed in increment of FSA at 25°C ± 2 °C /75% ± 5% RH condition for all the coated tablets. The increase in the FSA content was very significant at 40°C ± 2 °C /75% ± 5% RH condition in the order as –

Uncoated >> Aquarius® MG > Kollicoat® Protect > Opadry® AMB

The moisture barrier efficiency of the particular coating system depends on the property and chemistry of key moisture barrier providing ingredient present in the coating systeme. In the selected three commercially available coating system, the Kollicoat® Protect and Opadry® AMB

are two system which are based on the Polyvinyl alcohol while Aquarius® MG is based on the Hypromellose coating system. The partially hydrolysed polyvinyl alcohol is known as the excellent film former and poly(vinyl alcohol) (PVA) is a synthetic, hydrophilic polymer that is widely studied for various pharmaceutical applications, including use in controlled release formulations, transdermal delivery systems, and tablet coating. Addition of plasticizers, heat treatment, polymer blends, copolymers, and cross-linking enhance the moisture barrier properties. Opadry® AMB contains partially hydrolysed polyvinyl alcohol. Kollicoat® Protect contains Polyvinylalcohol-Polyethelene glycol copolymer, here PEG was introduce to provide more plasticity to the film, But it is well documented that, PEG is a hydophylic polymer and may compromise the efficiency of the coating system. Introduction of PEG could be one of the reason for compromised performance of Kollicoat® Protect as compare to the Opadry® AMB. Aquarius® MG is a Hypromellose coating system, Hypromellose is hydrophilic and water swellable, hence least moisture protection ability was expected and was confirmed from the results of the current study. It is also reported that, the film adherence property of the cellulose based coating system is lower compare to the PVA based coating system. Hence it can be conclude that the PVA based coating system has a good performance than the cellulose based coating system.

CONCLUSION:

The stability of tablet containing moisture sensitive drugs like Ranitidine hydrochloride and Aspirin was studied and could be improved. Water uptake during storage and, thus, drug degradation could significantly be reduced by applying moisture-protective aqueous polymer coatings. Opadry® AMB system was shown to provide a significantly better moisture barrier than that of Kollicoat® protect and Aquarius® MG coating systems.

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