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Opinion note

Development and challenges of herbal injectables – a possible emerging area of drug delivery

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Article history	ABSTRACT
Received : July 10, 2020 Accepted : August 04, 2020	Herbal drugs have been employed in the treatment of diseases since ancient time. People have confidence in their efficacy and safety even today. The main reason for the popularity of these drugs is their limited side-effects when consumed in the
Keywords	and long gestation period remain challenging. This can be remedied by administering these drugs through parenteral routes in the form of herbal injectables. This article aims to draw the attention of the researcher toward the
Herbal drugs	formulation and development of herbal injectables. Besides, the emphasis has given
Herbal extracts	to the current scenario, challenges and perspectives of herbal injectables.
Herbal injectables	
Herbal preparations Parenteral route	© 2020 Global SciTech Ocean Publishing Co. All rights reserved.

INTRODUCTION

Herbal drugs are used in the form of crude extract, tincture, galenical and isolated individual compound. The easy preparation techniques make them cost-effective. There are several techniques available for the preparation of herbal extracts in which maceration, percolation, decoction, diffusion and digestion are some common techniques. The selection of the technique is based on the nature of the drug to be prepared. Herbal drugs are generally very popular in developing countries because of their economical nature and history of traditional use. These preparations are also popular in many developed countries including Germany, France, Italy and the United States where appropriate guidelines and regulations are existing in their preparation and use (Brevoort, 1995; Wagner, 1999; Calixto, 2000). In India, about 70% of the rural population follows Ayurvedic system of medicine whereas approximately 40% population of the western countries uses the herbal medicine for the treatment of various diseases (Pandey et al., 2013).

In recent days, fast treatment is the first choice of a patient which is mainly achieved using injectable drugs. These choices are usually preferred for a critically ill patient or one in an unconscious stage. The unavailability of herbal injectables in the market makes the population disappointed who prefers the herbal treatment and needs a speedy recovery. The herbal injectables can be a safe alternative treatment to the patients.

The injectable preparations are the sterile preparations which are administered to the body with the help of a syringe. The aseptic conditions are required to manufacture these preparations. The injectables can be administered the drug through intra-dermal, intramuscular, subcutaneous, intra-arterial and intra-vinous routes. However, intra-vinous is generally preferred because 100% bioavailability occurs with this route along with the lesser pain during administration. As herbal provide injectables effective and speedy treatment, they are a better alternative when GIT does not respond and need some quick symptomatic relief (Jain, 2017).

ADVANTAGES

Herbal injectable preparations provide more bioavailability as compare to oral preparations of the same drug. The side effects of herbal preparations are generally not seen if the optimum dose regimen is followed. Injectables provide effective targeting of drugs to the particular site of the body. Therapeutic efficacy might be increased because there is no drug-food and druggastrointestinal fluid interaction with injectable preparations. The dose of a drug can be reduced in the form of injection because of limited absorption window of the gastrointestinal tract. The onset of therapeutic action occurs instantly in case of drug administered directly to the systemic circulation.

CURRENT SCENARIO

At present, there is no popular herbal injectable formulation available in the market. Very scarce of literature is available on the research in this field. Some traditional systems such as the system are working Chinese with these formulations but their worldwide acceptability is still questionable. In some reports, it has been seen that researchers administered the herbal formulation to the animals by parenteral route but the basis of that administration is not clear (Wynn and Fougère, 2007).

Traditional Chinese medicine (TCM) has long been regarded as integral to the Chinese national essence and the development of TCM injections is considered to be a great achievement in the field of herbal injectables. TCM injection is a sterile preparation made with one or more purified extract of Chinese herbal drugs. TCM is injected into the human body as a solution, emulsion, concentrated solution or reconstituted powder that is made into a solution before administration (Wu and Zhang, 2011). The Chaihu herbal injection was the first herbal injection developed and used in China for the abatement of fever. Interestingly, a long list of TCM injections is now available in China to treat a variety of disorders (Kong et al., 2010; Tan L. et al., 2019).

A group of the researcher in China evaluated the therapeutic efficacy and safety of Xiaoaiping Chinese herbal medicine injections. for chemotherapy-induced thrombocytopenia in nonsmall cell lung cancer (NSCLC) and gastric cancer which is registered in the Chinese Clinical Trial Registry under Reg. No. ChiCTR-TRC-13003888. They conducted a trial on 120 patients with 60 patients in the intervention group and 60 patients in the control group and reported that Xiaoaiping injection may provide a safe and for chemotherapy-induced effective option thrombocytopenia in patients with NSCLC (Qi et al., 2019). Zhang et al. (2019) expanded the previous work to compare the efficacy and safety of Chinese herbal injections in combination with radiotherapy to treat oesophagal cancer. This study conducted 55 trials which included 12 Chinese herbal injections and 4114 participants. The study revealed that Compound kushen injection combined with radiotherapy can become an effective option for patients with oesophagal cancer in terms of efficacy and safety.

Jain (2017) reported a list of 96 Ayurvedic injections manufactured by Bundelkhand Ayurvedic Unani Pharmaceutical Works, Jhansi (Uttar Pradesh, India) and 28 Ayurvedic injections manufactured by Pratap Pharma Private Limited, Dehradun (Uttarakhand, India) which were available in the market till 1983. The major reason for their removal from the market might be their poor quality control and optimization. If this huge number of herbal injections were available at that time, these can be developed again by following the existing guidelines of governing bodies because a long history of their use showed their compatibility with human blood and body fluid.

A clinical study on 45 subjects was conducted to find out the effect of Kshara injection of 5% and 10% solution in the internal haemorrhoids by dividing subjects into the three groups, Group A (received 10% Kshara injection), Group B (received 5% of Kshara injection) and Group C (received distilled water as Placebo). The study concluded that Kshara Injection would be an integrated approach having a safe and simpler procedure in its application because a success rate of 88.3% in Group A and 86.6% in Group B was achieved (Rao, 1999). The study also found no complications during and after the treatment. Hence, such herbal injectables might be used for other purposes too. Similarly, Reddy et al. (2014) reported the controlled clinical study of herbal sclerosant injection of Apamarga Kshar on internal haemorrhoids (I^0 and II^0). They conducted a trial on 100 subjects by dividing them into two groups in which Group A was given herbal Sclerosant injection of Apamarga Kshara consisted of a wellprepared drug in liquid form and Group B was given 3% Polidocanal marketed injection as a control. The study found that herbal injection was effective without showing any complications.

A subcutaneous intralesional Ksharodaka injection was also used to treat warts in different patients. It has been observed that all warts took a minimum of 2-6 days to shed off, leaving minor scars and there were no adverse reactions reported in any of the cases (Manohar et al., 2014). Burghart (1987) reported that the administration of drugs through injection is not new but it was practised by Ayurvedic healer since a long past. He has given the example of penicillin, which was known to Brahmanical sages of the past and was given intravenously in ancient Ayurvedic practices.

LIMITATIONS AND CHALLENGES

If a dose of the drug is directly administered to the body fluid or systemic circulation, then particle size optimization requires special attention. The "Good Manufacturing Practices" guidelines of different governing bodies being followed during manufacturing are challenging for small scale manufacturers. At the same time, the manufacturing cost increases by maintaining aseptic conditions in the manufacturing area. The storage of injectables requires more attention as compared to the other dosage forms.

In the development of a new dosage form or exploration of a new route for the drug administration, there are many challenged to be faced. Since 1978, at least 65 cases of heavy metal intoxication associated with Ayurvedic HMPs in adults and children have been reported in the United States and abroad (Eisenburg et al., 1998; Robert et al., 2004). So, the purification of herbal drugs is needed to limit the use of heavy metals. The crude raw herb material has many variations as per geographical locations, climatic conditions, environmental hazards, harvesting methods, and collection protocols which make it a difficult task to standardize the end product for a reproducible quality (Bauer and Tittel, 1996). To overcome the variation and keep uniformity in the concentration of herbal material components of different sources, the quantitative estimation must be kept in concern.

Herbal medicines used in traditional systems are used without any toxicity studies. Their embryotoxic, foetotoxic, and carcinogenic effects are likely to remain unrecognized in a traditional practice. The embryotoxic effect of Pippalyadi vati, a traditional contraceptive consisting of Embelia ribes, Piper longum and Borax, has been reported (Chan, 2003). The selection of dosage regimen may also create problems. The dose must be calculated based on crude drug or extract to be used. The dose of the extract has to be calculated based on extractive value (Thatte, 2005). Additionally, wellcontrolled and appropriate randomized clinical trials are still needed to prove their efficacy (Sharma et al., 2010). In the context of herbal injectables, comparatively more challenges occur in comparison of oral preparations. The parenteral route for herbal drugs is not explored well in current research so challenges might be faced during the development of the same.

PERSPECTIVES

Based on the confidence on herbal drugs enjoyed by people, it could be said that the herbal drug would be the choice of drugs over allopathic drugs in near future if some other formulations like herbal injectables are introduced in the system. There is the opportunity of formulating various injectable formulations like solutions, concentrated mixtures, suspensions, solutions. emulsions. reconstituted powders etc. The field of novel drug delivery system could be seen as an opportunity in future, under which we can control the drug release or target the drug to a particular site of the body for the treatment of a particular disease. The herbal injectables might be set a milestone in the field of healthcare in terms of revenue generation, employment generation and better treatment.

In the development of herbal injectables, there is a need for new research focusing model. Starting from the purifications and sterilization of raw material the development of herbal injectables requires the standardization, dosage regimen calculation, drug interaction, blood compatibility, toxicological studies and all the quality control testing such as formulation clarity, particle size optimization, pH range optimization, isotonicity, stability, viscosity, pyrogens testing along with sterility testing in the same pattern of allopathic injectables.

CONCLUSION

The earlier studies revealed that the herbal injectables might be an effective alternative for the treatment in the near future. This mode of therapy might be the preferred choice of patients over allopathic injectables if available in the market. For the same, extra precautions should be taken for the optimization of the drug to be injected. In this direction, a roadmap should be prepared to develop the herbal injectables with the help of uniform research policy. As a result, there may be a good future of herbal injectables if developed with proper guidelines framed for this purpose.

CONFLICTS OF INTEREST

The author declares no conflicts of interest.

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