Pharmaceutical Sciences, 2022, 28(4), 638-642
doi:10.34172/PS.2021.80
https://ps.tbzmed.ac.ir/

Short Communication

Review and Comparison of Acceptance Criteria for Senna and Its Preparations According to BP (2015 and 2020) and USP-NF (39-34 and 43-38)

Laleh Khodaie[1,2*], Saurabh Bhatia[3,4], Ahmed Al-Harrasi[3]

[1]*Department of Traditional Pharmacy, Faculty of Traditional Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.*
[2]*Department of Pharmacognosy, Faculty of Pharmacy,Tabriz University of Medical Sciences, Tabriz, Iran.*
[3]*Natural and Medical Sciences Research Center, University of Nizwa, Nizwa, Sultanate of Oman.*
[4]*School of Health Science, University of Petroleum and Energy Studies, Uttarakhand, 248007, India.*

Article Info

Article History:
Received: 27 October 2021
Accepted: 19 December 2021
ePublished: 27 December 2021

Keywords:
-*Cassia acutifolia*
-*Cassia angustifolia*
-Quality control
-Pharmacopoeia
-Senna
-Standardization

Background: Quality and quantity assurance of herbs are global concerns. This study aimed to classify and compare the monographs and test procedures of Senna parts and preparations according to two editions of BP and USP-NF. The monographs and specifications were compared to suggest a practical approach to extract relevant data.

Methods: BP 2015 and 2020, USP-NF 39-34 and 43-38, and scientific databases were used for literature review.

Results: In both editions of USP-NF, determination of heavy metals was solely included for the powder and tablet of sennosides. In both editions of BP, assessment of microbial contamination was merely included in the monograph of dry extract of Senna, not for the rest of the monographs. Comparing two editions of BP indicated that in BP 2020, LC and HPTLC methods were added to assure the quality of pods and leaflets of Senna species.

Conclusion: Preparation of tabular data will assist analysts in extracting desired information and guidelines to prepare licensed herbal products. This approach could be applicable to select relevant tests according to the facilities and equipment of laboratories.

Introduction

Herbs and herbal products are the oldest healthcare agents known to human beings.[1] In this day and age, they could successfully preserve their position in the healthcare system. A high proportion of the population relies on herbs, herbal products, and phytomedicines, especially in developing countries.[2] Despite the widespread and global usage of herbal products and ethnobotanicals, in some cases, the level of their verification, safety, and efficacy has not been addressed sufficiently.[3,4] Regarding these concerns, several requirements, guidelines, and test procedures should be fulfilled to vouch for their verification, safety, and efficiency. These requirements are described as quality and quantity assurance guidelines.[5] These guidelines guarantee the degree of excellence of botanicals and phytopharmaceuticals. Quality control incorporates sensory and analytical inspection of botanicals to identify genuine products and prevent adulteration. Quantity affirmation is defined as quantifying typical phytochemicals responsible for the pharmacological effects of herbs and their products.[4] Even though quality and quantity control of herbs are not equally addressed as chemical and conventional drugs, recently, that of herbal pharmaceuticals are in the growing demand to prevent consequences. Reported side effects of herbs, morbidity, and mortality could be addressed by undertaking standard and accepted test procedures. These approaches could efficiently prevent herbs' hazardous effects, such as their toxicity and carcinogenicity.[2,6] There are some frequently used herbs that physicians and healthcare practitioners widely prescribe. Among these herbs, diverse species of Senna (Fabaceae) and related products are highly utilized to treat constipation in communities.[7] Moreover, they are used for bowel clearance before medical examinations such as colonoscopy.[8] Due to Senna's efficiency, availability, low cost, and toxicity, it is sold for treating constipation even without being prescribed by a physician.[9] It is used for self-medication in various forms of either crude or registered herbal preparations.[10] It has two important species used in commerce, with scientific names of *Cassia acutifolia* Delile. (*Cassia senna* L.) or Alexandrian or Khartoum Senna, wildly grown in Egypt and the Middle East, and *Cassia angustifolia* Vahl, known as Tinnevelly Senna, native to India.[9] Their pods and leaves are pharmacologically active due to containing anthraquinones or anthracene glycosides, known as sennosides A, B, C, and D. They are

*Corresponding Author: Laleh Khodaie, Email: khodaiel@gmail.com

active phytochemicals of herbs that act as pro-drugs to trigger stimulation of intestinal smooth muscles. Being metabolized in the colon by bacterial glycosides, they influence fluid secretion and induction of defecation.[11] Being an officially known herb, monographs of Senna and its products were included in globally known pharmacopeias, BP, and USP-NF backed by years of experimentation and observations.[12-15] British Pharmacopeia, generally known as BP, is the national pharmacopeia of the United Kingdom. As a public and freely available tool, it incorporates roughly 4000 monographs of medicinal standards, which contain guidelines to analyze pharmaceuticals, dosage forms, herbal products, and excipients. Monographs undergo inclusions, omissions, or updates to safeguard the health of individuals. BP consists of 6 volumes; particularly, volume IV is allocated to herbs, herbal products, and homeopathic preparations.[16] The United States Pharmacopeia (USP) and the National Formulary (NF) forms the USP-NF. Similar to BP, it incorporates standards of therapeutics and excipients. It is enforceable for the manufacturing and marketing of medicines in the United States, as an official document. The monographs of USP-NF get regular revisions and updates to ensure the safety of the individuals. USP-NF includes five volumes.[17] Monographs of BP and USP-NF include specifications and several test procedures to affirm the quality and quantity of herbal products and phytopharmaceuticals such as senna leaves, pods, and related products.[9] According to BP and USP-NF, quantity assurance of this herb could be undertaken by analytical methods, especially spectroscopic and chromatographic procedures.[3] Quality assurance of Senna, both as raw material and phytopharmaceutical, could be carried out by macroscopic, microscopic examinations, chromatographic methods, and several physical, phytochemical and chemical tests.[12-15] Besides the mentioned tests, other criteria could affect the quality of Senna, including time and area of growth, and manufacturing procedures.[18] Although pharmacopeial procedures and requirements are useful and comprehensive; an analyst could be confused to select the most suitable guidelines among the offered ones. Far too little attention has been paid to classifying and categorizing herbal monographs and their test procedures. Classification of BP and USP-NF guidelines could be practical for analysts, typically for the manufacturers, scholars, and students willing to apply those methods in the lab. Therefore, the first purpose of this paper was to provide an informative overview, comparative and classified data on quality and quantity assurance of Senna based on conventional methods introduced in two editions of global pharmacopeias, BP and USP-NF. The second objective was to unravel the inclusions of guidelines in revised versions of BP and USP-NF relevant to Senna pods, leaflets, and preparations.

Methods

This manuscript was authored in 2021 via reviewing pharmacopeias BP (2015 and 2020) and USP-NF (39-34 and 43-38), and using scientific databases including PubMed, Web of Science, and Scopus. Herbal monographs of BP and USP-NF contain qualitative and quantitative measures of herbs and herbal preparations. Generally, each monograph contains seven parts covering title and definition, identification, tests for contaminants/impurities, physicochemical tests, some other specific tests, and packaging, labeling, and storage. In this study, data were extracted regarding quality and quantity control of 2 species of Senna as a raw material powder and herbal preparations. Some keywords were used to review the literature in databases published from 2000 to 2021. They were as follows: quality assurance, standardization, quality control, Senna, Cassia, pharmacopeia, phytochemical marker, herb, and medicinal plant.

Results and Discussion

BP (2015 and 2020) and USP-NF (39-34 and 43-38) were used to prepare the tables. The results were classified into three tables; Table S1 (supplemetary data) presented specifications and requirements of herbal monographs in mentioned pharmacopeias. However, it is unlikely to find all the mentioned requirements in monographs of herbs and herbal products. Thus, the type and number of requirements of monographs differ in each pharmacopeia.

Table S2 (supplemetary data) indicated requirements of monographs, including the parts and products of Senna, related identification tests (macroscopic and microscopic examinations, TLC, chromogenic tests, LC and HPTLC), quantitative analysis, and phytochemical biomarkers. Table S3 (supplemetary data) illustrated further licensing requirements (physical and chemical tests) in both editions of BP and USP-NF, including foreign substance determination, loss on drying, and determination of ash, and insoluble ash in hydrochloric acid for quantity assurance. Also, contamination tests were included in Table S3 for raw materials, products, and phytopharmaceuticals.

Comparison of monographs and specifications in two editions of BP and USP-NF

Regarding Senna parts and products in BP and USP-NF, both manuscripts contain monographs for leaves and pods of Senna. In BP, monographs of Senna tablets, granules, and dry extract were included when it comes to the Senna preparations, while USP covered monographs of Senna oral solution, sennosides tablets, and powder. As far as differences in monograph specifications in BP and USP-NF are concerned, only sennosides powder and tablets were required to be analyzed for heavy metals. Hence, in USP-NF, assessment of microbial contamination was included for leaves and pods of Senna, while in BP, only dry extract of Senna had to be assessed for microbial contamination. Contrary to expectations, both versions of BP did not contain any test procedure to measure microbial contamination of Senna pods and leaves.

Identification and quality assurance by sensory approach and physicochemical tests

As an OTC medicine, leaves and pods of Senna and their preparations were already included in BP and USP-NF. Macroscopic and microscopic examinations and powder characteristics of Senna parts are essential to authenticate the herb and prevent adulteration. Evaluation of physicochemical properties of Senna is of utmost importance, which was discussed in both BP and USP-NF;[12-15] firstly, the percentage of foreign matter should be measured to assure the absence of unwanted material. Mainly, it was merely reported for pods and leaves of *Cassia* species. Senna preparations were exempted for mentioned tests in both editions of BP and USP-NF. The foreign matter was mainly Senna stems or other organs and elements. Secondly, for measuring volatile substances and moisture of herbs, a loss on drying test ought to be carried out. This test is necessary since moisture could catalyze both hydrolyses of phytochemicals, bacterial and fungal contamination.[19] Thirdly, total ash, as a diagnostic test, should be evaluated to depict plant-derived (organic compounds) and non-plant-derived ash (inorganic compounds). It is substantial to determine the purity of powdered herbal parts. Fourthly, acid insoluble ash indicates siliceous contamination coming from the soil.[20] Besides the mentioned four physicochemical tests, additional tests are required to evaluate Senna liquid extract, tablets, oral solution, sennosides powder, and tablets, which were presented in Tables S2 and S3.

Identification and quality assurance by chromatography methods and chromogenic tests

As shown in Table S2, authentication, in crude terms, fingerprint profiling of Senna parts and products could be analyzed quickly and accurately by TLC (Figure 1). Marker standards (sennosides A, B, C, D, rein8-glucoside, Senna extract CRS) could carry out TLC of Senna parts and preparations in BP and USP-NF. If the zones of the chromatogram were similar in terms of position, size, and color, qualitative and semi-quantitative assessments of products could be undertaken.[21] As far as the chromogenic test concerned, two procedures and reagents were introduced in BP and USP-NF. The mentioned procedures could be found in more detail in the mentioned

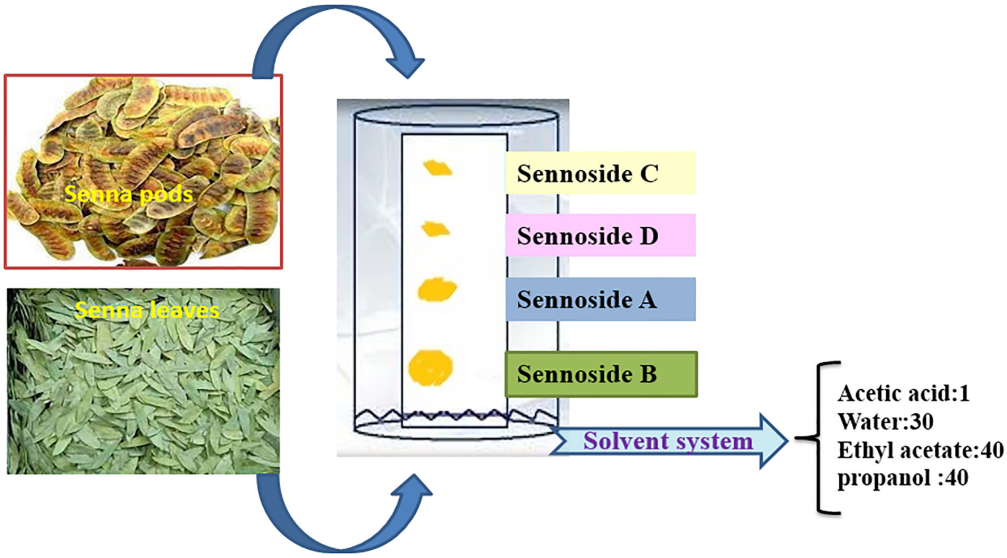

Figure 1. TLC profile of Senna extract. Sennosides appear on TLC plate according to their retention factors.

pharmacopeias.[12-15] In BP 2020, HPTLC was included as an additional approach to assure the quality of Senna pods and leaves. This method is applied using plates and a lower amount of solvents to detect contaminations with higher sensitivity and reproducibility than classic TLC. LC is also included for quality assurance of Senna and its products. LC is one of the efficient, accurate, and precise methods to determine both the quality and quantity of Senna and its preparations.[22] Regarding quality assurance, detection of main phytochemicals could be carried out by this method (Figure 2).

Measurement of bioactive compounds

In Table S2, quantitative measurements of senna parts and products were categorized. That could be undertaken by measurement of the minimum required amount of biomarkers. According to BP and USP-NF, quantity control could be carried out by LC, HPLC, UV, and fluorescence spectroscopy. By HPLC documentation of chromatograms, a retention time of peak, as well as UV-Vis absorption spectra could be available.[16] For analysis by HPLC, a column based on end-capped octadecylsilyl silica gel (5µ) as well as an isocratic elusion by mobile phase of acetonitrile (17 volumes) and 1% v/v glacial acetic acid could be used for detecting sennosides, typically sennoside B. Sample and standard solutions could be prepared according to the procedures explained in BP 2015.[12] This guideline elaborates how to measure the percentage of

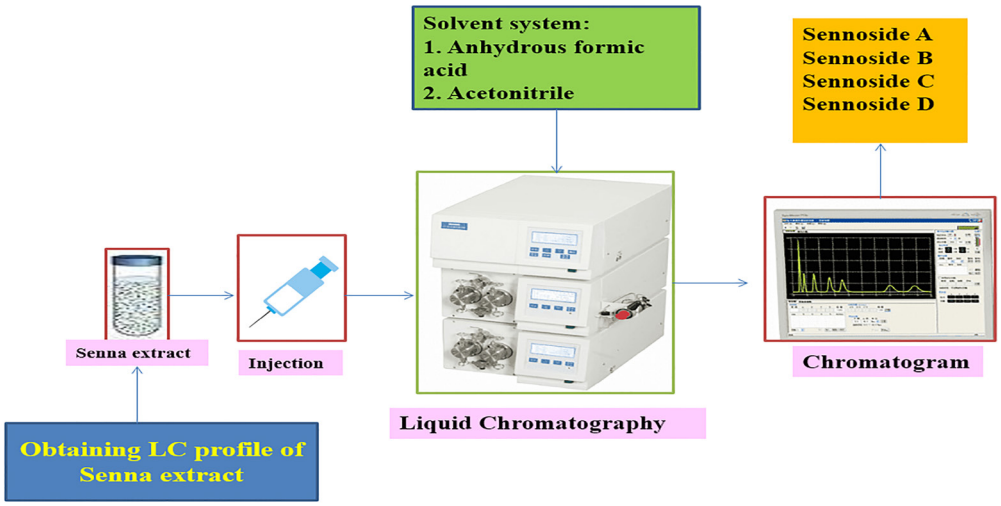

Figure 2. LC profile of Senna extract.

sennoside B in a sample solution. According to two editions of USP-NF, fluorescence spectroscopy could be utilized to measure phytochemical biomarkers in sennoside powder and sennoside tablets.[14] In previous editions of BP and USP-NF, assays using UV-Visible spectroscopy were the dominant approach of biomarker analysis in pods and leaves of Senna and dry extract of leaves. However, in the revised edition of BP, the LC method was also included to measure total anthraquinones (aloe-emodin and rhein) in pods and leaflets of senna. This measurement was based on rhein, with an amount of a maximum 7%. Moreover, in BP 2020, a minimum amount of anthraquinone glycosides based on sennosides B was determined 2% instead of 3.4%.[13]

Conclusion

The evolution of the global pharmacopeias of BP and USP-NF, as legal standards, goes through rigid screens of governing body policy. These widely acceptable resources include monographs of enormously utilized herbal parts and preparations. Postgraduate students of pharmacy and pharmacognosy, scholars, pharmaceutical companies, and manufacturers who opt for quality and quantity assurance of herbs and their preparations could refer to mentioned resources, find the relevant monographs, and categorize the requirements according to Tables S2 and S3. Tabular data concisely presents required guidelines for licensing process of herbs. They assist in efficiently extracting desired information and procedures. Also, they offer an opportunity to select relevant tests according to the facilities and equipment of laboratories. Tabular data could also assist analysts in defining appropriate and validated procedures to assure acceptable quality and quantity of herbal products.

Acknowledgments

This study was supported by a grant (grant No: 65879) from Tabriz University of Medical Sciences.

Author Contributions

LK: Conception, design, acquisition of data from BP and USP, and drafting introduction, methods, and results. SB: classification and categorizing data in tabular form and checking plagiarism. AA: drafting the discussion and conclusion parts. All authors read and approved the final manuscript.

Conflict of Interest

The authors report no conflicts of interest.

Supplementary Data

Supporting data (Tables S1-S3) is available on the journal's website along with the published article.

References

1. Wińska K, Mączka W, Łyczko J. Essential oils as antimicrobial agents-myth or real alternative? Molecules. 2019;24(11): 2130. doi:10.3390/24112130
2. Leonti M, Verpoorte R. Traditional Mediterranean and European herbal medicines. J Ethnopharmacol. 2017;199:161-7. doi:10.1016/j.jep.2017.01.052
3. Ip SP, Zhao M, Xian Y, Chen M, Zong Y, Tjong YW, et al. Quality assurance for Chinese herbal formulae: standardization of IBS-20, a 20-herb preparation. Chin Med. 2010;5:8. doi:10.1186/1749-8546-5-8
4. Liu SH, Chuang WC, Lam W, Jiang Z, Cheng YC. Safety surveillance of traditional Chinese medicine: current and future. Drug Saf. 2015;38(2):117-28. doi:10.1007/s40264-014-0250-z
5. Haleem RM, Salem MY, Fatahallah FA, Abdelfattah LE. Quality in the pharmaceutical industry - A literature review. Saudi Pharm J. 2015;23(5):463-9. doi:10.1016/j.jsps.2013.11.004
6. Brown AC. Kidney toxicity related to herbs and dietary supplements: Online table of case reports. Part 3 of 5 series. Food Chem Toxicol. 2017;107(PtA):502-19. doi:10.1016/j.fct.2016.07.024

7. Budzynska K, Gardner ZE, Dugoua JJ, Low Dog T, Gardiner P. Systematic review of breastfeeding and herbs. Breastfeed Med. 2012;**7**(6):489-503. doi:10.1089/bfm.2011.0122
8. Kesavelu D, Sr. The efficacy and safety of combined senna and probiotic-based bowel preparation for colonoscopy in children. Cureus. 2020;12(9):e10180. doi:10.7759/cureus.10180.
9. Cirillo C, Capasso R. Constipation and botanical medicines: An overview. Phytother Res. 2015;29(10):1488-93. doi:10.1002/ptr.5410
10. Vitalone A, Di Giacomo S, Di Sotto A, Franchitto A, Mammola CL, Mariani P, et al. *Cassia angustifolia* extract is not hepatotoxic in an in vitro and in vivo study. Pharmacology. 2011;88(5-6):252-9. doi:10.1159/000331858
11. Waltenberger B, Avula B, Ganzera M, Khan IA, Stuppner H, Khan SI. Transport of sennosides and sennidines from *Cassia angustifolia* and Cassia senna across Caco-2 monolayers--an in vitro model for intestinal absorption. Phytomedicine. 2008;15(5):373-7. doi:10.1016/j.phymed.2007.03.008
12. British Pharmacopoeia Commission. British Pharmacopoeia. volume 4, London: The Stationary Office; 2015. p. 362-7
13. British Pharmacopoeia Commission. British Pharmacopoeia. volume 4, London: The Stationary Office; 2020. p. 455-61
14. Council of experts and its experts commmitees. The United States pharmacopeia39. National formulary34. Vol. 3. Rockville (MD): United States Pharmacopeial Convention; 2015, p. 5825-30.
15. Council of experts and its experts commmitees. The United States pharmacopeia43. National formulary38. Vol. 2-2. Rockville (MD): United States Pharmacopeial Convention; 2020, p. 4023-29.
16. Cartwright A.C. The British Pharmacopeia, 1864-2014. London and New York: Routledge; 2015.
17. Roger LW. Official USP Reference Standards: Metrology concepts, overview, and scientific issues and opportunities. J Pharm Biomed Anal. 2006;40(1):3-15. doi:10.1016/j.jpba.2005.07.017
18. Bauer R, Franz G. Modern European monographs for quality control of Chinese herbs. Planta Med.2010;76(17):2004-11. doi:10.1055/s-0030-1250532
19. Kim D, Kim B, Yun E, Kim J, Chae Y, Park S. Statistical quality control of total ash, acid-insoluble ash, loss on drying, and hazardous heavy metals contained in the component medicinal herbs of "Ssanghwatang", a widely used oriental formula in Korea. J Nat Med. 2013;67(1):27-35. doi:10.1007/s11418-012-0640-4
20. Donggyu K, Bogsoon K, Eunsun Y, Junghun K, Youngzoo C, Seungkook P. Statistical quality control of total ash, acid-insoluble ash, loss on drying, and hazardous heavy metals contained in the component medicinal herbs of "Ssanghwatang", a widely used oriental formula in Korea. J Nat Med. 2013;67(1):27-35. doi:10.1007/s11418-012-0640-4
21. Shufen C, Boqiang F, Frank SCL, Xiaoru W. Application of microemulsion thin layer chromatography for the fingerprinting of licorice (Glycyrrhiza spp.). J Chromatogr B. 2005;828 (1-2):33-40. doi:10.1016/j.jchromb.2005.09.042
22. Jing J, Harendra SP, Ming W, Wie CR, Si BC. Advances in analytical technologies to evaluate the quality of traditional Chinese medicines. Trends Anal Chem. 2013;44:39-45. doi:10.1016/j.trac.2012.11.006