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Review Article

Effects of processing adjuvants on traditional Chinese herbs

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ABSTRACT

Processing of Chinese medicines is a pharmaceutical technique that transforms medicinal raw materials into decoction pieces for use in different therapies. Various adjuvants, such as vinegar, wine, honey, and brine, are used in the processing to enhance the efficacy and reduce the toxicity of crude drugs. Proper processing is essential to ensure the quality and safety of traditional Chinese medicines (TCMs). Therefore, sound knowledge of processing principles is crucial to the standardized use of these processing adjuvants and to facilitate the production and clinical use of decoction pieces. Many scientific reports have indicated the synergistic effects of processing mechanisms on the chemistry, pharmacology, and pharmacokinetics of the active ingredients in TCMs. Under certain conditions, adjuvants change the content of active or toxic components in drugs by chemical or physical transformation, increase or decrease drug dissolution, exert their own pharmacological effects, or alter drug pharmacokinetics. This review summarizes various processing methods adopted in the last two decades, and highlights current approaches to identify the effects of processing parameters on TCMs.

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1. Introduction

Chinese medicinal processing is a pharmaceutical technique that transforms medicinal raw materials into decoction pieces for use in different therapies based on traditional Chinese medicine (TCM). Processing of crude drugs into decoction pieces is a precious heritage and traditional practice in China, which plays an important role in disease prevention and treatment. The Chinese medicinal materials (CMM) originate from plants, animals, or minerals must undergo appropriate treatments before use as a decoction or other TCM preparations. The Chinese herbal property theory, one of the basic theories in TCM, provides directions for the clinical use of herbs. This theory classifies Chinese herbal properties into four natures, five flavors, ascending or descending, floating or sinking, channel tropism, and toxicity [1]. According to this theory, herbs have special affinities to certain organs and channel systems of the body, and exhibit special effects on diseases of these systems and organs [2]. The potency and toxicity of these herbs may be standardized by processing them according to their characteristics and clinical purpose. Traditional methods, such as stir-frying and steaming, are widely used in herb-processing to prevent exaggerated pharmacological actions, alleviate side effects, modify energy properties (nature, flavor, and channel tropism), mask disagreeable odors, or prolong the shelf-life of crude herbs [3]. Adjuvants are often added to enhance therapeutic effects or minimize drug toxicity, thereby broadening the spectrum of clinical application of the processed drugs. Commonly used adjuvants include vinegar, honey, wine, brine, ginger juice, bran, and rice. Drugs are processed with selected adjuvants based on their specific properties—frying with vinegar adds to the liver-soothing and analgesic effects of drugs, and honey confers Qi-nourishing and lung-moistening effects. Accordingly, the source and quality of adjuvants notably affect the efficacy of processed drugs. The Chinese Pharmacopoeia (2015 edition) lists 117 decoction pieces that are processed with various adjuvants, accounting for 55% of the total number of listed drugs [4]. Compared to simple heat treatment, addition of adjuvants allows tailored enhancement of therapeutic properties of drugs. However, it also complicates the standardization of drug processing methods. Despite being officially described in the Chinese Pharmacopoeia, standards of quality control for processing adjuvants and processed drugs are still lacking. Zhao et al. have discussed the various problems in CMM processing, and emphasized that traditional processing procedures need to be further organized, validated and implemented with scientific understanding to safeguard the quality of decoction pieces [3].

Processing makes TCMs different from other oriental and Western herbal medicines. However, classical TCM theories emphasize on the holistic understanding of diseases and drugs,

instead of studying their isolated details. Though classic processing theory and methods have been proven reasonable and reliable in the long-standing clinical practice of TCM, the underlying scientific principles remain largely unknown, affecting the production and use of decoction pieces. Standardization of processing methods, quality control of adjuvants, and related clinical studies were neglected in the past until serious drug misadventures occurred due to improperly processed herbs. Approximately 2396 of 12,354 (19.4%) adverse events, associated with TCM use between 1949 and 2008 in China, are reported to be ascribable to improper processing; besides, over 7000 cases of poisoning due to unprocessed aconitum plants have been reported in the past decade [5,6]. A multi-herb formula is therapeutically more beneficial than a single herb, due to its effects on multiple targets. Synergistic pharmacological effects are often observed with herbal medicines because plant extracts contain compounds that potentiate the action of each other [7]. We speculate that adjuvants similarly act to potentiate the pharmacological effects of drugs. However, identifying their targets at a molecular level is challenging. Fortunately, advanced analytical tools such as MS, NMR, high-throughput screening and omics, offer new avenues to conduct research on TCM at the cellular and molecular level [8]. Significant progress made in this direction in the past two decades necessitates a systematic review to summarize the accumulated knowledge. This review summarizes the commonly used adjuvants and their chemical, pharmacological, and pharmacokinetic mechanisms of synergistic potentiation of drug therapy as well as recent methodological approaches to identify these mechanisms.

2. Mechanisms of interaction between herbs and various processing adjuvants

2.1. Vinegar

Vinegar is consumed as a food condiment worldwide, especially in Chinese cuisines, and also has medicinal uses due to its physiological effects. Different types of vinegars contain organic acids, aldehydes, esters, alcohols, phenols, flavonoids, and ligustrazine [9]. Traditionally, vinegar is widely used in the processing of herbs that soothe the liver, relieve depression, prevent blood stasis, relieve pain, and act as purgatives.

Bupleuri Radix (Chaihu in Chinese), the dried root of Bupleurum falcatum L., is used as a herbal medicine in East Asia to treat influenza, common cold, fever, inflammation, malaria, and menstrual disorders [10]. Vinegar-baked Chaihu has a stronger effect than unprocessed Chaihu on soothing liver and relieving depression. Volatile oils and saikosaponins are the main active ingredients of Chaihu. Baking in vinegar is reported to significantly decrease the content of volatile oils and other antipyretic and anti-inflammatory components, including

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