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Formulation and development of aqueous film coating for moisture protection of hygroscopic *Herniaria glabra* tablets

Higroskopik Herniaria glabra tabletlerinin nemden korunması için sulu film kaplamanın formülasyonu ve geliştirilmesi

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Abstract
Objectives: The aim of the present study is to develop a moisture protective coating solution and using it to film coat hygroscopic *Herniaria glabra* tablets.
Materials and methods: Five coating formulations were developed and applied on *Herniaria glabra* core tablets by fluidized-bed coating. The film coated tablets were evaluated by appearance, percentage of moisture gain, disintegration time and percent of drug release. Physicochemical properties and stability during storage of the best obtained coated tablets were studied.
Results: The results of this study showed that the film coating F5 containing 25% HPMC, 20% Shellac, 10% PEG 1500, 29.6% PEG 4000, 5% tween 80, 10% titanium dioxide and 0.4 % acid red 2 offered good protection for coated tablets against moisture. Coated tablets showed physical and dissolution stability during storage.
Conclusion: Combination of hydrophilic polymer HPMC and hydrophobic polymer shellac is a suitable way to balance moisture protective properties and attain fast release of drugs. This study could make it useful to develop a pharmaceutical moisture barrier film coating system for immediate release tablets. However, more studies will be needed to further evaluate the moisture resistant film.

Keywords: HPMC; Shellac; Moisture protection; Coating; *Herniaria glabra* tablets.

Öz
Amaç: Bu çalışmanın amacı, nem koruyucu bir kaplama solüsyonu geliştirmek ve higroskopik Herniaria glabra tabletlerini kaplamak için kullanmaktır.
Gereç ve yöntemler: Beş kaplama formülasyonu geliştirildi ve akışkan yataklı kaplama ile Herniaria glabra tablet çekirdeğine uygulandı. Film Kaplı tabletler, görünüm, nem Kazanım yüzdesi, dağılma süresi ettik ilaç salma yüzdesi ile değerlendirildi. En iyi elde edilen film kaplı tabletlerin fizikokimyasal özellikleri ve stabilitesi depolama sırasında incelenmiştir.
Bulgular: Bu çalışmanın sonuçları, aşağıdakileri içeren F5 kaplama filminin olduğunu göstermiştir: %25 HPMC, %20 Şellak, %10 PEG 1500, %29,6 PEG 4000, %5 tween 80, %10 titanyum dioksit ve %0,4 asit kırmızısı 2, kaplanmış tabletler için iyi koruma sağladı. Kaplanmış tabletler, depolama sırasında fiziksel ve çözünme stabilitesi göstermiştir.

Sonuç: Hidrofilik polimer HPMC ve hidrofobik polimer gomalak kombinasyonu, neme karşı koruyucu özellikleri dengelemek ve ilaçların hızlı salınımını sağlamak için uygun bir yoldur. Bu çalışma, hemen salınan tabletler için farmasötik bir nem bariyeri film kaplama sistemi geliştirmeyi faydalı kılabilir. Bununla birlikte, neme dayanıklı filmi daha fazla değerlendirmek için daha fazla çalışmaya ihtiyaç duyulacaktır.

Anahtar Kelimeler: HPMC; Shellac; Nem koruması; Kaplama; Herniaria glabra tabletleri.

Introduction

The tablets are the most popular dosage form of the drugs in use today. However, tablets may contain moisture sensitive active pharmaceutical ingredients (APIs). The stability of API in tablet during its shelf life is necessary to ensure its effectiveness. Thus, absorb moisture can cause hydrolysis and oxidation which conduct to degradation of the active substances and consequently decrease in therapeutic efficiency of the medicine.[1] Therefore, the most suitable is to protect the core tablets with a moisture protective film that could efficiently prevent water vapor from attaining the cores and hence prevent the hydrolytic degradation of API.[2,3]

Moisture protective films are used for protecting from moisture as well as for improving physical appearance, mechanical resistance and masking unpleasant odor and taste.[4]

A perfect coating film should exhibit various qualities to attain the function of moisture barrier. Thus, the coating film should be uniform, smooth and guarantee stability of drug during the shelf life. Such a coating film should also possess an adequate thickness with a low permeability to water vapor.[5]

The use of the coating film with water-soluble polymers has seen great success in recent years due to drawbacks of organic solvents (toxicity, pollution and explosion hazards) utilized in water-insoluble polymers.[6,7] Therefore, water soluble polymers, including hydroxypropyl methyl cellulose (HPMC), hydroxyethyl cellulose (HEC) and polyvinyl alcohol (PVA) are widely used in moisture barrier coating.[8]

A coating films formed with entero-soluble polymers, such as shellac polymer could efficiently provide both moisture protection and enteric functionalities due to their insolubility at acidic and neutral pH.[9,10] Shellac polymer can be used in coating film to achieve enteric applications, immediate-release properties, taste masking and sealcoating.

Different methods have been developed to test the moisture uptake of drugs. The most common method is to measure the weight increase of the dosages at various constant temperature and humidity conditions. Therefore, both uncoated and coated pharmaceutical dosages are investigated for their moisture uptake at these various humidity conditions created by a saturated salt.

Tablets containing *Herniaria glabra* extract, potassium citrate and sodium citrate were developed in laboratory in order to study their diuretic and antilithiasic effect.[11, 12, 13] However, studies have shown that obtained tablets are moisture sensitives (figure 2). Thus, absorb moisture can cause degradation of the active substances and consequently a reduction of their therapeutic efficacy.

The objective of this study was to develop a moisture barrier films based on HPMC and Shellac polymers, to film coat hygroscopic Herniaria glabra core tablets and evaluate moisture barrier properties of the films at different humidity conditions. The drug release of coated tablets was investigated. In addition, the stability of the coated tablets during storage was also evaluated.

Materials and methods

Chemicals and reagents

Herniaria glabra herb was supplied by HERBSMOROCCO (Rabat, Morocco), Potassium citrate, Sodium citrate, Schellac, Lactose monohydrate, Calcium stearate, Tween 80 and Titanium dioxide were provided by Merck (Darmstadt, Germany); Hydroxypropyl methyl cellulose (HPMC 6FC) was obtained from Dow Chemical Company (Midland, MI, USA); PEG 1500 and PEG 4000 were provided by Stepan company (Northfield, USA) and Stearic acid was received from Tianjin Damao Chemical

Reagent Factory (Tianjin, China); Acid red 2 was supplied by Spectrum Chemical (New Brunswick,USA).

Preparation of film coated Herniaria glabra tablets

Preparation of saponin-rich extract of Herniaria glabra

Herniaria glabra herb was initially defatted with petroleum ether in the Soxhlet apparatus and then extracted with ethanol 70% for 7 days by maceration.[14] The obtained extract was purified from ballast and accompanying substances using the selective liquid-liquid extraction method with organic solvents (cyclohexane, chloroform, ethyl acetate) and then precipitated in cold acetone obtaining purified saponin-rich extract.[15] The obtained extract was dried at 60˚C.

Preparation of core tablet

The core tablet containing 50 mg saponin-rich extract *Herniaria glabra*, 100 mg Potassium citrate, 100 mg Sodium citrate, 245 mg Lactose and 5 mg Calcium stearate was obtained by wet granulation method. All the ingredients were properly weighed and sieved through a 20 mesh sieve. Saponin-rich extract *Herniaria glabra*, Potassium citrate and Sodium citrate as drug substances and Lactose monohydrate as diluent were loaded into a Laboratory High Shear Mixer Granulator (STE Techpharm, Spain) and mixed for 5 min.[16] The powder blend was granulated using purified water as granulating fluid. The purified water was sprayed onto the powders with the 3g/min and 0.11 MPa spray air pressure. During the spraying, the impeller speed was 600 rpm. The wet granules obtained, were air dried in the Lab Fluid Bed Dryer (STREA-1, Aeromatic Fielder, Switzerland) at an inlet temperature of 60°C for 10 min.[17] The dried granules were milled through 850 µm sieve and lubricated for 5 min with calcium stearate and stored for compression into tablets. The tablets were compressed with a single punch machine (Korsch EK0, Germany). The average weight of the tablets was 500.0 mg.

Preparation of film coating suspensions

Five coating formulations were developed using HPMC and Shellac as film-forming agent, stearic acid, PEG 1500 and PEG 4000 as plasticizers, tween 80 as surfactant, titanium dioxide as pigment and acid red 2 as colorant; detailed compositions were showed in table I and II.

Formulation F1 contained 8% Shellac, 0,6% stearic acid, 6% PEG 4000, 0.4% tween 80, 1.5% TiO2, 0.05% acid red 2 dye, 10% ammonia 25% and 73,45% distilled water. Polymeric Shellac solution was obtained by dissolving 40 g Shellac polymer in a mixture of 200 ml water and 50 g 25% ammoniated aqueous solution under stirring and heating at temperature between 50-60 ºC.[18] The obtained polymer Shellac solution was cooled to room temperature. 30 g polyethylene glycol (PEG) 4000, 2.0 g tween 80 and 3.0 g stearic acid were added progressively and mixed to the polymeric shellac solution until they were evenly dispersed. In a separate container, 7.5 g titanium dioxide was dispersed in 100 ml purified water using magnetic stirrer during 2 hours. The obtained Shellac mixture was thoroughly mixed with titanium dioxide suspension, 0.25 g acid red 2 dye and remaining water under stirring for 60 minutes in order to obtain a homogenized distribution.

Formulation F2 contained 7.5% Shellac, 7.5% PEG 4000, 0.5% tween 80, 1.5% TiO2, 0.05% acid red 2 dye, 10% ammonia 25% and 72,95% distilled water. Formulation F2 (not containing stearic acid) was prepared in the same way as F1.

Formulation F3 contained 6% HPMC, 6% PEG 4000, 0.3% tween 80, 1% TiO2, 0.05% acid red 2 dye and 86.65% distilled water. Polymeric HPMC solution was obtained by dissolving 30.0 g HPMC polymer in 300.0 ml purified water with magnetic stirring at 80 ºC for 60 minutes. The obtained polymeric HPMC solution was cooled to room temperature and mixed with 30.0 g PEG 4000 and 1.5 g tween 80. In a separate container, 5.0 g titanium dioxide was dispersed in 100 ml purified water using magnetic stirrer during 2 hours. The obtained HPMC mixture was mixed with titanium dioxide suspension, 0.25g acid red 2 dye and remaining water under stirring for 60 minutes in order to obtain a homogenized distribution.

Formulation F4 contained 2.4% shellac, 3% HPMC, 2.8% PEG 4000, 1% PEG 1500, 0.6% tween 80, 1.2% TiO2, 0.05% acid red 2 dye, 4% ammonia 25% and 84.95% distilled water. Polymeric Shellac

solution (12.0 g Shellac prepared in the same way as F1) was mixed with 14.0 g PEG 4000, 5.0 g PEG 1500 and 3.0 g tween 80 in order to obtain a homogenized shellac mixture. Polymeric HPMC solution (15.0 g HPMC prepared in a similar fashion as F3), was mixed with the shellac mixture, titanium dioxide suspension (6.0 g TiO2), 0.25g acid red 2 dye and remaining water under stirring for 60 minutes in order to obtain a homogenized distribution.
Formulation 5 contained 2.4% shellac, 3% HPMC, 3.6% PEG 4000, 1.2% PEG 1500, 0.6% tween 80, 1.2% TiO2, 0.05% acid red 2 dye, 4% ammonia 25% and 83.95% distilled water. Formulation F5 was prepared in the same way as F4.
The coating solutions were filtered through sieve number 140 equivalent to 160 µm (ASTM E-11, Cole Parmer, USA) and stored in airtight container.

Preparation of free films
Free films were prepared by casting polymer solution onto glass petri dishes, and placed in an oven at 50 ºC for 24 h. Dried films were removed and cut carefully into strips with an average thickness of 200-300 µm, width 10 mm and length 50 mm. Free film were kept in a dessicator with 50% RH at room temperature until mechanical analysis were performed. The mechanical properties of the films including tensile strength and elongation at break were evaluated by a Texture Analyzer (TA-XT plus, UK) using 50 N load cell and cross head speed of 5 mm/min.

Coating process
The coating of the tablets was carried out in a fluid bed coater (Strea-1 Aeromatic Fielder, Switzerland) and the coating parameters were as follows: Batch size 500.0 g, Inlet air temperature 60°C, outlet air temperature 45°C, air flow 90 m^3/h, atomizing air pressure 2.0 bar, spray rate 3 g/min, drying temperature 50°C and drying time 15 min. The tablets were coated until a weight gain of 6% w/w. Coating solution was stirred continuously over coating process.
Evaluation of tablets core and coated tablets
The thickness, friability, hardness and disintegration time of the core tablets and coated tablets were studied according to the methods described in the Russian Pharmacopoeia 14.[19] The thickness was determined with a micrometer (Moore and right 1965B, UK), the friability was determined with a friabilator (Erweka TA 100, Germany), the hardness was measured using a hardness tester (Erweka TBH 125, Germany) and the disintegration time was studied in distilled water (disintegration medium) at 37 ± 0.5 °C using disintegration tester (Erweka ZT 120, Germany).

Dissolution test of tablets
The dissolution test was performed using the Russian Pharmacopeia 14, paddle method.[20] Drug release was measured in Erweka dissolution tester (DT 720, Germany) using distilled water as the dissolution medium, maintained at 37± 0.5 °C and agitated at 50 rpm (n = 6). The samples were withdrawn at 5, 10, 15, 20, 30, 45 and 60 min.
Drug release of saponins was determined spectrophotometrically based on the method of HIA et al.[21] To 0,5 ml of sample and standard (Escin), 0,5 ml of 8% Vanillin solution and then 5,0 ml of 72% Sulfuric acid were added and mixed well in an ice water bath. The mixture was warmed in a bath at 60°C for 10 min, then cooled in water at the ambient temperature for 5 min. The absorbance of the standard and samples was measured at 560 nm using a UV 1240, spectrophotometer Shimadzu, Japan.
Preparation of reagents: 8 % (w/v) vanillin solution: 800 mg of vanillin was dissolved in 10 ml of 99.5% ethanol. Prepared freshly for each determination.
72% (v/v) sulfuric acid: to 28 ml of deionized water, 72 ml of sulfuric acid was added.
Drug release of citrates was determined using non-aqueous acid-base titrimetry method described in European pharmacopeia 8.[22] 20 ml of sample was evaporated gently on a hot plate until dryness, then dissolved in 20 ml of anhydrous acetic acid, heating to about 50 °C. Allowed to cool. 0.25 ml of naphtholbenzein solution as indicator was added and the solution was titrated with 0.1N perchloric acid until a green color was obtained.

Preparation of reagents: Preparation of anhydrous acetic acid: 104 ml of acetic anhydride poured into glacial acetic acid in small portions with stirring. The acid container was left to stand for about a day. *Preparation of 0.1N. titrated solution of perchloric acid in anhydrous acetic acid*: approximately 8.5 ml of 72% perchloric acid was dissolved in 100 ml of anhydrous acetic acid, about 30 ml of acetic anhydride was added in small portions with constant cooling of the solution to bind water. The bottle was closed with a cork and leaved for a day in a dark place, then the volume of the solution was brought to 1 liter.

Moisture uptake of tablets

The moisture uptake of the tablets was determined by placing the tablets in desiccators of 25°C/75% RH, saturated sodium chloride solution and 25°C/91% RH, saturated potassium nitrate solution.[23] Weight gain was measured at predetermined time points.

Stability test of coated tablets

The samples of coated tablets were blister packed in aluminum by using packing machine DP-210 (Wenzhou T&D Packaging Machinery Factory, China). Stability studies were realized according to ICH guidelines.[24] Tests were conducted under room temperature (RT) and accelerated stability conditions. The samples designed for RT were kept at 30 ± 2 °C and 65 ± 5 % relative humidity, while the accelerated stability samples were kept at 40 ± 2 °C and 75 ± 5 % RH in humidity chamber (Binder KBF 115, Germany). The RT samples were tested at 0, 3, 6, 9 and 12 months. The accelerated stability samples were tested at 0, 1, 2, 3 and 6 months. During storage the coated tablets were tested for their physical appearance, hardness, friability, disintegration and dissolution.

RESULTS AND DISCUSSION

It has been shown that coatings affect the physicochemical properties of the tablet to varying degrees and these changes are suggestive of the effect of the coating materials.[25,26] The moisture uptake behavior of coated tablets exposed to different relative humidity conditions can be utilized as a measure for the ability of a film coating to protect the core tablet against moisture.[27] Thus, Core tablets of Herniaria glabra were coated using the prepared coating solutions (table I and II). The results of the tested parameters were presented in the table 3 and figures 1, 2 and 3.

For formulation F1 and F2

TCF1 (tablets coated with formulation F1) showed good physical appearance with a smooth surface. The coated tablets exhibited the best moisture protection compared to others coated tablets (moisture gain 5.1% at 75% RH and 6.4 at 90% RH). The disintegration time of coated tablets was increased in comparison to core tablets (from 3 min in core tablets to 25 min in coated tablets). The dissolution profile of TCF1 showed decrease of drug release (80.2% of saponins and 84.4% of citrates).
TCF2 (tablets coated with formulation F2) showed also a good physical appearance and a good moisture protection. Removing Stearic acid from F2 has slightly decreased disintegration time (22 min) and increased dissolution of coated tablets (82.3% of saponins and 87.2% of citrates).
Free shellac films F1 and F2 presented lower tensile strength and higher elongation (figure1). Interestingly, shellac coated tablets showed lowest moisture uptake compared with other coated tablets at 75% and at 90% relative humidity (figure 2). However, shellac coating led to a long disintegration time and a considerable reduction of the resulting drug release rate. Therefore, it is convincing to suggest that these findings can be attributed to the poor water solubility of shellac and also to a hydrophobic character of the stearic acid (in F1) which both have led to form a coating film with a low permeability. [28,29,30]

For formulation F3

TCF3 (tablets coated with formulation F3) showed the shortest disintegration time (7min) and exhibited the best drug release (90.2% of saponins and 93.1% of citrates) in comparison to others

coated tablets. However, coated tablets manifested high moisture uptake (moisture gain 8.4% at 75% RH and 10.5% at 90% RH) and showed signs of cracking.
Therefore, the tablets coated by HPMC film showed high moisture uptake compared to tablets coated by shellac film, this might indicate that HPMC has a lower potential for moisture protection than shellac. This obviously is a result of the hydrophilic nature of the HPMC film. Then, HPMC polymer being a hydrocolloid, absorbs water molecules due to hydrogen bonding with water molecules and itself. As a result, when the film is exposed to water/moisture it tends to allow a water vapor permeability.[31]

For formulation F4 and F5
TCF4 (tablet coated with formulation F4) showed lower water uptake rates compared with HPMC coated tablets (moisture gain 5.6% at 75% RH and 7.3% at 90% RH). The disintegration time of TCF4 was reduced (15 min) in comparison to HPMC coated tablets. The dissolution profile of TCF4 showed increase of drug release (86.1% of saponins and 89.3% of citrates) in comparison to HPMC coated tablets. However, TCF4 have shown signs of cracking which was attributed to a lack of plasticizer concentration in film.
By increasing concentrations of plasticizers 1.2% PEG 1500 and 3.6% PEG 4000 in coating solution F5 (10% PEG 1500 and 29.6% PEG 4000 in film coating F5), the signs of cracking have disappeared and a good coated tablets (TCF5) with smooth surface were obtained. Increasing the amount of plasticizers has also led to decrease tensile strength and increase percent elongation (figure1). The TCF5 showed a low moisture uptake. Thus, the weight gain was decreased from 16.1% of core tablets to 5.7% of TCF5 at 75% RH and from 18.2% of core tablets to 7.5% of TCF5 at 90% RH.
In the Shellac-HPMC composite film, shellac is a hydrophobic component that repels water molecules from forming a bond due to its hydrophobicity and hence reduces the permeability of water vapor through the composite film.[32,33]
TCF5 showed satisfactory disintegration time within 15 min and drug release achieved 88% of Saponins and 90.6% of citrates which complied with the Russian dissolution requirements.
Therefore, the combination of 3% HPMC and 2.4% Shellac in coating solution (25% HPMC and 29.6% shellac in film coating) has led to a good protection for coated tablets against moisture and provided satisfactory dissolution.
According to this findings, the formulation F5 showed most satisfactory results and was selected as an optimized formulation after comparative evaluation.
The properties of uncoated and coated tablets can be seen in Table 4. TCF5 showed a small increase in hardness and decrease in friability. The tablets weight variation also decreased, which is indicative of the good coating uniformity provided by the fluid bed process. The disintegration time was increased from 3 min (core) to 15 min. From the results uncoated and coated tablets showed suitable characteristics which complied with the Russian Pharmacopoeia 14.

Stability studies
CTF5 were stored in stability chamber with controlled temperature and humidity in order to study their stability. Thus, physicochemical properties were studied. The results were showed in table 5.
Long term and accelerated stability studies showed no major change in physical characteristics, hardness, friability and disintegration of coated tablets. Drug release was within acceptable limits and complied with the Russian dissolution requirements. Thus, CTF5 were stable under stability testing conditions.

CONCLUSION

Combination of hydrophilic polymer HPMC and hydrophobic polymer shellac is a suitable way to balance moisture protective properties and attain fast release drugs. The results of this study showed that formulation of film coating containing 25% HPMC and 20% Shellac as film-forming agent, 10% PEG 1500 and 29.6% PEG 4000 as plasticizers, 5% tween 80 as surfactant, 10% titanium dioxide as pigment and 0.4 % acid red 2 as colorant offered good protection for coated *Herniaria glabra* tablets

against moisture. Moreover, coated tablets showed physical and dissolution stability during storage. This study could make it useful to develop a pharmaceutical moisture barrier film coating system for immediate release tablets. However, more studies will be needed to further evaluate the moisture resistant film.

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Table 1: Composition of coating solutions (% w/w)

Component	F1	F2	F3	F4	F5
Shellac	8.0	7.5	-	2.4	2.4
Stearic acid	0.6	-	-	-	-
HPMC 6FC	-	-	6.0	3.0	3.0
PEG 4000	6.0	7.5	6.0	2.8	3.6
PEG 1500	-	-	-	1.0	1.2
Tween 80	0.4	0.5	0.3	0.6	0.6
TiO2	1.5	1.5	1.0	1.2	1.2
Acid red 2	0.05	0.05	0.05	0.05	0.05
Ammonia 25%	10.0	10.0	-	4.0	4.0

Distilled water	73.45	72.95	86.65	84.95	83.95

Table 2: Compositions of film coating (%)

Component	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)
Shellac	48.3	44.0	-	21.7	20.0
Stearic acid	3.7	-	-	-	-
HPMC 6FC	-	-	45.0	27.1	25.0
PEG 4000	36.3	44.0	45.0	25.3	29.6
PEG 1500	-	-	-	9.1	10.0
Tween 80	2.4	2.9	2.2	5.5	5.0
TiO2	9.0	8.8	7.4	10.9	10.0
Acid red 2	0.3	0.3	0.4	0.4	0.4
Ammonia 25%	*	*	*	*	*
Distilled water	*	*	*	*	*
Total	100.0%	100.0%	100.0%	100.0%	100.0%

*Distilled water and Ammonia 25% are volatile components, which do not remain in the film coating

Table 3: Physicochemical properties of uncoated and coated Herniaria glabra tablets

Formulation	Disintegration, min	%, Saponins release	%, Citrates release	Physical appearance
Tablet cores	3±1	94.1±1,2	96.0±1,3	
CTF1	25±1	80.2±1,5	84.4±0,5	Smooth shiny surface
CTF2	22±1	82.3±0,7	87.2±1,2	Smooth shiny surface
CTF3	7±1	90.2±1,2	93.2±0,9	Signs of cracking
CTF4	15±1	86.1±0,9	89.3±1,1	Signs of cracking
CTF5	15±1	88.0±1,6	90.6±0,8	Smooth shiny surface

Table 4: Physicochemical properties of uncoated and film coated *Herniaria glabra* tablets CTF5

	Uncoated	CTF5
Average weight of tablet (mg)	500.0 ± 1.7	530.0 ± 0.8
Diameter (mm)	11.0 ± 0.4	11.5±0.5
Thickness (mm)	3.11 ± 0.12	3.35 ± 0.14
Hardness (N)	12.1 ± 0.8	12.4±0.7
Friability (%)	0.15	0.12
Disintegration time (min)	3 ± 1	15±1
Saponins content (%)	94.1 ± 1.2	88.0 ± 1.6
Citrates content (%)	96.0 ± 1.3	90,6 ± 0,8

Table 5: Stability testing of *Herniaria glabra* coated tablets at Room Temperature and under Accelerated conditions

	Period (Month)	Physical Characteristics (pink Tablet)	Hardness (N)	Friability %	Disintegration, min	%, Saponins release	%, Citrates release
CTF5 at Room Temperature	0	Appropriate	12.4± 0.8	0.10±0.12	15±1	88.0±1.6	90.6± 0.8
	3	Appropriate	12.4± 0.6	0.10±0.11	15±1	88.0±1.0	90.6± 1.2
	6	Appropriate	12.3± 0.4	0.11±0.09	15±1	87.9±1.1	90.5± 1.3
	9	Appropriate	12.2± 0.3	0.13±0.08	15±1	87.8±1.5	90.3± 0.9
	12	Appropriate	12.2± 0.9	0.14±0.14	15±1	87.6±0.9	90.1± 1.1
CTF5 under Accelerated conditions	0	Appropriate	12.4± 0.8	0.10±0.12	15±1	88.0±1.6	90.6± 0.8
	1	Appropriate	12.3± 0.5	0.11±0.13	15±1	87.9±1.2	90.4± 1.4
	2	Appropriate	12.3± 0.7	0.12±0.07	15±1	87.8±1.5	90.2± 1.2
	3	Appropriate	12.2± 0.6	0.12±0.12	15±1	87.6±1.4	90.1± 0.8
	6	Appropriate	12.1± 0.9	0.14±0.15	15±1	87.3±0.7	89.9± 1.5

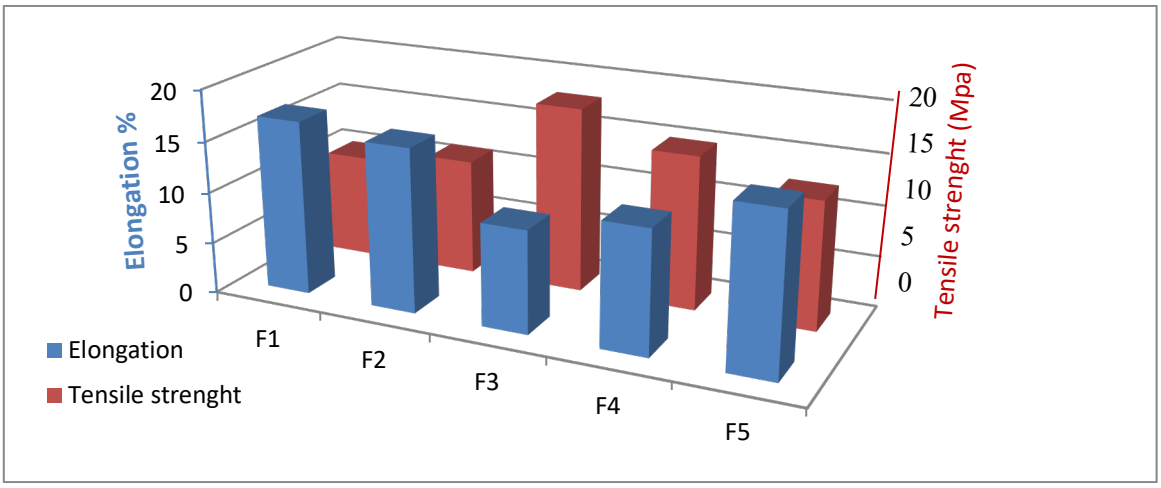
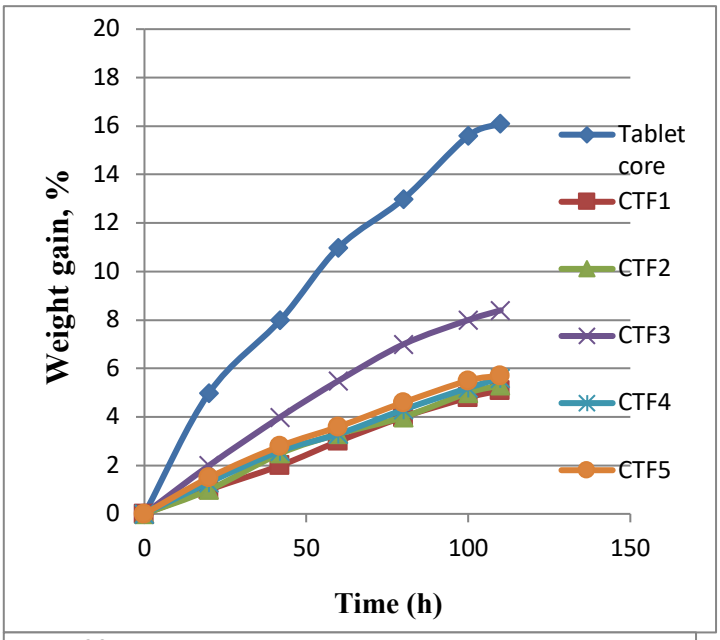


Figure 1: Tensile strength and percentage elongation of free films



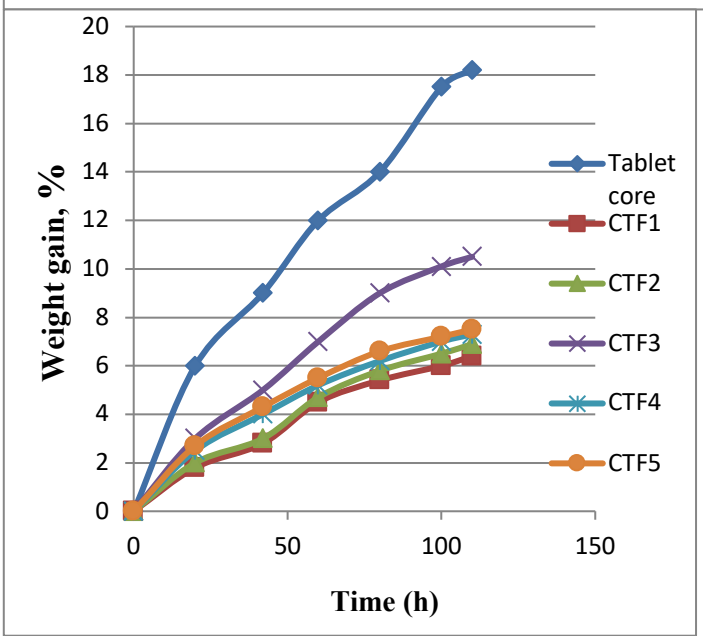


Figure 2: Percent moisture (weight) gain of coated tablets at 25°/75% RH and at 25°/90% RH

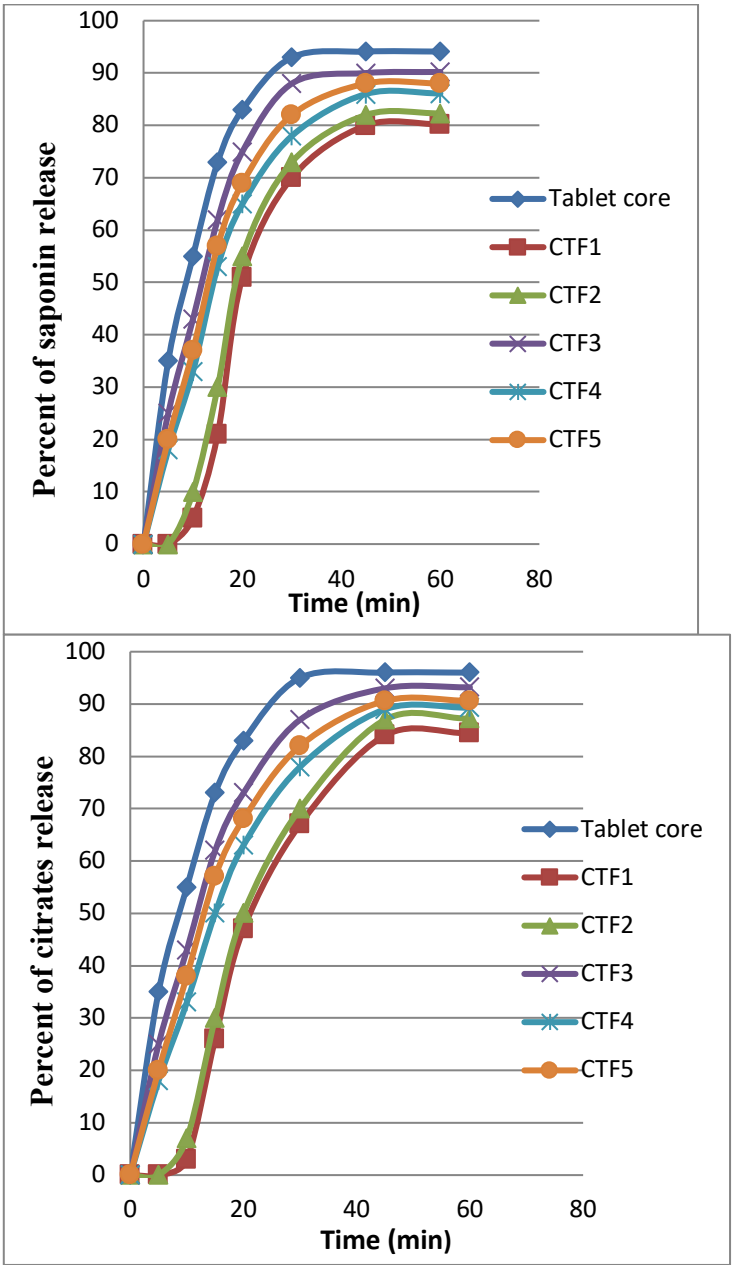


Figure 3: Drug release of *Herniaria glabra* coated tablets with different coating solutions (F1, F2, F3, F4, and F5)