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Quality Evaluation of Multicomponent Medicines Using Mahalanobis Distance

– Examination of Design Process of Unit Space –

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1. Introduction

Kampo and other medicines derived from natural substances are multiple-component drugs (referred to below as multicomponent medicines). The quantitative and qualitative profiles of these medicines vary according to geological and ecological factors, the time, place, and year of harvest, the weather conditions under which they were grown, and other factors (all of which will be referred to below as environmental factors), and the variations are greater than in single-component medicines. Fixed quality standards are therefore established to guarantee the safety and effectiveness of multicomponent medicines, and quality of the medicines is evaluated on the basis of those standards. The quality standards currently in use for these quality evaluations are set on the basis of, for example, the included amount or amounts of one or more selected marker components characterizing the multicomponent medicine[1]. This method of evaluation, however, evaluates only a limited set of components, leaving many components unevaluated. Current quality tests may, accordingly, ascribe identical quality to preparations with different numbers of components or different quantities of these components. To supply medicines of higher quality, we are therefore studying quality evaluation methods that apply the Mahalanobis-Taguchi (MT) method to evaluate patterns with a wider range of medicine-characterizing components. Although there have been many reports of the use of correlation coefficients and the like to characterize multicomponent medicines numerically,[2)-5)] there are no reported examples of the use of Mahalanobis distance in relation to the characteristic patterns of medicines.

A related topic is the merits of simulation. Since the crude drugs used as raw materials are natural substances, the data employed are strongly affected by 'noise factors' such as differences between individual organisms and environmental factors. Furthermore, even after these differences and factors have been accounted for, they vary over time, so in order to keep the market supplied with products manufactured from such varying raw materials, variations over time must be dealt with. That is, differences due to temporal drift (i.e., years of good and bad harvest) within the extent that does not affect safety and effectiveness must be included, together with the effects of upward and downward drifts in the included quantities of the materials, and all this must be built into the unit space. In view of the above, the present report deals with methods of designing the unit space, which lies at the heart of this evaluation methodology.

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