PROCEEDING

Approach to novel functional foods for stress control
1. Toward structure-activity relationship and data mining of food compounds by chemoinformatics

Takashi Kinoshita, Zsolt Lepp, and Hiroshi Chuman

Department of Molecular Analytical Chemistry, Institute of Health Biosciences, The University of Tokushima Graduate School, Tokushima, Japan

Abstract : Over the past several decades, thousands of natural organic compounds have been isolated from foods, and the information about their structures and biological activities has been accumulated. Despite the long research history of food products and their potential great promise as a medicine and functional food, the systematic research and development have not been carried out extensively. For understanding of the comprehensive structure-activity relationship, we have developed the database system of flavonoids, which are frequently found in vegetables and fruits. We also plan to execute a virtual screening of flavonoids with antidepressant activity by using the database and an advanced chemoinformatic tool. In this section, we will briefly describe (1) flavonoid database and (2) virtual screening of antidepressant compounds. J. Med. Invest. 52 Suppl. : 240-241, November, 2005

Keywords **:** *antidepressant, flavonoid database, structure-activity relationship, support vector machine,*

COMPREHENSIVE DATABASE OF FLAVONOIDS

A group of flavonoid consists of approximately 4000 natural organic compounds with "flavonoid skeleton". Structural and biological information about flavonoids and their structurally related compounds was extracted from USDA Flavonoid Database (1), Functional Food Factors Database (2-4), National Cancer Institute Database (5), MDL Screening Compound Directory (6) and MDL Drug Data Report (6). The combined database, as shown schematically in Figure 1, now consists of about 8000 flavonoids ("extended flavonoids"). Molecular physicochemical parameters such as log *P* (*n*-octanol/water partition coefficient) and numbers of hydrogen bonding acceptors/donors are known to be definitely important in the structure-activity relationship and drug discovery. These quantities of each compound in the database were added as additional information. From this database, useful information is expected to be extracted by various softwares in chemoinformatics and computational chemistry. This database will be open to the public through Web as the University of Tokushima Food Database in near future.

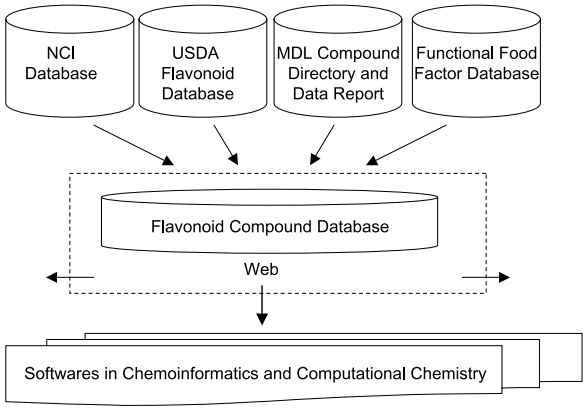

Figure 1. Overall architecture of flavonoid database system

Received for publication September 9, 2005 ; accepted September 16, 2005.

Address correspondence and reprint requests to Hiroshi Chuman, Ph.D., Department of Molecular Analytical Chemistry, Institute of Health Biosciences,The University of Tokushima Graduate School, 1-78, Shomachi, Tokusima 770-8505, Japan and Fax:+81-88-633-9508.

VIRTUAL SCREENING OF ANTIDEPRESSANT COMPOUNDS

The objective of virtual screening described here is to mine promising food compounds with antidepressant activity. However, the information concerning the activity of food compounds is very limited. On the other hand, an antidepressant medicine has been widely recognized as one of the most important therapeutic drugs and a huge number of studies about their structure and mechanism have been reported. Thus, our strategy approaching the aforementioned objective is to understand the structure-activity pattern relationship of medicinal drugs and to apply it to food compounds later. The result of the former part is briefly introduced here. One of emerging and promising statistical methods in the field of informatics is now Support Vector Machine (SVM) (7,8), which can be used for classification and regression in general multivariable problems. By using SVM with 39 structural descriptors, we carried out a virtual screening of more than 30,000 compounds against 21 target enzymes involved in antidepressant activity. It was found that 56-89 % of test compounds were assigned correctly to each target enzyme, as shown in Figure 2. Based on with this encouraging result, we will continue to work for deeper understanding of the structure-activity patter relationship and mining of a promising antidepressant food compound.

The flavonoid database and virtual screening mentioned above are reported in the subsequent papers. We will publish more details elsewhere.

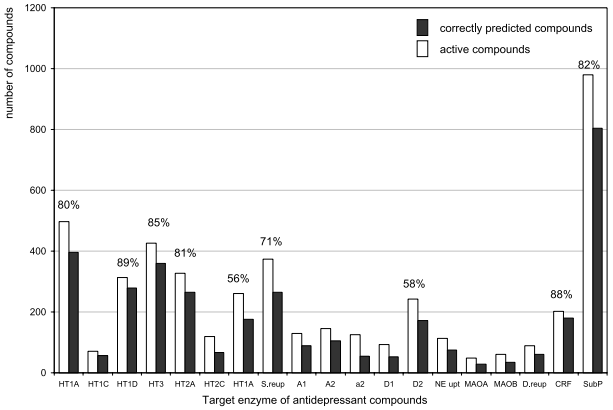

Figure 2. Success rate in prediction of antidepressant compounds by Support Vector Machine Success ratio (%) is shown in the top of the bar for each target enzyme with more than 200 active compounds.

REFERENCES

1. http://www.nal.usda.gov/fnic/foodcomp/Data/Flav/flav.html.
2. Watanabe S, Zhuo XG, Kimira M : "Food safety and epidemiology : new database of functional food factors". Biofactors 22 : 213-219, 2004
3. Zhuo XG, Watanabe S :"The construction of web database server-client system for functional food factors". Biofactors 22 : 329-332, 2004
4. http://www.life-science.jp/FFF/index.jsp.
5. http://dtp.nci.nih.gov/webdata.html.
6. The MDL Screening Compound Directory and Drug Data Report is available from MDL Information Systems Inc., San Leandro, CA94577, USA. http://www.mdl.com/.
7. Vapnik VN : "Statistical Learning Theory", John Wiley & Sons, New York, 1998
8. Chen N, Lu JY, Li G : "Support Vector Machine in Chemistry";World Scientific Publish-ing Co. Pte. Ltd., Singapore, 2004