

Regular Article

Standardization and evaluation of safety of a herbomineral formulation Articulin® forte tablets

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In the earlier days physicians used to be the formulator and all the processes right from collection to dispensing were controlled by them. In last few decades, there has been tremendous growth in the field of herbal medicines. It has become necessary to lay down stringent parameters to ensure batch to batch consistency and reproducibility. Therefore, standardization of herbal formulations has become extremely essential in order to assess the quality, purity, safety and efficacy of drugs based on the amounts of their active principles. Heavy metal toxicity being a major safety issue in Ayurvedic formulations, it is essential to evaluate them for heavy metal content. Articulin® Forte Tablet is a well-known herbomineral formulation used for rheumatoid arthritis. In present studies, Articulin® Forte Tablets were evaluated for heavy metal contents.

Key Words: Ashwagandha, Arsenic, Herbomineral, Articulin® Forte

The American medical research community has sounded a heavy metal warning against Ayurvedic cures. "Users of Ayurvedic medicine may be at risk for heavy metal toxicity, and testing of Ayurvedic and Herbal Medical Products for toxic heavy metals should be mandatory," Dr Robert Saper and his colleagues have interpreted in their study on Ayurvedic and herbal medicines (Shukla, 2006). India having a rich heritage of traditional medicine constituting with its different components like Ayurveda, Siddha and Unani. The development of these traditional systems of medicines with the perspectives of safety, efficacy, and quality will help not only to preserve the traditional heritage but also to rationalize the use of natural products in healthcare (Tekeshwar et al, 2011). Classical Ayurveda prescribes metals and minerals or in combination with herbs as herbomineral formulations. Manufacturing procedures for these formulations are stringent and adverse reactions are possible if precautions are not taken (Shastri,1994). Although the medicines are used widely in India, doubts about their long term safety come up due to presence of toxic metals in them and adverse reactions are reported (Saper et al, 2004 and Parab,2003). There are 8403 licenced Ayurvedic pharmacies and approximate turnover is 4000 crores. This commercialization has brought with many challenges about safe use of Ayurvedic medicines and need of standardization (Thatte, 2008). Articulin Forte is a well-known herbomineral formulation containing Ashwagandha, Guggul, Haldi and Jasad Bhasma which is used for osteoarthritis, rheumatoid arthritis, painful conditions and inflamed joints. Turmeric is anti-inflammatory and antiseptic. Curcumin, an alkaloid isolated has anti-inflammatory, antirhumatoid activity (Arora, 1971). Guggul is well known anti-inflammatory drug. Zinc deficiency has shown to be a consistent finding in rheumatic disorders and its supplementation is claimed to be useful(Shimpkin,1976 and Prasad, 1979).

Materials and Methods

Articulin® Forte Tablets containing Ashwagandha, Guggul, Turmeric powder and purified Jasada Bhasma were manufactured in Eisen Pharmaceutical Co Pvt Ltd Pune. Guggul purchased from local market was purified on the basis of Indian Medicinal Systems of Ayurveda (Charak Samhita, 1949).

Chemicals: All the solvents and chemicals used were of analytical grade and purchased from Qualigens.

Determination of moisture content (Anonymous, 1990)

Place about 10 G of drug in tared evaporating dish and place it in oven at 105°C for 5 hrs and weigh. Continue the drying and weighing at one hour interval until the difference between two successive weighing corresponds to NMT 0.25%. Weigh the sample till constant weight is obtained

Determination of total ash (Anonymous, 1996)

Total ash determination constitutes detecting the physiological ash and non-physiological ash. For its detection, 2g of powdered material was placed in a suitable tared crucible of silica previously ignited and weighed. The powdered drug was spread into an even layer and weighed accurately. The material was incinerated by gradually increasing the heat, not exceeding 450°C until free from carbon, cooled in desiccator, weighed and percentage ash was calculated by taking in account the difference of empty weight of crucible & that of crucible with total ash.

Determination of Acid insoluble ash

The ash obtained as above was boiled for 5min with 25ml of dilute hydrochloric acid; the insoluble matter was hot water and collected on an ash less filter paper, washed with ignited to constant weight. The percentage of acid-insoluble ash with reference to the air-dried drug was calculated.

Determination of solvent Extractive values

Alcohol soluble extractive value

5g of coarsely powdered air-dried drug was macerated with 100ml of alcohol in a closed flask for twenty-four hours, shaking frequently during six hours and allowing standing for eighteen hours. It was then filtered rapidly; taking precautions against loss of solvent. 25ml of the filtrate was evaporated to dryness in a tared flat-bottomed shallow dish at 105°C to constant weight and weighed. The percentage of alcohol-soluble extractive was calculated with reference to the air dried drug and is represented as % value.

Water soluble extractive value

5g of coarsely powdered air-dried drug was macerated with 100ml of chloroform water in a closed flask for twenty-four hours, shaking frequently during six hours and allowed to stand for eighteen hours. It was then filtered rapidly, taking precautions against loss of solvent. 25ml of the filtrate was evaporated to dryness in a flat bottomed shallow dish at 105°C to constant weight and weighed. The percentage of water-soluble extractive was calculated with reference to the air-dried drug and is represented as % value.

Heavy Metal Analysis: Articulin® Forte Tablets were analysed for heavy metal content using Inductively Coupled Plasma Mass Spectrometry. Individual ingredient was analysed for arsenic content by Inductively Coupled Plasma Mass Spectrometry at DAL Pune.

Microbial Analysis: Microbial analysis for confirming absence of pathogens was done as per procedure given in IP 2010.

Results and Discussion

Articulin®Forte Tablets is a safe and clinically tested herbomineral formulation for rheumatoid arthritis and osteoarthritis and other inflammatory conditions (Kulkarni, 1992 and Kulkarni, 1991). This formulation was evaluated for different parameters like moisture content, ash value and extractive value. The results are given in Table 1.

Table 1: Proximate analysis of Articulin®Forte Tablets

No	Parameter	Result
1	Moisture on IR balance	1.8%
2	LOD	2.07%
3	Total ash	36.53%
4	Acid insoluble ash	2.86%
5	Alcohol soluble extractive	0.82%
6	Water soluble extractive	3.77%

It was observed that total ash value was found to be very high due to presence of Jasad Bhasma. Rest of the parameters were found to comply with the standards. Heavy metal toxicity is a major issue in the Ayurvedic formulations. Each individual component of the formulation was studied for Arsenic content. (Table 2)

Table 2: Arsenic content of each ingredient of Articulin® Forte Tablets

No	Crude drug	Detection limit	Result
1	Haldi	0.01µg/g	<0.01µg/g
2	Ashwagandha	0.01µg/g	<0.01µg/g
3	Guggul	0.01µg/g	<0.01µg/g
4	Purified Jasad Bhasma	0.01µg/g	<0.01µg/g

All the components were found to be within specified limit. Therefore, each ingredient of Articulin® Forte Tablets was tested for presence of heavy metal. (Table 3)

Table 3: Heavy metal analysis of Articulin®Forte Tablets

No	Heavy metal tested	Detection limit	Result
1	Arsenic	0.01µg/g	<0.01µg/g
2	Mercury	0.01µg/g	<0.01µg/g
3	Lead	0.05µg/g	0.05µg/g
4	Cadmium	0.05µg/g	<0.05µg/g
5	Nickel	0.05µg/g	<0.05µg/g

The results indicate that the formulation is very safe as it contains heavy metals within specified limits. Jasad Bhasma used in the formulation is purified by the method given in Ayurvedic text. Microbial analysis showed the formulation is free from pathogens like *E.coli*, *Salmonella*, *Pseudomonas* and *Staphylococcus*. (Table 4)

Table 4: Microbial tests Articulin® Forte Tablets of for pathogens

No	Micro-orgaism	Present/ Absent
1	<i>E.coli</i> (NCTC 9002)	AB
2	<i>Salmonella abony</i> (NCTC 6017)	AB
3	<i>Pseudomonas aerogenosa</i> (NCIM 2200)	AB
4	<i>Staphylococcus aureus</i> (NCIM 2079)	AB

Conclusion:

Articulin®Forte Tablets, a herbomineral formulation is a clinically tested formulation which is standardized by modern scientific methods. On the basis of clinical trials and standardization by different methods, safety and efficacy of the formulation is confirmed.

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