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Phytopharmaceuitcals Ingredients' – A new category of Monographs in Indian Pharmacopoeia

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ABSTRACT

Indian Pharmacopoeia Commission (IPC) is mandated amongst others to publish, The Indian Pharmacopoeia (IP), with the focuses on promoting the quality standards for pharmaceuticals including herbal medicines. In 2015, phytopharmaceutical regulations were notified to pave way for scientific development of herbal / botanical based drugs. IPC is moving towards developing Phytopharmaceuticals Ingredients (PPIs) category monographs. In the present paper we describe the process adopted at IPC in developing PPIs monograph. The IPC has recognized certain PPIs monograph with a reason to demonstrate that four marker compounds can be characterized in the raw herbs in order to promote the quality standards for phytopharmaceuticals.

INTRODUCTION

The Indian Pharmacopoeia Commission (IPC), under the Ministry of Health & Family Welfare, Government of India through the publication of Indian Pharmacopoeia (IP), a book of official standards of quality for drugs, vaccines,

blood products, radio pharmaceuticals and herbal medicines achieves its mandate. IPC plays a vital role as it publishes IP and its addenda from time to time in order to promote them. It is pertinent to state that IP plays a major role in promoting the quality standards for herbal medicines [1]. The current edition of I.P i.e. 2018 contains total 168 monographs on raw herbs, processed herbs (extracts) and finished herbal formulations such as tablets, capsules. Till today one of the criteriae for inclusion of a monograph on herbs, processed herbs and herbal products was to test for at least one bio active or analytical marker compound that has been characterized in that herb both qualitatively and/or quantitatively.

Besides promoting the quality standards for herbal medicines, IPC is also moving towards developing standards for phytopharmaceuticals as the necessary regulations already have been made in some countries [2-4]. In India, as per the Gazette notification 2015 the regulatory provisions for phytopharmaceuticals and regulatory submission requirements for scientific data on quality, safety, and efficacy to evaluate and permit marketing approval for Phytopharmaceuticals drug on similar lines to synthetic, chemical moieties have been made under the Drugs & Cosmetics Act 1940 and rules 1945 there under. As per the Gazette notification, Phytopharmaceuticals drug is defined as purified and standardized fraction with defined minimum four bio-active or phytochemical compounds (qualitatively and quantitatively assessed) of an extract of a medicinal plant or its part, for internal or external use of human beings or animals for diagnosis, treatment, mitigation, or prevention of any disease or disorder but does not include administration by parenteral route [5,6]. The requirements for phytopharmaceuticals are under the purview of Central Drugs Standard Control Organization (CDSCO) as it differs from Ayurvedic, Siddha or Unani drugs which include all medicines intended for internal or external use for or in the diagnosis, treatment, mitigation or prevention of (disease or disorder in human beings or animals, and manufactured) exclusively in accordance with the formulae described in, the authoritative books of ayurvedic, siddha and unani tibb systems of medicine specified in the First Schedule. However, phytopharmaceutical drugs are fraction of crude extract and are distinctly differentiated by being purified and standardized. Further, CDSCO in collaboration with IPC and other similarly placed organizations such as Indian Council of Medical Research, Council for Industrial and Scientific Research (CISR) laboratories have engaged in capacity building and facilitating Phytopharmaceuticals drug approval process. It is learnt that development of a few identified PPIs as a phytopharmaceutical drug has been undertaken by CSIR on a mission mode. The draft Good Manufacturing Practices guideline for phytopharamceuticals also has been published under the Schedule M.

Since this regulatory provision on Phytopharmaceuticals is expected to promote the innovations and also it would encourage research in phytopharmaceutical drug development for academia, researchers, and industry, there is an

emerging need to begin with developing the standards for Phytopharmaceuticals Ingredients (PPIs). The IPC has initiated its scientific process to publish a PPIs category monograph in IP. The IPC has recognized certain PPIs monograph with a reason to demonstrate that four marker compounds can be characterized in the raw herbs and their purified fractions. However, such monographs may or may not strictly meet the requirements of definition of phytopharmaceuticals. The purpose of the PPIs monograph is to provide the scientific information on the quality standards of the herbal drug and characterization of minimum four of its bio markers / analytical markers in order to facilitate appropriate maintenance of the standards by the stakeholders. As an example of this effort the modified monograph on *Andrographis paniculata* is cited here (Figure 1). The existing monograph in IP, on *Andrographis paniculata* has been modified to provide for testing qualitatively/quantitatively for four bio / analytical markers namely, Andrographolide, Andrograpanin, Neo - andrographolide and 14-deoxy -11,12 didehydro andrographolide. This modified monograph is being included in the next addendum of IP. Such monographs in the next addendum would be identified by the suffix PPI next to the name of the monograph to denote that such ingredients demonstrate potentially meeting the defined criteria for a phytopharmaceutical in IP.

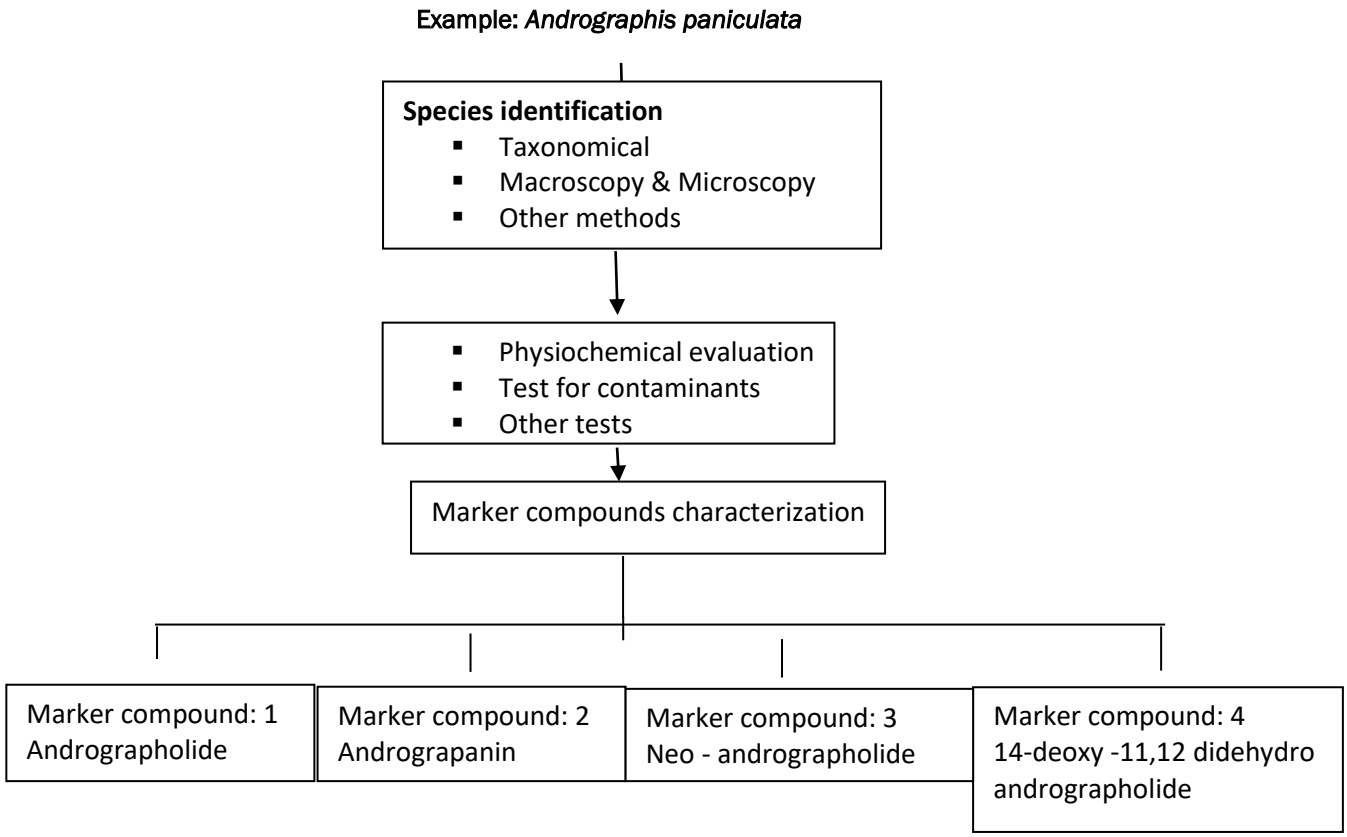

Figure 1: Process of PPIs category monograph development in IP

Other monographs on similar lines would be included in the next addendum to IP, namely *Aegle marmelos* (bio markers: Psoralen, Marmelosin, Umbellifereone and Scopoletin), *Silybum marianum* (bio markers: Silychristine, Isosilybin A, Isosilybin B, and Silybibn A &B) and *Plumbago zeylanica (bio markers: Lawsone, Plumbagin, 2,4-di bromide Plumbagin and Plumbagic acid)* under the category of PPI monograph. It is further work in progress and IPC is requesting its collaborating institutions and other stakeholders to establish and compile a list of most widely used medicinal plants of having at least four markers, and share the data with Pharmacopoeia Commission. Such data received shall be verified and characterized at IPC before accepting them for inclusion in IP addendums as PPIs. The General Chapter on herbs, processed herbs and herbal products is being amended to include appropriate statements related to Phytopharmaceuticals. The PPIs category monographs in IP will be supplemented and updated periodically as new information provided by the stakeholders or available in the literature or established at IPC will be reviewed and approved. It is to be recognised that mere inclusion of a monograph for a herb or extract or PPI in IP does not give it a status of drug and relevant regulations need to be complied with, and approval as a drug is to be obtained from the office of Drugs Controller General of India after submission of relevant applications. Keeping in mind the interest of patients and in National interest IPC encourages stakeholders to provide data and quality standards parameters for PPIs for review and validation at the Commission's Laboratory for inclusion in the Pharmacopoeia. As to ensure its effective and safe practices many users of the monographs of this category in IP have informed about the usefulness of monographs in IP on herbs for various purposes. To avoid supplier - buyer controversies, recognition of an acceptable safety profile, supporting researchers especially those who undertake human intervention studies / clinical trials to get herbs of specified quality for use are some of the advantages. It is also a fact that appearance of a monograph in IP has assisted regulatory authorities in other nations during review of herbs for acceptance. It is a fact that IP has shown leadership beginning in 2007 by inclusion of objectively accessible quality parameters for herbs through its monographs inclusion in IP and the current approach to identify some of the monographs as PPI is continuation of such scientific effort.

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