IJPSR (2010), Vol. 1, Issue 8 (Suppl.) **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 28 April, 2010; received in revised form 20 June, 2010; accepted 28 July, 2010

RELEASE PROFILE OF EXTRACTS OF *BRIDELIA FERRUGINEA* LEAF AND *CANTHIUM GLABRIFLORUM* STEM BARK FROM DIFFERENT ABSORBENTS

R Johnson*[1], J Adotey [1], M T Bayor[1] and K Annan [2]

Department of Pharmaceutics, Faculty of Pharmacy and Pharmaceutical Sciences, College of Health Sciences, Kwame Nkrumah University of Science and Technology [1], Kumasi, Ghana
Department of Pharmacognosy, Faculty of Pharmacy and Pharmaceutical Sciences, College of Health Sciences, Kwame Nkrumah University of Science and Technology[2], Kumasi, Ghana

Keywords:

Bridelia ferruginea,
Canthium glabriflorum,
Absorbents,
Release profile

Correspondence to Author:

R Johnson

Department of Pharmaceutics, Faculty of Pharmacy and Pharmaceutical Sciences, College of Health Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana

E-mail:
rjohnson.pharm@knust.edu.gh

ABSTRACT

The aqueous decoctions of *Bridelia ferruginea* leaf and *Canthium glabriflorum* stem bark were converted into granules by absorbing into different types of absorbents in different quantities. *In vitro* dissolution studies were then used to assess the release of the extracts from the granules. Comparative and ranking studies of the effects of different weights of the different absorbents on the release of the extracts by Duncan's multiple range tests (p=0.05) were used to assess the performance of the absorbents. The λ_{max} for the extracts were obtained with 0.01 %w/v solutions at 267 nm and 279 nm for *B. ferruginea* and *C. glabriflorum*, respectively. The UV absorbances at these frequencies were used as indices for the assay of the active constituents in the respective extracts. The cumulative percentage release of the extracts was generally higher from the extract-absorbent systems than from the pure extracts, for all the different types and weights of absorbents used. The results also indicated significant differences (p = 0.05) in the mean cumulative percent release of both extracts from the different absorbents. There were however, optimised weights of the effective absorbents per dose (weight) of the extracts that produced the best release effects. 76 mg of Microcrystalline cellulose per dose of *B. ferruginea* extract (155.2 ± 2.0 mg) had the best and most significant release profile (75.3 ± 0.7 %), whilst, 48 mg of bentonite per dose of *C. glabriflorum* extract (170 ± 2.0 mg), was the most significant with the highest cumulative percent release (99.4 ± 0.2 %) after 45 minutes, indicating their suitability for use in formulating these extracts into solid dosage form.

INTRODUCTION: *Bridelia ferruginea* (Euphorbiaceae) leaf and *Canthium glabriflorum* (Rubiaceae) stem bark are used traditionally to treat diabetes and hypertension respectively [1]. The incidence of these two diseases is increasing in developing countries. The conventional drugs for their treatment have many adverse effects [2]. There is therefore the need to develop conventional dosage forms from plants with documented evidence of activity and with less adverse effects. In developing solid dosage forms such as tablets and capsules, the goal is to prepare a formulation with good flow properties that result in standard product with accurate dosing and good bioavailability characteristics [3]. In such formulations, the active components and excipients are blended thoroughly to ensure a uniform powder mix for compression or encapsulation.

Gelatin capsules are unsuitable for the encapsulation of aqueous liquids. As such, rather than place a liquid in such capsules, it is desirable to absorb the liquid by mixing with a suitable absorbent [4]. This technique was employed in the formulation of *B. ferruginea* and *C. glabriflorum* aqueous decoctions which were difficult to dry completely without loss of integrity and activity, into granules using bentonite, light magnesium carbonate, microcrystalline cellulose and kaolin as absorbents. To obtain a product of good bioavailability characteristics, *in vitro* dissolution testing is mandatory for solid dosage forms [3]. Though dissolution testing is not a predictor of therapeutic efficiency, it is a qualitative tool which can provide valuable information about the biological availability of a drug as well as batch-to-batch consistency. It is considered as one of the most important quality control tests performed on pharmaceutical dosage forms. This study therefore, investigated the release of the extracts of *B. ferruginea* and *C. glabriflorum* from the different absorbents by *in vitro* dissolution tests in order to determine the most appropriate type and quantity of absorbent for use in converting the extracts into solid dosage forms.

MATERIALS AND METHODS:

Absorbents: Microcrystalline cellulose (Pacegrove Medical & Pharm Lab, UK); Bentonite powder (Drug Pharm Trading, Holland); Light Magnesium carbonate and Kaolin (Fisons Scientific, England) were used as the absorbents. All other chemicals and reagents used were of analytical grade.

Plant Materials: The fresh leaves of *B. ferruginea* and stem bark of *C. glabriflorum* were harvested from the Akwapim range and authenticated at the Centre for Scientific Research into Plant Medicine (CSRPM), Ghana, in November 2008, where voucher specimens with numbers CSRPM/08/62 and CSRPM/08/01, respectively, have been deposited in their herbarium. The plant materials were dried at room temperature for 15 days and then comminuted into coarse powder for extraction.

Preparation of Decoctions: The decoctions were prepared according to how they are used locally and at CSRPM (i.e. *B. ferruginea*; 5 %w/v and *C. glabriflorum*; 8 %w/v). Samples of 300 g *B. ferruginea* in 6 L of water and 400 g *C. glabriflorum* in 5 L of water were boiled for 1 hour and allowed to cool and macerate for 12 hours. The liquid extracts were decanted, the marc pressed and the extracts clarified by filtration. Each extract was then concentrated at 50 ^{o}C into a thick viscous mass and kept in desiccators until used further.

Determination of Wavelength of Maximum Absorption (λ_{max}): Serial dilutions of 1 %w/v stock solutions of *B. ferruginea* leaf and *C. glabriflorum* stem bark extracts were prepared in

distilled water and their absorbance measured on a UV-Visible Spectrophotometer (Cecil 7200 Series) in order to determine the wavelength of maximum absorption for each extract. Concentrations of 0.01 %w/v of both extracts gave λ_{max} at 267 nm and 279 nm for *B. ferruginea* and *C. glabriflorum*, respectively.

Formulation of Granules: Various samples of the concentrated decoctions obtained were absorbed into 5 different quantities of the selected absorbents as indicated in **Tables 1** and **2**. The choice of weights of the absorbents used was based on the weight of extract per dose of their respective formulations. Each decoction-absorbent system was then dried in an oven at 50 ^{o}C to a constant weight and the resultant dry mass passed through a Retsch analytical sieve (No. 20; 850 µm) to obtain the appropriate granules.

TABLE 1: FORMULATION OF GRANULES OF *B. FERRUGINEA*

INGREDIENTS	Bf1	Bf2	Bf3	Bf4	Bf5
***B. ferruginea* decoction (5 %w/v)**					
Plant material (g)	300	300	300	300	300
Water (L)	6	6	6	6	6
Absorbents					
Bentonite (g)	1.9	3.8	5.7	7.6	9.5
Kaolin (g)	1.9	3.8	5.7	7.6	9.5
Light Magium carbonate (g)	1.9	3.8	5.7	7.6	9.5
Microcrystalline cellulose (g)	1.9	3.8	5.7	7.6	9.5

TABLE 2: FORMULATION OF GRANULES OF *C. GLABRIFLORUM*

INGREDIENTS	Cg1	Cg2	Cg3	Cg4	Cg5
***C. glabriflorum* decoction (8%w/v)**					
Plant material (g)	400	400	400	400	400
Water (L)	5	5	5	5	5
Absorbents					
Bentonite (g)	1.95	3.90	5.86	7.81	9.76
Kaolin (g)	1.95	3.90	5.86	7.81	9.76
Light Mag. carbonate (g)	1.95	3.90	5.86	7.81	9.76
Microcrystalline cellulose (g)	1.95	3.90	5.86	7.81	9.76

Dissolution profile of the granules

The study of the *in vitro* release of the extracts from the granules was conducted using the six vessel USP type II rotating paddle apparatus (Erweka). The dissolution medium was 900 ml distilled water, pH 6.9, at 37 ± 0.5 ^{o}C, with a paddle speed of 50 rpm. Samples of 20 ml solution were withdrawn at predetermined time intervals and replaced with fresh dissolution medium. The samples were filtered through 0.2 µm Whatman filter paper and diluted appropriately to obtain 0.01 %w/v solutions. The absorbance of these solutions were then measured on a UV/Visible double beam Spectrophotometer at 267 nm for *B. ferruginea* and 279 nm for *C. glabriflorum*, and the concentration of the extracts in these solutions determined using the equations of the calibration curves. The cumulative percent releases of the extracts were then calculated.

Statistical Analysis: Two-way ANOVA was used for the comparison of the mean percent release of the extracts from the different weights of the different absorbents. Duncan's multiple range tests were used in ranking the absorbents and their various weights employed, on Excel 2007 software.

RESULTS AND DISCUSSION: Accurate methods of assay for herbal remedies are rare, and in instances where the active constituents are unknown there is difficulty in assessing therapeutic potency. The measurements of UV absorbance of natural products have been used to quantify the amount of active constituents present, especially values obtained at the wavelength of maximum absorption (λ_{max}). The λ_{max} obtained for 0.01 %w/v solution of both *B. ferruginea* and *C. glabriflorum* were at 267 nm and 279 nm, respectively. The relationships of concentration of extracts against UV absorbances at these wavelengths were linear (R^2 = 0.9941; *B. ferruginea* and R^2 = 0.9971; *C. glabriflorum*)

which enabled the determination of the concentration of the extracts from the samples in the dissolution studies.

The drying of the aqueous decoctions of both plants resulted in gummy-like materials which were very hygroscopic. The use of absorbents in the formulation of such extracts into solid dosage forms makes processing easier and reduces the hygroscopicity of the extracts [5]. However, from biopharmaceutical viewpoint such absorbents affect the release of the extract after administration of the drug [4]. A good absorbent should therefore release the extract readily in order for it to exert its desired therapeutic effect. The bioavailability exhibited by a drug involves the quantity and rate at which the intact form of the drug appears in the systemic circulation following administration. It is important in determining whether a therapeutically effective concentration is achieved at the site(s) of action of the drug. Current bioavailability assessments depend on measurement of the concentration of the drug in a suitable body fluid, usually blood plasma, urine or occasionally saliva, over a period of time after administration as a correlation of the clinical efficacy of the drug in treating a given disease condition [6]. Some drugs require the time of peak concentration as a monitoring parameter and others, the maximum concentration at a given time. Though dissolution testing is not a predictor of therapeutic efficiency, it is a qualitative tool that can provide valuable information about the biological availability of a drug. The parameter of assessment used depends on the drug, the type of disease and duration of treatment.

In Ghana, aqueous decoctions of *B. ferruginea* leaf and *C. glabriflorum* stem bark are used for the management of diabetes and hypertension, respectively. The maximum concentration of these extracts in the blood within a given period of time will be an important parameter for assessing their bioavailability and effectiveness, since such remedies will be used over long periods of time.

From the dissolution profile of the pure extracts (without any absorbent), 35.0 ± 1.2 % of *B. ferruginea* and 42.1 ± 0.9 % of *C. glabriflorum* were released after 45 minutes, as against 70 % as specified in the BP (2007)[7]. The cumulative percent releases of the extracts were generally higher from the extract-absorbent systems than from the pure extracts for all the different types and weights of absorbents used (**Figs. 1 and 2**).

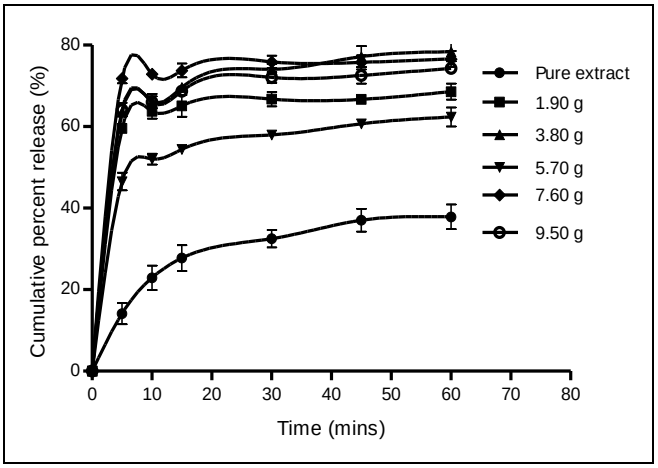

FIG. 1: RELEASE OF *B. FERRUGINEA* FROM THE PURE EXTRACT AND DIFFERENT EXTRACT-ABSORBENT (MICROCRYSTALLINE CELLULOSE) SYSTEMS

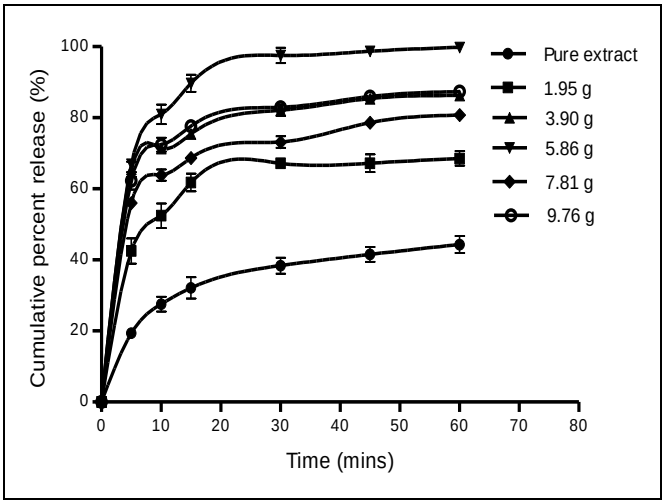

FIG. 2: RELEASE OF *C. GLABRIFLORUM* FROM THE PURE EXTRACT AND DIFFERENT EXTRACT-ABSORBENT (BENTONITE) SYSTEMS

The surface area and the solubility of a solid affect its dissolution in a liquid. Surface area is inversely proportional to the particle size. Materials that tend to form coherent masses in the dissolution medium, as was in the case of the pure extracts, leads to a reduction in the surface area available for dissolution [3]. The granules from the extract-absorbent systems provided discrete particles with larger surface area, hence the improved dissolution profiles and higher cumulative percent release of extracts.

Generally, there was a relative increase in the cumulative percent release of the extracts as the weight of absorbent increased to some level, for almost all the absorbents (**Figs. 1** and **2**). However, there was an optimised weight of each absorbent per dose (weight) of the extracts that produced the best release, especially after 45 minutes (**Tables 3** and **4**). The results also indicated significant differences (p = 0.05) in the mean cumulative percent release of both extracts from the different absorbents used, as ranked by Duncan's multiple range tests (**Tables 5** and **6**).

TABLE 3: CUMULATIVE PERCENT RELEASE OF THE EXTRACT OF *B. FERRUGINEA* FROM DIFFERENT WEIGHTS OF THE ABSORBENTS AFTER 45 MINUTES

Sample		Bf1 (1.9 g)	Bf2 (3.8 g)	Bf3 (5.7 g)	Bf4 (7.6 g)	Bf5 (9.5 g)
		Cumulative Percent Release (%) (Mean ± SD, n=3)				
Extract only	35.0 ± 1.2					
Bentonite		49.3 ± 0.4	55.1 ± 0.9	59.2 ± 0.2	52.8 ± 0.7	57.4 ± 0.6
Kaolin		60.9 ± 0.6	44.2 ± 0.9	45.9 ± 1.4	64.1 ± 0.5	67.9 ± 0.3
Light Mag. carb.		44.1 ± 0.8	46.5 ± 0.4	50.3 ± 0.7	43.3 ± 0.8	52.1 ± 0.7
Micro. cellulose		66.4 ± 0.5	68.4 ± 1.2	74.5 ± 0.3	75.3 ± 0.7	71.1 ± 0.3

TABLE 4: CUMULATIVE PERCENT RELEASE OF THE EXTRACT OF *C. GLABRIFLORUM* FROM THE DIFFERENT WEIGHTS OF ABSORBENTS AFTER 45 MINUTES

Sample		Cg1 (1.95 g)	Cg2 (3.90 g)	Cg3 (5.86 g)	Cg4 (7.81 g)	Cg5 (9.76 g)
		Cumulative Percent Release (%) (Mean ± SD, n=3)				
Extract only	42.1 ± 0.9					
Bentonite		66.4 ± 0.4	84.8 ± 0.3	99.4 ± 0.2	89.2 ± 0.5	86.7 ± 0.8
Kaolin		27.9 ± 0.6	28.9 ± 0.2	26.4 ± 0.7	29.1 ± 0.4	28.5 ± 1.1
Light Mag. carb.		26.2 ± 0.5	27.2 ± 0.6	48.9 ± 0.8	40.8 ± 1.2	28.9 ± 0.9
Micro. cellulose		32.8 ± 0.3	37.1 ± 0.7	39.5 ± 0.6	37.5 ± 1.1	40.7 ± 0.2

TABLE 5: MEAN CUMULATIVE PERCENT RELEASE OF *B. FERRUGINEA* FROM THE DIFFERENT ABSORBENTS RANKED BY DUNCAN'S MULTIPLE RANGE TESTS

Rank order	Absorbent	Mean release (%)	n	Ranked
1	Microcrystalline cellulose	66.72	30	A
2	Kaolin	54.14	30	B
3	Bentonite	48.73	30	C
4	Light Magnesium carbonate	46.24	30	D

TABLE 6: MEAN CUMULATIVE PERCENT RELEASE OF *C. GLABRIFLORUM* FROM THE DIFFERENT ABSORBENTS RANKED BY DUNCAN'S MULTIPLE RANGE TESTS

Rank order	Absorbent	Mean release (%)	n	Ranked
1	Bentonite	76.49	30	A
2	Microcrystalline cellulose	35.61	30	B
3	Light Magnesium carbonate	31.56	30	C
4	Kaolin	27.89	30	D

$LSD_{0.05} = 2.69$

For *B. ferruginea*, microcrystalline cellulose produced the best release effects. The 7.60 g/15.5 g absorbent-extract system [i.e. 76mg of microcrystalline cellulose per dose of *B. ferruginea* extract (155.2 ± 2.0 mg)], had the best properties in terms of ease of processing (percentage loss, 2.03 ± 0.02 %) [8] and good flow, and recorded a release of 75.3 ± 0.7 % of extract after 45 minutes. With *C. glabriflorum* extract, bentonite was the most suitable absorbent.

An optimum weight of 5.86 g of bentonite per 20.74 g of extract [i.e. 48 mg of bentonite per dose of *C. glabriflorum* extract (170 ± 2.0 mg)], made processing easier (percentage loss, 2.42 ± 0.03 %)[8], had good flow properties and gave the best release of extract (99.4 ± 0.2 %) after 45 minutes. The results therefore, indicated that microcrystalline cellulose and bentonite were the most suitable among the absorbents used, for formulating *B. ferruginea* and *C. glabriflorum* extracts, respectively, into solid dosage forms.

CONCLUSION: The study demonstrated that absorbed plant extracts present different release profiles dependent on the source of the extract and the type of absorbent used, and that an optimum amount of an effective absorbent is required to make the extract readily available after oral administration. 76 mg of microcrystalline cellulose per dose of extract (155.2 ± 2.0 mg) had the best release profile for *B. ferruginea*, whilst, 48 mg of bentonite per dose of extract (170 ± 2.0 mg) was the most appropriate for *C. glabriflorum*.

ACKNOWLEDGEMENT: The authors wish to thank the technical staff of CSRPM, Mampong-Akwapim, Ghana, for their support and supply of the plant materials.

REFERENCES:

1. Ghana Herbal Pharmacopoeia. Advent press, Ghana, First Edition 1992.

2. Meri Kay VVS and Popovich NG: Diabetes Supplement. *US Pharmacist*. Nov. 1994.

3. Martins EW: Remington's Pharmaceutical Sciences. Mack Publishing Co. Easton, Thirteenth Edition 1965.

4. Ansel HC and Popovich NC: Pharmaceutical dosage forms and Drug delivery systems. William and Wilkins, Sixth Edition 1995.

5. Johnson R: Formulation of Camber and Bredina liquid extracts into solid dosage form. M. Pharm. Dissertation, Department of Pharmaceutics, KNUST, Ghana, March 2006.

6. Proudfoot SG: Introduction to Biopharmaceutics. Pharmaceutics-The science of dosage form design, Churchill Livingstone, Edinburgh, 1998: 174-177.

7. British Pharmacopoeia. Version 11.0. Appendix XII D. System Simulation Ltd, 2007.

8. United States Pharmacopoeia 30/National Formulary 25. Convention Inc, 2007: p. 277.