

Survey Study

Evaluation of package inserts of Ayurveda drug formulations from Mumbai city

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Abstract

Introduction: Package insert (PI) is a vital document accompanying a prescribed medication to provide information to the prescriber and end-user at a glance. Studies regarding PIs of Ayurvedic medicines in accordance with standard guidelines are lacking. **Aim:** Present study was undertaken to evaluate PI of Ayurveda drugs. **Materials and Methods:** PIs of Ayurveda drugs were obtained from five randomly selected Ayurveda medical shops located in three main zones of Mumbai. From each medical shop, a range of 15–20 PI was planned to be collected for different formulations. It was decided to collect a minimum fifty PIs/group for equitable distribution of various formulations in period of January–June 2013. Checklist was prepared, and content validity was achieved. Final validated checklist contained a total of 13 items, and the presence or absence of information pertaining to these items on the PI was evaluated. Any other additional information present on PI was also noted. Each item was analyzed and expressed as percentages. **Results:** The information on 258 PIs included: Name of ingredients (67%), quantity of ingredients (47.27%), route of administration (86.8%), dosage form (86.8%), indications (18%), dose (18%), contraindications (18%), side effects (9%), shelf life (5.81%), storage conditions (11%), and manufacturers name with contact details (34%). **Conclusion:** PIs accompanying Ayurveda medicinal products in India are deficient in information required to be furnished by them.

Key words: Ayurvedic drugs, drug information, Mumbai, package insert

Introduction

In today's era, information about a particular drug is readily available on internet, books, and scientific journals. Most of these sources are directed toward medically literate person and not toward patient/common man. "Package Insert" (PI) is one such document which creates awareness about the drug among medical professionals. "Package Insert" is defined as a document accompanying a prescribed medication to provide information at a glance about the contents, dosing instructions, indications, adverse effects, contraindications, and precautions to be followed with the use of the drug.^[1] The extent of information contained in these PIs as well as their design is usually governed by regulatory bodies that control manufacturing and sales of the drugs for the country.^[1] In India, requirements for a PI for

Allopathic drugs are clearly defined in the Drugs and Cosmetics Rule 1945 Section 6 of Schedule D (II).^[2] However, there is no regulatory requirement for providing PI for Ayurvedic drugs.

Sales of Ayurveda formulations are increasing in India as well as internationally. The overall international trade in medicinal plants and their products reported by the WHO is 6.2 billion USD, which has the potential to grow to 5 trillion USD by 2050.^[3] Alternative systems of plant-based medicine form an important part of the health care systems in most of the Asian, African, Latin American, and some developed countries. Among Asian countries Japan, China, and India have the highest

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per capita consumption of traditional medicine. Most of the population in Africa and Latin America also relies on traditional medicine.^[3] While conducting a thorough literature search, relevant, and authentic guidelines designed specifically for herbal formulations with the WHO and Chinese medicinal regulations were obtained. The Sixth International Conference of Drug Regulatory Authorities, which was held in Ottawa, Canada, in October 1991, recommended the WHO Guidelines for the Assessment of Herbal Medicines be adopted by all member states and adapted to their local needs as a means of ensuring adequate standards of quality, efficacy, safety, and information.^[4]

Majority of Ayurveda drug manufacturing companies do provide PI with their formulations. However, after extensive electronic search (till December 2012), published studies on PI accompanying Ayurveda formulations were not found. Hence, present pilot study was designed to evaluate PI of Ayurveda drugs for their content.

Materials and Methods

For the purpose of the study, PIs of Ayurveda formulations (for sale in India only) were obtained from five randomly selected Ayurveda medical shops selling exclusively non allopathic drugs located in three main zones, i.e. South Mumbai, Eastern suburbs, and Western suburbs of Mumbai (total 15 medical shops were selected). From each medical shop, a range of 15–20 PI was planned to be collected for different formulations. The Ayurveda formulations for study purpose were divided into four groups according to the method of preparation, namely, Group I: *Kadha* (or *Kashayam* [medicinal decoction]) and *Asava–Arishta* (alcohol containing Ayurvedic medicines), Group II: Tablets (*Ghanavati*, *Guggulu*, *Gutika* [pill preparation] etc.), Group III: *Churna* (powdered mix preparation), Group IV: Other (*Taila* [oil preparation], *Ghrita* [ghee preparation], *Lepa* [paste preparation], ointments-liniments, etc., for local application and other). It was decided to collect a minimum fifty PIs per group for equitable distribution of various formulations. Thus, target was to collect minimum 200 PI from 15 Ayurveda medical shops from three different zones of Mumbai in period of six months from January to June 2013.

For the evaluation of contents in the PIs “checklist” was prepared by the authors. This checklist was prepared on the basis of the guidelines given for herbal drugs on China and WHO website.^[5,6] This checklist was sent for review to Ayurveda physicians ($n = 10$) for content validity who were practicing Ayurveda for a minimum period of 8 years. The final validated checklist contained a total of 13 items and the presence or absence of information pertaining to these items on the PI was evaluated [Table 1].

Any other additional information (language, special instructions includes diet, lifestyle modification, *Anupana* [vehicle], etc.), present on the PI was also noted. Each item was analyzed and expressed as percentages.

Results

From fifteen Ayurveda medical shops, 258 PIs of Ayurveda formulations were collected. Among these, 53 PIs for Group I, 62 PIs for Group II, 59 PIs for Group III, and 84 PIs for

Table 1: Analysis of the content of package inserts of Ayurveda formulations ($n=258$)

Item on the checklist	Number of package inserts containing information (%)
Name of ingredients	173 (67)
Quantity of ingredients	122 (47.27)
Route of administration	224 (86.8)
Dosage form	224 (86.8)
Therapeutic indications	46 (18)
Dose	46 (18)
Contraindications	46 (18)
Warning and precautions	23 (9)
Interactions	-
Side effects	-
Shelf life	15 (5.81)
Storage conditions	28 (11)
Manufacturers name and contact details	88 (34)

Group IV Ayurveda formulations. Out of these 258 marketed formulations, 69 were “*Granthokta*” (as per authoritative books of Ayurvedic system) and 189 were proprietary formulations. Further, out of these 258 formulations, 113 were herbomineral and 145 were herbal preparations. No single formulation was found to having a single herb or mineral. Analysis of content of PIs of Ayurveda formulations is presented in Table 1.

Among the PIs, only 15 (5.8%) had mentioned about *Anupana* (vehicle) and *Pathya-Apathya* (do’s and don’ts). All PIs were printed in multiple languages. PIs printed in English language were 215 (83.33%), whereas PIs printed in Hindi language were 201 (77.90%). Other languages found were Marathi, Gujarati, Kannada, Malayalam, Urdu, and Tamil. PIs having 2 languages were 153, 3 languages were 78, and 4 languages were 42. Moreover, 3 PIs were printed in more than 6 languages. Only two of the PIs had a mention of conduct of clinical trials to the claims made.

Discussion

PI of a drug is a scientific document providing all essential information regarding the drug use in a comprehensive manner. From the results of study, it is evident that PIs provided with Ayurveda formulations did provide information on ingredients, dose, and route of administration (ROA) but were deficient in several aspects: Adverse effects, precautions, dosing instructions, etc., PI assessed in the study did not provide the health care professional with necessary information that may adversely affect the outcome of therapy. In India, rules for PIs of pharmaceutical preparations have been mentioned in Section 6.2 and 6.3 in Schedule D (II) of Drugs and Cosmetic Rules, 1945.^[2] Guidelines for PIs of the Ayurvedic medicines have not been mentioned in these rules; however, rules for labels of Ayurvedic medicines are enlisted in rule 161 of part XVII in the Drugs and Cosmetic Rules, 1945.^[2] Thus, rules for PIs of Ayurvedic formulations are lacking in India. Previous studies evaluating the PIs of Ayurvedic medicines have never been conducted. Studies evaluating the labels of Ayurvedic medicines in compliance with the rule 161 were done.^[7] Researchers found

some missing information in labels of all Ayurvedic medicines in their study, while another researcher observed that 30% of labels were noncompliant with rule 161.^[7,8] Since rules for PIs are not available in India for Ayurvedic medicines, PIs of Ayurvedic drug formulations cannot be expected to be compliant to Schedule D (II) which have been laid for pharmaceutical preparations. Hence, this study highlights a need for guidelines to be formulated for PIs of Ayurvedic medicines.

Schedule D (II) mandates the mention of posology of medicine on PIs.^[2] In present study, mention of content of the preparations was noted in 67% PIs, and quantity specifications were present in 47.27%. WHO guidelines^[5] suggest that name along with quantity of all active ingredients must be available on the PI. Guidelines of China government are more explicit and clearly notify that product name should be consistent with the name of the registry: Proprietary Chinese medicine, including the product name and trademark text (if any). The font, size, and color of the words should be consistent. It should not be named using both Chinese medicine and Western medicine theory, and it should not be misleading or exaggerated in any way.^[6] At least botanical names of medicinal ingredients should be mentioned. Sanskrit names also can be used with proper authentic references. Knowing ingredients would help patients to identify any substance to which he/she has a known allergy and avoid consumption of such formulations. As regard to the quantity of the ingredients, the Chinese herbal medicine directive have strict rules about master formula, weight or volume, net weight/net volume of each unit, display of these measurements metric system, excipients, and conversion factor wherever necessary.^[6] The dosage should be indicated in terms of daily dose or each dose (subject to the dose form), while ROA of medicine and precautions should be clearly indicated under the method of usage. Method of usage and dosage should be clearly listed if the product is suitable for different groups of people such as children. Dosage forms in the study were mentioned in 86.8% of PIs.

ROA was mentioned in 86% of PIs. Many herbs are effective in both ways; externally and internally for same disease. Schedule D (II) recommends the mention of method of administration on the PIs.^[2] Thus, patients and physicians should have clear idea about ROA, many externally indicated liniments/ointments may be harmful when ingested. WHO guidelines clearly state that dosage of application, frequency of use, and method of usage should be listed clearly and accurately.^[5]

Indications for use should be mentioned as it is vital information. Schedule D (II) requires therapeutic indications to be enlisted on PIs.^[2] About 18% of PIs in the present study had mention of therapeutic indications for which the medicine can be used. Indications of the Ayurvedic medicine should be well defined as many Ayurveda drugs have more than one indication. Moreover, there should be a clear cut mention of purpose i.e. tonic, nutraceutical, cosmetic, medicine, or otherwise. Ideally, names of the diseases must be mentioned preferably from Ayurveda texts. As per the Chinese recommendations on PIs, the indications of the product should be consistent with those under the Chinese Pharmacopoeia or National Drug Standards.

It is well known fact that both over treatment as well as under treatment with any formulation is harmful; hence, appropriate dosing instructions must be mentioned for the safety and

efficacy of the formulation. Furthermore, some formulations may have interactions with foods consumed; hence, the time with respect to meals should be specified. In addition, warnings/precautions were not specified in 91% of the PIs. Schedule D (II) mandates mentioning about the precautions or warnings and interactions with use of the medicines on PIs.^[2] Many patients resorting to Ayurveda formulations may be already on a cocktail of allopathic (or other system of medicine) medications for chronic ailments such as diabetes mellitus, hypertension, skin diseases, gout, and rheumatoid arthritis. Combining Ayurveda formulations and allopathic medications may give rise to interactions which may result in either failure of treatment. The possibilities of such interactions should be mentioned in PIs of Ayurveda formulations meant for such chronic indications.

If Ayurveda formulations are associated with certain known side effects; the patient should be warned of such side effects through the PIs. In the current study, none of the PIs mentioned the side effects. Schedule D (II) instructs mention of side effects on PIs of medicine.^[2] WHO guidelines do mention that section on major side effects (if any) and over dosage information, contra-indications, warnings, precautions, major drug interactions, use during pregnancy, and lactation must be specified on the PI.^[5] In addition, the conditions requiring cautions of the medicine (e.g., problems of liver and kidney functions), factors affecting the curative effects of the medicine (e.g., food, cigarette, alcohol etc.), conditions requiring observations during the process of the use of the medicine (e.g., allergic reaction), drug abuse, and drug dependence, must be specified.

Many PIs (94%) were lacking information about shelf life of a formulation. Ayurveda itself distinctly mentions shelf life period of formulation that should be followed. Various process performed during preparation of drug may increase shelf life period of Ayurveda drug. Knowing the shelf life period, helps in avoiding adverse effect of a drug after its expiry date. Inappropriate storage of Ayurveda formulations may result in the formulations losing their efficacy and cause failure of treatment. Thus, any special precautions to be taken for the storage of a given product should be emphasized upon in the PIs. Schedule D (II) has directives regarding mentioning of shelf life of packaged materials on PIs.^[2] WHO guidelines and Chinese guidelines for herbal drugs do state that Instructions should be given accurately on the PIs if the product is required to be kept under specific conditions (temperature such as “store at 2–5°,” humidity such as “keep in a cool and dry place,” lighting such as “protect from light”).

Availability of manufacturers contact details is also a vital part from patients' side. Any information regarding the formulation can be asked if these details are provided with. Schedule D (II) has no clauses regarding mention of name and address of the manufacturer along with the manufacturing license number on the PIs of medicines. However, this information has to be mentioned on labels of Ayurvedic medicine as per rule 161.^[2] This information should also be made available on the PIs.

Language used in PI matters a lot as this piece of paper provides information to medical person as well as patient too. Manufacturer may provide other information in other language as per need. Schedule D (II) instructs the PIs to be in English;

however, some PIs in the present study were in additional local languages. PIs generally are meant to be of importance and use for the medical community. There are no guidelines for the use of multiple languages in the PIs. However, PIs of Ayurvedic formulations in present study might have been designed for understanding of local population. This may be of advantage as persons using Ayurvedic medicine may be accessed by population not learned in English but may have knowledge of other languages. Concept of *Matra*^[9] (dose), *Kaala*^[10] (time), *Anupana*^[10] (vehicle taken along with main medicine), and *Kashaya Kalpana*^[11] (dosage form) had given immense significance in Ayurveda texts already. *Anupana* is an essential concept given by Ayurveda. Though lukewarm water is assumed most commonly but there are several other drugs (milk, butter milk, honey, butter, etc.),^[10] which are used in consideration with disease, *Srotas* (channels/pores), etc. as *Anupana*. While prescribing formulations, to increase efficacy, *Anupana* instructions are key factor. Ayurveda drugs work excellently when *Pathya-Apathya Kalpana*^[12] (comprehensive diet and lifestyle for disease) is followed along with the course. It is the most vital point of instructions provided by physician to patients, but if PI offers this information, then it is very convenient, time saving, precise, and helpful for patient as well as physician.

In case of allopathic medicines there are several national and international regulatory bodies which ensure quality control, formulate guidelines for the stringent manufacture, packaging, distribution, and disposal of products. In India, the PIs of the allopathic medicines have to meet strict guidelines according to Schedule D (II) of the Drugs and Cosmetic Rules, 1945.^[2] Though the rules for PIs of the allopathic medicines are stringent, the same do not follow for the Ayurvedic medicines as discussed above. To change the current scenario of Ayurveda formulations, it is essential that existing bodies such as AYUSH/Ministry of Health implement similar measures as with allopathic medications to Ayurveda formulations. Provision of PIs complete with all essential information as highlighted in the study should also form an important component of quality control process. Thus, in China, all PIs are approved by the Chinese Medicines Board. As a pilot study, it was decided to restrict the study area to Mumbai not only because authors were from Mumbai but also Mumbai is a city which is densely populated and has diversity in each aspect such as socioeconomic status, religion, and disease. In Mumbai, more than 1000 Ayurveda medical shops are selling exclusively non allopathic drugs. There were no previous studies available from Mumbai for Ayurveda drugs.

In Drugs and Cosmetic Act 1940, combined guidelines for labels and PI are mentioned. However, PI is the material where manufacture can provide all scientific and important information whereas labels may contain various attractive design, pictures, etc., Information on labels was not scope of the study. Previous studies concluded that Ayurveda drug container labels were deficient in most of the requirements specified in the Act.^[7,8] WHO also recommends that PIs should be understandable to the end user/patient with simplicity. Patient friendly PIs are mandatory in several countries, particularly in the European Union,^[13] where they contain information pertaining to the drug in a legible and comprehensible manner. Such a directive has proved to be extremely beneficial to both the patient and the health care providers. It not only provides

the patient with essential information regarding the drug but also bridges any miscommunication between the patient and doctor with regards to its consumption, dosage, storage, and much other vital aspect. This would ensure safe and efficacious use of the product and would also help Ayurveda formulations attain a wider acceptance.

Limitation

Though this study represents limited data of only five shops in three main regions of Mumbai, the data may not be representative of all the herbal medicines marketed in Mumbai, and, similarly, for the entire country. However, this being a pilot study, further studies involving herbal medicines available all over India should be conducted to get an exact estimate of deficiencies in their PIs.

Conclusion

From the present study, it can be concluded that currently PIs accompanying Ayurveda medicinal products in India are deficient in the information required to be furnished by them. PIs should provide information for the safe and efficacious use of drugs both for the prescriber and patient.

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Conflicts of interest

There are no conflicts of interest.

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हिन्दी सारांश

मुंबई शहर के आयुर्वेदिक औषधियों के दवाई जानकारी पत्र का मूल्यांकन

सुदत्त शिरोलकर, राखी के. त्रिपाठी, अनिरुद्ध व्ही. पोटे

दवाई जानकारी पत्र यह एक महत्वपूर्ण दस्तावेज है, जिससे औषध निर्देश करने वाला और अंतिम उपयोगकर्ता, दवाइयों की जानकारी प्राप्त कर सकते हैं। आयुर्वेद दवाई जानकारी पत्र मानक के दिशा निर्देशों के अनुसार है या नहीं, इसमें अभी तक अध्ययन नहीं हुआ है। यह अध्ययन आयुर्वेदिक दवाइयों के दवाई जानकारी पत्र का आंकलन करने के लिए किया गया है। मुंबई के ३ प्रमुख क्षेत्र के ५ आयुर्वेदिक दवाई के दुकानों से आयुर्वेदिक दवाइयों के दवाई जानकारी पत्र प्राप्त किये गये। प्रत्येक दुकान से आयुर्वेदिक दवाइयों के निर्माण पद्धति के अनुसार १५-२० दवाई जानकारी पत्र चुने गये। जनवरी से जून २०१३ तक कम से कम ५० दवाई जानकारी पत्र प्रति/समूह के अनुसार इकट्ठा किये गये। जांच सूची तय की गई और उसकी सामग्री वैधता की गई। अंतिम वैद्य जांच सूची में १३ विषयों का समावेश था और इनकी उपस्थिति या कमी के अनुसार दवाई जानकारी पत्र का मूल्यांकन किया गया। अधिक जानकारी भी नोट की गई। प्रत्येक विषय की जांच की गई और उसे प्रतिशत में अंकित किया गया। २५८ दवाई जानकारी पत्र में यह जानकारी प्राप्त की गई-घटक के नाम (५६%) घटक की मात्रा (८६.२६%), औषध मार्ग (८५.८%), औषध रूप (८६.८%) संकेत (१८%), औषध मात्रा (१८%), औषध निषेध (१८%), दुष्प्रभाव (९%), जीवनकाल (५.८९%), भंडारण की स्थिति (९९%) संपर्क विवरण के साथ निर्माताओं के नाम (३८%)। भारत में आयुर्वेदिक दवाई के दवाई जानकारी पत्र पर जो जानकारी होनी चाहिए, वह अपूर्ण है।