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### **Review Article**

## An analysis of the combination frequencies of constituent medicinal herbs in prescriptions for the treatment of bone and joint disorder in Korean medicine: determination of a group of candidate prescriptions for universal use

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#### ABSTRACT

*Background*: This study aimed to select prescriptions (mixtures of medicinal herbs) used in the treatment of bone and joint disorders in Korean medicine, and through the analysis of medicinal herb combination frequencies, select a high-frequency medicinal herb combination group for further experimental and clinical research.

Methods: We systematically searched for terms related to bone and joint disorder in the "Dongeuibogam (Dong yibaojian)", a seminal Korean medicine book. We reviewed the results of published papers regarding the effects in bone and joint disorders (especially in osteoporosis, osteomalacia, osteopenia, rheumatoid arthritis, and degenerative arthritis).

Results and Conclusion: We selected 34 candidates of a medicinal herb combination and nine candidates of a medicinal herb for the treatment of bone and joint disorders.

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#### 1. Introduction

Natural products and their derivatives have historically been invaluable as a source of therapeutic agents.<sup>1</sup> Although their application is often viewed with skepticism by the Western medical establishment, they are used in ancient medical traditions such as Ayurveda and traditional Chinese medicine (TCM) which are a rich source of therapeutic leads for the pharmaceutical industry.<sup>2</sup> However, it is very difficult to get a 'discovery' from traditional medicine.<sup>2</sup>

This study is a kind of 'discovery', namely 'mining' from Korean medicine(KM) that is one of traditional medicine.

We aimed to sort candidates of medicinal herb combinations which have a high probability of treatment effect for more than one disorder among high morbidity rate disorders such as osteoporosis, osteomalacia, osteopenia, rheumatoid arthritis, and degenerative arthritis by analyzing constituent

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### **ARTICLE IN PRESS**

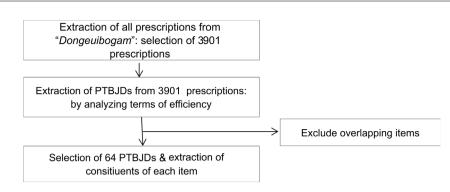


Fig. 1 – First research step; establishing a list of PTBJDs and constituents of each item in "Dongeuibogam". PTBJD, prescription for the treatment of bone and joint disorder.

herbs from prescriptions (mixtures of medicinal herbs) which are widely used for various kinds of bone and joint disorders (BJD) in KM.

Furthermore, in this study, the frequency of medicinal herb combinations comprising each prescription for the treatment of bone and joint disorder (PTBJD) was analyzed after selecting all of the prescriptions recorded in "Dongeuibogam (Dong yi bao gian)", a principal piece of Korean medicine literature, for the treatment of BJDs.

Although commonly used prescriptions for specific symptoms are fixed in Western medicine, the prescription could be different for individuals in KM since the prescriptions are customized based on patient's age, gender, etc. Therefore, many prescriptions exist for specific symptoms in KM, and that is why we combined all individual medicinal herbs from PTBJDs when analyzing the frequency of individual medicinal herbs and combinations of medicinal herbs from PTBJD.

#### 2. Materials and methods

This methodology assumed that the higher the dose within a PTBJD, the stronger the effect, and that the more frequently used medicinal herbs are in PTBJDs, the more important it is.<sup>3</sup>

In this paper, we found frequency of individual medicinal herbs and combinations of less than seven medicinal herbs from PTBJD in "Dongeuibogam" and made a list of high-ranked combinations.

By assessing the efficacy of the medicinal herbs of the combinations via analysis of previous studies, we would like to suggest preliminary data for experimental and clinical researchers to develop new herbal formulae for osteoporosis, osteomalacia, osteopenia, rheumatoid arthritis, and degenerative arthritis.

Since it is practically hard to develop herbal formulae using more than six medicinal herbs, the number of medicinal herbs is limited from one to six.

This study is comprised of three steps. Each step was performed as described in the following section.

## 2.1. Establishing a list of PTBJDs and constituents of each item in "Dongeuibogam"

According to the medical information website produced by the National Library of Medicine (MedlinePlus; https://www.nlm.nih.gov/medlineplus/), definitions of osteoporosis, osteomalacia, osteopenia, rheumatoid arthritis, and degenerative arthritis are "a condition that affects especially older women and is characterized by decrease in bone mass with decreased density and enlargement of bone spaces producing porosity and brittleness", "a disease of adults that is characterized by softening of the bones and is analogous to rickets in the young", "reduction in bone volume to below normal levels especially due to inadequate replacement of bone lost to normal lysis", "a usually chronic disease that is considered an autoimmune disease and is characterized especially by pain, stiffness, inflammation, swelling, and sometimes destruction of joints", and "arthritis typically with onset during middle or old age that is characterized by degenerative and sometimes hypertrophic changes in the bone and cartilage of one or more joints and a progressive wearing down of apposing joint surfaces with consequent distortion of joint position and is marked symptomatically especially by pain, swelling, and stiffness" respectively.

However, as there is no correspondent definition in "Dongeuibogam", we tried to select specific indications which are the most similar to symptoms of Western medicine by analyzing terms describing effects and selected all prescriptions which have one of the specific indications.

To sum up, in the first step, after selecting all of the prescriptions recorded in "Dongeuibogam", their indications were analyzed and the medicinal herbs constituting each of the PTBJD were selected (Fig. 1). Data of "Dongeuibogam" was obtained from a state-run website, "Korean traditional knowledge portal" (http://www.koreantk.com/ktkp2014/).

## 2.2. Selection of medicinal herb combinations from 64 PTBJDs in order of frequency

In the second step, the combinations with the highest repeat frequencies were selected as candidates of a medicinal herb combination for the treatment of bone and joint disorders (CMHCTBJD), and all medicinal herbs which comprise these combinations were selected as candidates of a medicinal herb for the treatment of bone and joint disorders (CMHTBJD). Only the medicinal herbs with doses in the upper 80% cumulative proportion per prescription were included in the CMHCTBJD

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