

Design, Formulation, and Evaluation of Senna Effervescent Tablets

Ali M. El-hassan¹; Shayoub M E²; Abdalkreem M. abdalkreem³; Osman H M⁴ and Kamal Khalifa^{5*}

¹Omdurman Islamic University, ² Department of Pharmaceutics, Faculty of Pharmacy, University of Khartoum.

³Department of Pharmaceutics, Faculty of Pharmacy, University of Omdurman Islamic

⁴ Department of Biochemistry, Faculty of Pharmacy, University of National Ribat.

⁵ College of Applied & Industrial Sciences, University of Bahari.

(Received October 15, 2012. Accepted November 3, 2012)

Abstract— Cassia leaves and pods extracts has been used in traditional or herbal medicine since ancient times. The pods and leaves contain anthraquinone glycosides that have a significant laxative effect. In this study anthraquinone was extracted from *Senna* (*Cassia acutifolia* Delile) pods and the active constituents were checked to confirm the presence of both Anthraquinone compounds (sennosides A and B). Effervescent tablets were formulated using the senna extract as the active ingredient in addition to other tableting constituents. The formulated tablets were then subjected to the known official monographs requirements like: resistance to crushing (hardness test), weight variation, disintegration time/ effervescent time, friability test, content uniformity test and pH. The results obtained were: 7.4 kg / cm², 10%, 59.01 s, 0.74 %, 97.30 %) and 5.4 for resistance to crushing, weight variation, disintegration time, friability test, content uniformity test and pH respectively. The values obtained indicate the effervescent comply with the pharmaceutical standards set by British Pharmacopoeia (BP) and United States Pharmacopoeia (USP). These tablets can be used as an alternative source of laxative medicine in Sudan due to the abundance of *Cassia acutifolia* as a wild plant.

Index Terms— Senna, (*Cassia acutifolia*) Extract, Anthraquinones, Effervescent Tablets.

I. INTRODUCTION

According to the World Health Organization [1] traditional medicine or herbal medicine is the accumulation of the knowledge, skills, and practices based on the theories, beliefs, and indigenized by different cultures, to maintain health. Herbal medicines include herbs, herbal materials, herbal preparations and finished herbal products, which contain as an active ingredients parts of plants, or other plant materials, or combinations.

Herbal treatments are the most popular form of traditional medicine, and are highly lucrative in the international marketplace. Annual revenues of traditional medicine were US\$ 1.47 billion in Japan, US\$ 4.7 billion in China, and US\$ 7.4 million in Korea for 2008, 2009 and 2010, respectively [2].

Cassia acutifolia Delile., also known as *Alexandrian senna*, that belongs to a large genus of around 250 species of flowering plants in the family Fabaceae, subfamily Caesalpinioideae. Senna fruits contain about 2.5 to 4.5 % of sennosides A and B (not less than 2.2%) in *Alexandrian senna* [3] and from 1.2 to 2.5% in the *Tinnevely*. The pods are superior to leaves, as they contain more percentage of glycoside present in the pericarp of pods [4] while the seeds contain very little quantity of sennoside. The active constituents of senna are sennosides A, B, C, D, and free anthraquinones (aloe-emodin, chrysophanol, rhein) with sennosides A and B present in the greatest concentration [5].



Picture (1): *Senna alexandrian*

*Corresponding author: K. K. Taha : kamalth1012@yahoo.com

Sule *et al.* [6] reported the presence of anthraquinones in the bark of *Senna alata* Linn. crude stem bark extract. Ayo [7] reported the presence of sennosides in *Cassia nigricans* which is used by Nigerian herbal healer for treatment of gastrointestinal disorders.

Senna leave and pods have been shown to have laxative activity and anti-fungal activity [6]. It is useful in habitual constipation due to its laxative effects. Pharmacological investigations show that sennoside A and B account for the entire activity of the senna leave and pods. Sennosides A and B were used as laxative formulation [8] replacing the previously used carcinogenic phenolphthalein [9]. The glycosides are pro-drugs that are neither absorbed nor cleaved in upper gastrointestinal tract. They are degraded in the colon by bacterial enzymes to rheinanthrone, the laxative metabolite of which 90 % is bound to the feces in the colon and excreted as a polymer. It has been reported that the anthraquinone glycosides are capable to exert their laxative effect by small dose as they are not likely to enter the systemic circulation [10, 11]. Sultana *et al.* [12] reported the use of *Cassia angustifolia* as laxative drug against constipation in Indo-Pak subcontinent. In Thai medicine ripe cassia pods were used as laxative drug by boiling it with water and filtration through muslin cloth. The filtrate was made in small pills after evaporation [13]. Effervescent tablets liberate carbon dioxide when added to water thus facilitates tablets disintegration and dissolution [14]. In Sudan cassia leaves and pods decoction is used for the treatment of many problems of stomach disorder, but the quantity to be taken is unspecified due to the lack of the knowledge of the effective ingredients. The aims of the present study were to obtain the extract of the pods of *Cassia acutifolia* Delile and verify the presence of sennosides A and B and formulate an effective, non – expensive and stable preparation of senna pods extract then optimize it using different tablet additives for oral administration as effervescent tablets. The tablets will be subjected to the known official monographs of Pharmacopoeia to verify their compliance with the standards.

II. MATERIALS AND METHODS

Mature dry pods were collected from wild plants from Omdurman in November 2010. The pods were sorted, washed and dried in oven at 105 °C then kept in black polythene bags. The anthraquinone glycosides were extracted from the pod decoction and identified following the method reported by Aurapa and Wandee [15]. The anthraquinones were identified using the modified Borntrager's test where 200 mg pod powder was boiled in 5 ml 10% HCl and filtered. The filtrate was extracted with 5 ml benzene. The benzene layer was

separated and shaken with 5 ml 10% NH₄OH. A rose pink or cherry red colour solution that absorbed at $\lambda_{\text{max}} = 530 \text{ nm}$ was formed indicating the presence of anthraquinone derivatives [16].

The effervescent tablet of 600 mg was prepared as follows: The senna pods extract (active ingredient) 7.50 mg, polyvinyl pyrrolidone (PVP) binder 24.00 mg, Talc powder 7.50 mg, magnesium stearate 3.75 mg, saccharin 73.50 mg, polyethylene glycols (PEG) 12.00 mg, citric acid 79.33 mg, tartaric acid 158.66 mg and sodium bicarbonate 269.71 mg. The extract was dried in oven at 60 °C to constant weight and triturated in a mortar and pestle to make powder then mixed with calculated amount of the other components. The binder was added and formed into a paste and granulated using mesh 10. The granules were oven dried at 50 °C for one hour and resized using mesh 14. The granules were transferred to the hopper of a single punch tabletting machine (Erweka – Germany). The physical tests that included crushing (hardness test), weight variation, disintegration time/effervescent time, friability test, content uniformity test and pH were carried out to confirm their conformity with monographs of BP and USP requirements. Resistance to crushing was determined by taking 10 tablets from the formulation using a Pfizer hardness tester (Electrolab Pvt. Ltd., India). The average weight was determined by randomly picking 20 tablets and recording the weight of each tablet using a sensitive balance. Friability of the tablet determined using Roche friabilator. In this experiments the tablets are subjected to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at 6 inches height in each revolution. The pre-weighed sample of tablets were placed in the friabilator and subjected to the 100 revolutions. Tablets were then dusted using a soft muslin cloth and re-weighed. The friability (F) is given by the formula.

$$F = \frac{W_i - W_f}{W_i} \times 100$$

* where W_i and W_f stand for initial and final weights respectively.

The disintegration or effervescent time was determined by randomly taking three tablets. One tablet was individually placed in a beaker containing about 150 ml of tap water at 15-20 °C and the time of complete dissolution indicated by the cease of gas bubble for each tablet was recorded with the aid of stop watch. The pH of the solution was measured each time. Content uniformity test was carried out by taking one tablet of sennoside equivalent to 7.5mg

and dissolve in water. Then the mixture was diluted to 100ml with ether from which 10 ml were taken into a petri dish and evaporated to dryness. The dried residue was dissolved in 10 ml of 1.0 M KOH and the absorbance was immediately measured at 530 nm using 1.0 M KOH as a blank. A calibration curve using standard sennoside in 1.0 M KOH was constructed. The amount of sennoside in the tablet was determined and percent content was calculated

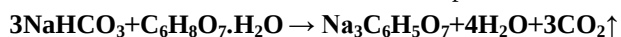


Picture (2): Effervescent Tablets

III. RESULTS AND DISCUSSION

Due to the high solubility of anthaquinone glycosides in water, decoction was employed as a reliable method for extraction [17]. The extract of senna pods decoction was

found to contain anthaquinone derivatives that has been identified phytochemically using the modified Borntrager's test and ultraviolet spectroscopy [15]. It has been reported that cassia species are rich in anthaquinone derivatives [18]. Due to its laxative effect [19] the extract was the active ingredient in the prepared tablets. The anthaquinones exert their laxative effects either by altering colonic motility leading to an accelerated large intestinal transit [20] or alteration in absorption or secretion of the colon causing diarrhea due to fluid accumulation [21]. In the tablets the quantity of anthaquinone derivatives sennoside A and B was small i.e. only 7.50 mg. It has been reported that sennoside A and B are not likely to enter the systemic circulation, hence they function at a low dose [10, 11]. The effervescent tablets are formed by adding an acid to a base to liberate carbon dioxide thus make the tablet content highly soluble. The reaction of sodium bicarbonate with tartaric acid is an example.



In this study the effervescent tablets were formulated using the granulation method which is superior to direct compression method as granulation reduces capping and protect the acid and base from environmental moisture [22]. The official monographs requirements were carried out to check the compliance of these tablets with the standards set by BP and USP.

Table (1)

The resistance to crushing (hardness) test for the tablets

Tablet No.	1	2	3	4	5	6	7	8	9	10	Mean
Force / kg	8.66	4.20	9.49	6.82	6.69	7.33	9.24	6.12	8.79	7.14	7.54

The resistance to crushing or hardness test is the measure of the ability of a tablet to withstand mechanical effect during storage and handling. It is an indication for its dissolution or disintegration rate i.e. the harder the tablet the longer is its dissolution time. The hardness can be varied by changing the binder ratio. According to BP the mean reading should fall in a

range equivalent to 4 – 8 kg/ cm² [23]. The 7.54 kg / cm² value obtained by this study (table (1)) is within this range.

According to BP and USP [22, 23] no tablet has a deviation of 10 % of the average and there should be no more than two tablets deviation by 5 % (30 mg). From table (2) it is clear that none of the weight loss that no deviation of 10 % (600 ± 60) and none has 5 % (±30 mg) deviation.

Table (2)

The weight variation test for the tablets

Tab	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Wt.	600	610	560	590	600	590	600	560	580	600	620	600	580	590	610	590	600	590	620	580

The average weight is 590 mg

Table (3)

Friability test for the tablets

Item	Value
Wt. of 20 tablets before the test	12.03 g
Wt. of 20 tablets after the test	11.94 g
Wt. loss for tablets	00.09 g
% Wt. loss for 20 tablets of the test	0.74 %

The total weight loss should not exceed 1 % and no tablet should exhibit any type of break or crack [24, 25]. The weight loss indicated is 0.74 % which is less than 1.0 % indicating the compliance of the sample with test.

Table (4)

Disintegration time and pH test for the tablets

Tab. No.	Dis. Time (s)	pH
1	59.30	5.3
2	58.31	5.5
3	59.43	5.4
Mean	59.01	5.4

The disintegration time for the tablets is 59.01 s making the formulation appropriate for use. A value of 62 s was reported by Srinath *et al.*[22] for effervescent paracetamol tablets compare to 55 s for marketed tablets in India.

Table (5)

Content uniformity test for the tablets

Item	Value
Wt. equivalent for 600 mg	7.50 mg
Experimentally obtained Wt.	7.30 mg
Content percent	97.30 %

The content uniformity test is a measure of the homogeneity of the tablet. Faure *et al.*[26] reported that wet granulation of tableting provides better uniformity of content especially at low drug concentration. In this study the value was found to be

97.30 %. This value lies within the range of 95 – 105 % set by [27] and similar results for the effervescent senna tablet was obtained by HPLC [28].

IV. CONCLUSIONS

- 1.The extract of cassia was found to contain sennosides A and B which are the active ingredients of a laxative drug. Effervescent tablets were formulated from the senna extract and optimized using different tablet additives for a convenient oral administration tablets.

- 2.The formulated tablets were subjected to the known official monographs requirements and were found to comply with the standards of the BP and USP. These tablets which were prepared from local plant that grows wild in Sudan can be used as a laxative drug with low price and short disintegration time.
- 3.The use of local binders like gum [29] which are also available, may even lower the cost, hence different

types of local binders can be used and analyzed to see their suitability.

REFERENCES

1. **World Health Organization (2000).** *General Guidelines for methodologies on research and Evaluation of traditional medicine* (document WHO/EDM/TRM/2000.1). Geneva.
2. **WHO 2011-2010.** Regional progress in traditional medicine.
3. **Anubha U., Yogendra C., Preeti S. N. and Noor A. K. (2011).** Sennoside contents in Senna (*Cassia angustifolia* Vahl.) as influenced by date of leaf picking, packaging material and storage period. *Journal of Stored Products and Postharvest Research* Vol. 2(5); pp. 97 – 103.
4. **Fairbairn J W. and Sheres AB. (1967).** The distribution of glycosides in *cassia senna* L. *Phytochemistry*, **6**; pp. 1303 – 1207.
5. **Tyler, V.E. Brady, L.R. Robbers J.E., (1988).** *Pharmacognosy*, 9th ed., Lea and Febiger, Philadelphia, PA, USA, , p. 65.
6. **Sule W. F., Okonko I. O., Omo-Ogun S., Nwanze J. C., Ojezele M. O., Ojezele O. J., Alli J. A., Soyemi E. T. and Olaonipekun T. O. (2011).** Phytochemical properties and *in-vitro* antifungal activity of *Senna alata* Linn. crude stem bark extract. *Journal of Medicinal Plants Research* , **5**(2); pp. 176-183.
7. **Ayo, R. G. (2010).** Phytochemical constituents and bioactivities of the extracts of *Cassia nigricans* Vahl: A review, *Journal of Medicinal Plants Research*, **4**(14), pp. 1339-1348.
8. **Verloop, Q. Leibenberg, W. Marais, A. F. Lötter, A. P. and de Villiers, M. M. (2004).** Compounded laxative formulations for substituting phenolphthalein with sennosides A and B in solid dosage form. *Trop J pharm Res*, **3**(1); pp. 265 – 277.
9. **Collins B. J., Grizzle T.B. and Dunnick J.K. (2000).** Toxicokinetics of phenolphthalein in male and female rats and mice. *Toxicol Sci*. **56** ; pp. 271 – 281.
10. **Moreau P., Moreau S. and Skinner S. (1985).** Comparative disposition of some anthraquinone glycosides and aglycones. *Biopharmaceutics and Drug Disposition*, **6**; pp. 325 – 334.
11. **DeWitte P. and Lemli L. (1990).** The metabolism of anthranoid laxatives. *Hepatogastroenterology*, **37**; 601 – 605).
12. **Shazia Sultana, Mushtaq Ahmad, Muhammad Zafar, Mir Ajab Khan and Muhammad Arshad.(2012).** Authentication of herbal drug Senna (*Cassia angustifolia* Vahl.): A village pharmacy for Indo-Pak Subcontinent, *African Journal of Pharmacy and Pharmacology*. **6**(30), pp. 2299-2308.
13. **Pongbunrod S. (1949).** *Mai Tet. Meuang Thai Kasembannakit*, Bangkok; pp. 137 – 139.
14. **Haac D., Gergely I. and Metz C. (2012).** The TOPO granulation technology used in manufacture of effervescent tablets. *TechnoPharm*, **2** (3); pp. 186 - 191.
15. **Aurapa S. and Wandee G. (2009).** Determination of anthraquinone glycosides in *Cassia fistula* leave extract for alternative source of laxative drug. *International J. of Biomedical and Pharmaceutical Sci.*, **3** (1); pp. 42 – 45.
16. **Evans W.C. (1996).** Trease and Evans Pharmacognosy, 14th Edition, Bailliere Tindall W.B. Saunders company ltd; London, pp 542 – 575.
17. **Sakulpanich A. and Gritsanapan W. (2008).** Extraction method for high content of anthraquinone from *cassia fistula* pods. *Thai Journal of Health Research*, **22**; pp. 167 – 172.
18. **Georges, K. Jayaprakasam, B. Dalavoy, S.S. Nair, M.G. (2008).** Pest-managing activities of plant extracts and anthraquinones from *Cassia nigricans* from Burkina Faso. *Bioresour. Technol.* **99**(6): 2037-2045.
19. **Bruneton, J. (1995).** *Pharmacognosy, phytochemistry, medicinal plants*, Lavoisier Publishing, Paris, pp. 349 – 354.
20. **Shi L., Xu L., Hou S., Lin S., Yang H. and Ma T. (2006).** Activation effect of cathartic natural compound rhein to CFTR chloride channel. *Chemical Research in Chinese University*, **22**; pp. 312 – 314.
21. **Van Gorkom B. A. de Vries E. C. Karrebeld A. and Kleibenker J. H. (1999).** Anthranoid laxatives and potential carcinogenic effects. *Alimentary Pharmacology and Therapeutics*, **13**; pp. 443 – 452
22. **K. R. Srinath, C. P. Chowdary, P. Palanisamy, A. Kishma, S. aparna, S. S. ali, P. Rakesh and K. Swetha (2011).** Formulation and evaluation of effervescent tablets of paracetamol. *IJPRD*, **3** (3); pp. 76 – 104.
23. **British pharmacopoeia (BP) 1998 - 2002-2004**
24. **British Pharmacopoei (BP), (2001).** Vol. II, Her Majesty's Stationary Office, London.
25. **US Pharmacopoeia National Formulary (1995).** USP 23/NF 18, United States Pharmacopoeial Convention. Inc., Rockville, MD.
26. **Faure A., York P. and Rowe RC. (2001).** Process control and scale up of pharmaceutical wet granulation process: A review *Euro. J. Pharmaceut. Biopharm.*, **52** (3); pp. 269 – 277.
27. **USP (1980).** 20th rev. Mac. Easton, p. 900.
28. **Sun, S.-W. 882 Su H.-T. (2002).** Validated HPLC method for determination of sennosides A and B in senna tablets *J. Pharm. Biomed. Anal.* **29**; pp 881–894.
29. **Taha, K. K, Elmahi, R. H. Hassan, E. A. Ahmed S. E. and shyoub, M. H. (2012).** Analytical study on three types of gum from Sudan. *Journal of Forest Products & Industries*, **1** (1); pp. 11 – 16.