國立交通大學

生物資訊研究所

碩 士 論 文

以計算方法探討抗氧化能力在補陽類中藥的

補益機轉中之角色

Computational characterization of the role of antioxidant

potential in the tonifying mechanism of

Yang-invigorating Chinese tonifying herbs

研 究 生：朱昭昉

指導教授：黃憲達 博士

中華民國 九十八 年 七 月

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研 究 生：朱昭昉　　Student：Chao-Fang Chu

指導教授：黃憲達　　Advisor：Hsien-Da Huang

國 立 交 通 大 學

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學生：朱昭昉　　　　　　　　　　　　　　　指導教授：黃憲達

國立交通大學 生物資訊研究所 碩士班

摘要

補益類中藥分為四類：補陰（Yin-nourishing）、補陽（Yang-invigorating）、補氣（Qi-invigorating）以及補血（Blood-enriching）。補陽類與補陰類中藥的特性，目前已知分別為刺激 ATP 的產生（ATP generation）以及免疫的調節作用（immunomodulatory activity）。然而，在補陽藥中卻發現了高度的抗氧化能力，而抗氧化能力被認為是一種陰的特性。這不合直覺，並且一直是個不解之謎。

在尋找補陽與補陰本質的過程中，在補陽藥裡並未找到共同的化合物，亦即能代表補陽作用的化合物。在我們使用支持向量機（SVM）的機器學習方法中，有一衍伸性的特徵，也就是每單位酚類化合物的 *ex vivo*（生物組織內、生物體之外）的抗氧化能力，可用來區分補陽藥與補陰藥。這顯示補陽藥、補陰藥本質上的差別，是在其單位抗氧化物質的 *ex vivo* 抗氧化能力。為了探討在粒線體中抗氧化能力以及生產 ATP 兩者之間的因果關係，以經過驗證之粒線體數學模型進行了模擬實驗，其模型範圍是粒線體的能量流轉以及自由基的代謝。粒線體系統的數學模型及代謝控制分析（MCA）之結果均指出，抗氧化作用對於 ATP 產生速率的影響有限。

本研究測試了抗氧化能力與產生 ATP 的因果關係；提出了一個全新的生化特徵，可用以區分補陽類與補陰類中藥；並且提出了補陽、補陰類中藥在中醫藥典中之所以被分為該類的可能原因。本研究的結果也顯示，現代中醫藥研究若要發掘出中醫藥的內在意義，必須築基於足夠的細胞或生理背景上。

Computational characterization of the role of antioxidant potential in the tonifying mechanism of Yang-invigorating Chinese tonifying herbs

Student: Chao-Fang Chu Advisor: Dr. Hsien-Da Huang

Institute of Bioinformatics and Systems Biology
National Chiao Tung University

ABSTRACT

Chinese tonifying herbs are classified into four categories: Yin-nourishing, Yang-invigorating, Qi-invigorating and Blood-enriching. Yang- and Yin-tonifying herbs are known to promote ATP-generation and exhibit immunomodulatory activity respectively. However, the high antioxidant activity, a supposedly Yin property, in Yang-tonifying herbs was counter-intuitive and remained an unresolved question.

In search of the essence of being Yang- and Yin-tonifying, common compounds present in and thus representative of Yang-tonifying herbs were not found. In our machine learning approach using support vector machine (SVM), the derived feature of *ex vivo* antioxidant activity divided by unit phenolic content was able to distinguish Yang- from Yin-tonifying herbs, suggesting that it is *ex vivo* antioxidant activity per unit antioxidants that is essentially different between Yang- and Yin-tonifying herbs. To characterize the causal relationship between antioxidant activity and ATP generation within mitochondria, simulations were performed using a validated mathematical model of mitochondrial energetics with ROS metabolism. Both mathematical modeling and metabolic control analysis (MCA) of the mitochondrial system showed a limited influence of antioxidation on ATP generation rate.

In the present study, the causal relationship between antioxidant activity and ATP-generation is examined, a novel biochemical feature distinguishing between Yang- and Yin-tonifying herbs presented, and a possible explanation of Yang- and Yin-tonifying herbs being categorized as such in TCM pharmacopoeia proposed. Results from this study also suggest that modern TCM investigations, in terms of TCM's essence, should be fruitful only if they are based on sufficient cellular or physiological context.

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國立交通大學　生物資訊研究所
碩士班研究生　朱昭昉
謹誌於 整合系統生物學實驗室（ISBLAB）
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1.1　Background

1.1.1　Yin vs. Yang: Core Theory in Traditional Chinese Medicine

Traditional Chinese medicine, in its unique understanding of pharmacology and human physiology, has effectively guided Chinese medical practitioners over thousands of years. In the core of TCM is the Yin-Yang theory, representing the dual qualities of matter; and a balance of Yin and Yang is essential to sustain optimal body function, akin to the modern concept of maintaining homeostasis. Counteractive properties such as water, coldness, stillness, inhibition and darkness belong to Yin, whereas those with proactive properties like fire, heat, movement, brightness, outward and upward direction, pertain to Yang (Liu et al., 1995, Ou et al., 2003). One instance to exemplify the Yin-Yang relationship is the association of decreased parasympathetic and sympathetic activities with the deficiency in Yin and Yang respectively in the human body, as shown in a psychophysiological study (Taitano, 2003).

1.1.2　Pharmacological Basis of Chinese Tonifying Herbs

Chinese tonifying herbs, or, according to the WHO International Standard Terminologies on Traditional Medicine in the Western Pacific Region (2007), “tonifying and replenishing medicinals” (code: 6.1.99) are “a category of medicinals that replenish the healthy qi and strengthen the body resistance, used for treating deficiency conditions."

These herbs are classified in TCM by their health-promoting actions into four tonifying categories: Yin-nourishing, Yang-invigorating, Qi-invigorating and Blood-enriching (Geng and Su, 1991). Yang- and Qi-tonifying herbs are further grouped in to the Yang family, whereas the Yin- and Blood-tonifying herbs are in the Yin family. Because of their potential in anti-aging remedies (**Figure 1**), much effort has been made to study the pharmacological basis of Yin- and Yang-tonifying herbs. An equivalence of antioxidation-oxidation to the action of Yin- and Yang-tonifying herbs was proposed (Ou et al., 2003), but was not supported by data on DNA protection against oxidative stress (Szeto and Benzie, 2006). Other studies on

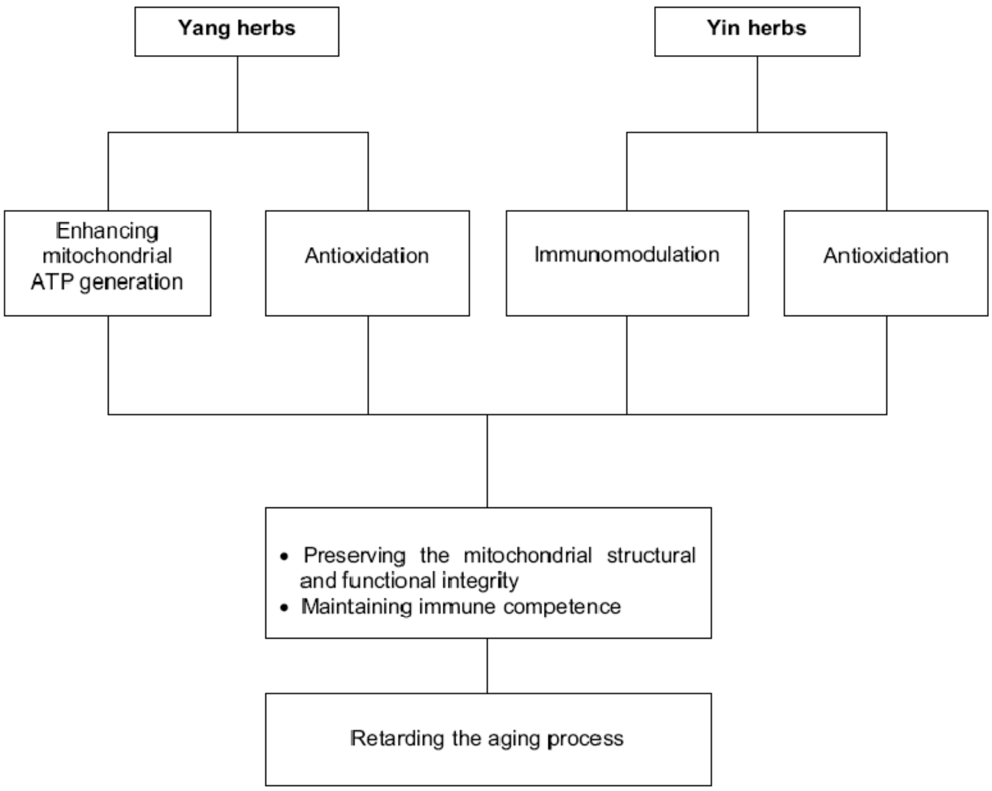

Figure 1. The currently accepted anti-aging rationale of Chinese tonifying herbs. (Ko and Leung, 2007)

Yang-tonifying herbs reported protective effects and enhancement of antioxidant status in human or rats (Mak et al., 2004, Leung et al., 2005, Chiu et al., 2008, Poon et al., 2008), indicating that antioxidant potential plays a physiologically significant role in the actions of Yang-tonifying herbs.

Currently, the characteristic pharmacological property of Yang-tonifying herbs is identified to be enhancement of mitochondrial ATP generation capacity (Yim and Ko, 2002, Ko et al., 2006, Ko and Leung, 2007).

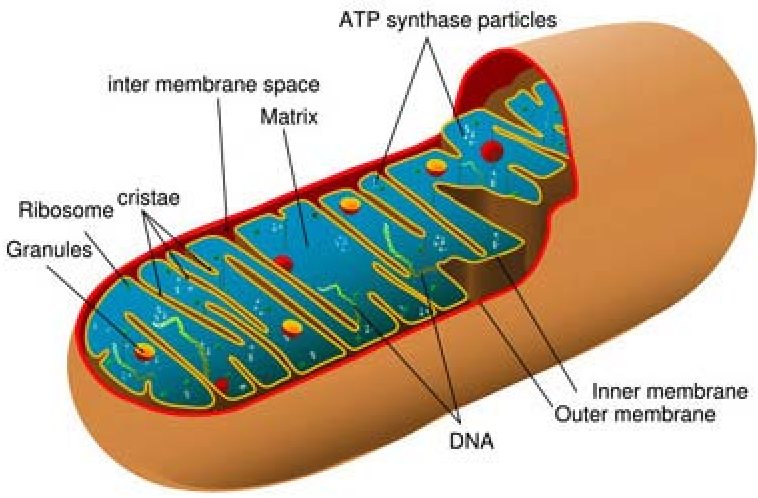

Figure 2. Simplified structure of a mitochondrion. This is a public-domain image.

1.1.3 Mitochondrial Energy Metabolism and Its Mathematical Models

Mitochondria are the main sites of ATP production in aerobic cells, containing two very different membranes, an outer one and an inner one, separated by the intermembrane space (**Figure 2**). The mitochondrion is a system with a level of complexity that needs computational modeling to aid in the study of mitochondrial energy metabolism (Wu et al., 2007). Therefore, numerous mathematical models based on experimental data and thermodynamic relations have been proposed (Korzeniewski and Zoladz, 2001, Vendelin et al., 2000, Cortassa et al., 2003, Cortassa et al., 2004, Beard, 2005, Zhou et al., 2005, Cortassa et al., 2006, Wu et al., 2007). Some of these models were expanded and modified, including the one expanded with reactive oxygen species production and scavenging (Cortassa et al., 2004, Cortassa et al., 2006, Wu et al., 2007). Since ROS production and scavenging are closely linked oxidative phosphorylation and hence ATP production (**Figure 3**), this Cortassa's model with ROS metabolism would be very valuable in studying the effect of antioxidant status in mitochondrial ATP generation.

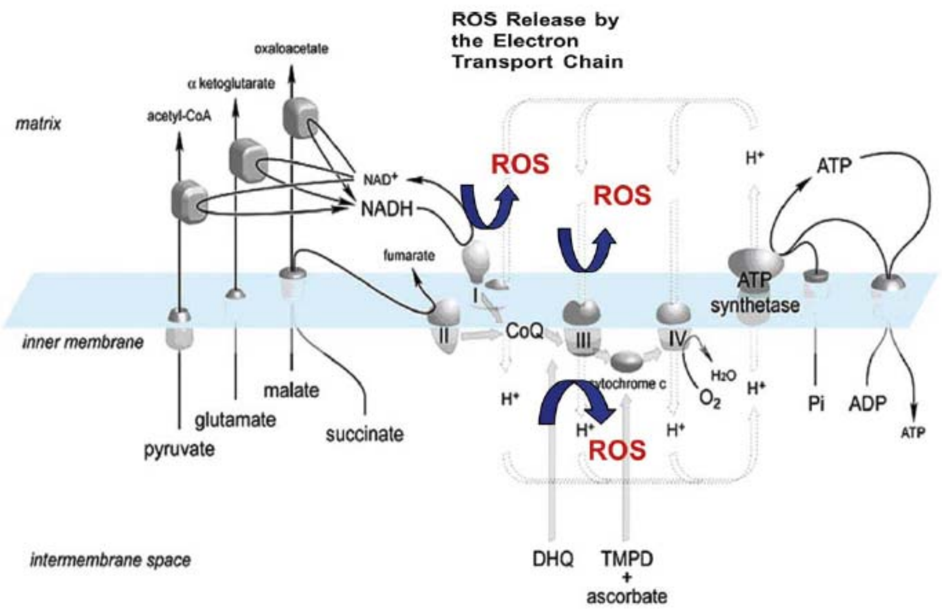

Figure 3. The integration of steps necessary for oxidative phosphorylation and the generation of ROS. (Sedensky and G. Morgan, 2006)

1.2 Motivation

1.2.1 The Counter-intuitive Presence of Antioxidant Potentials in Yang-tonifying Herbs

It is counter-intuitive for antioxidant potentials, which are considered a "Yin" property (Ko et al., 2004), to be present and even prevalent in "Yang"-tonifying herbs. Though antioxidant defense is known to be essential in sustaining mitochondrial ATP-generation (Melov, 2002), it remains a pharmacologically valuable question whether mitochondrial ATP generation is enhanced directly by accelerating the mitochondrial respiratory chain and/or indirectly by boosting mitochondrial antioxidant status (Ko et al., 2004, Ko et al., 2006).

1.2.2 Unresolved Systemic Roles of Antioxidant Potential in Yang-tonifying Herbs

The source of stimulated ATP generation was reported to be possibly caused by heightened activities of complex I and III (Leung, 2006, Leung and Ko, 2008) and antioxidation was not found to play a primary role in stimulating ATP generation (Ko et al., 2006). However, whether antioxidant potential or varied ROS-scavenging activities may at least play an adjunct role in stimulating ATP generation is still elusive. How is the dynamics of ATP generation affected by an enhanced antioxidant status? What is the systemic role of antioxidation exerted by Yang-invigorating herbs within cells? Such a systems topic is best prospectively addressed *in silico*, i.e., by computational modeling of the biochemical system of interest. The mathematical model will be described in detail in Materials and Methods.

1.2.3 Summary

In summary, the present study is motivated by (1) that the coexistence of ATP-generation capacity and high antioxidant potentials in Yang-tonifying herbs remains to be reconciled; (2) that a cross-talk and better mutual understanding between Western and traditional Chinese medicine in the science community is necessary; and (3) that identification of the systemic roles of these Chinese tonifying herbs within a particular system (e.g., mitochondria) can provide additional criteria for functional quality assessment of Chinese herbal products.

1.3 Research Goals

The following are the three main goals of this study (**Figure 4**) :

1. Determine the causal relationship between antioxidation and mitochondrial ATP generation; that is, clarify whether antioxidant potential in Yang-tonifying herbs is simply Nature's protective measure against oxidative stress created by accelerated ATP synthesis, or is causally related to ATP synthesis.

2. Discover the mechanism behind different antioxidant potentials and ATP generation capacities between Yang- and Yin-tonifying herbs.

3. Propose a rationale for Yang- and Yin-tonifying herbs being categorized as such in TCM literature.

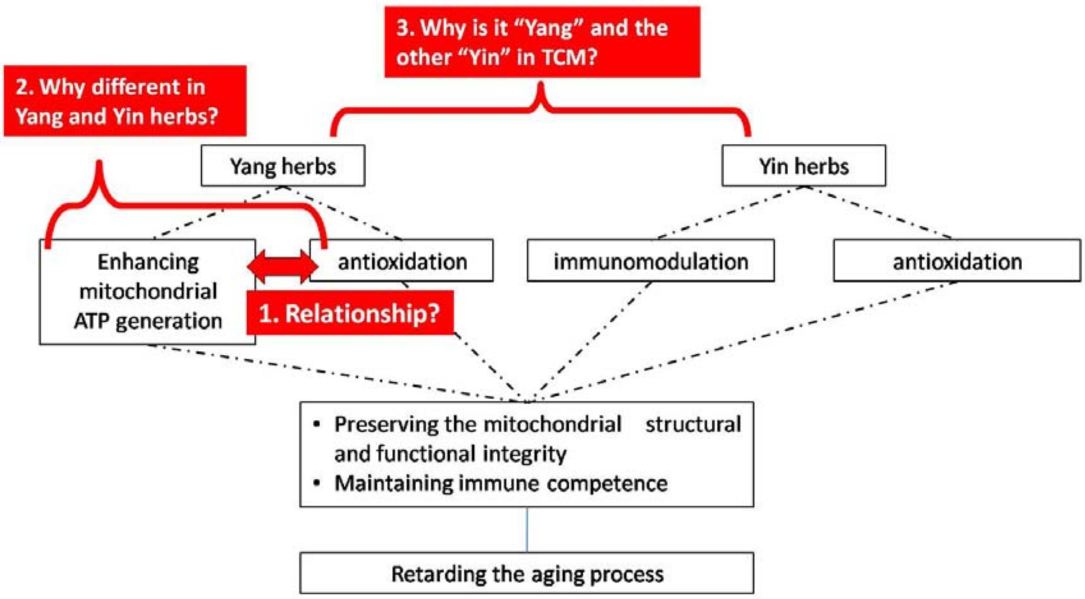

Figure 4. Research goals in the present study: answering these specific questions.

CHAPTER 2 MATERIALS AND METHOD

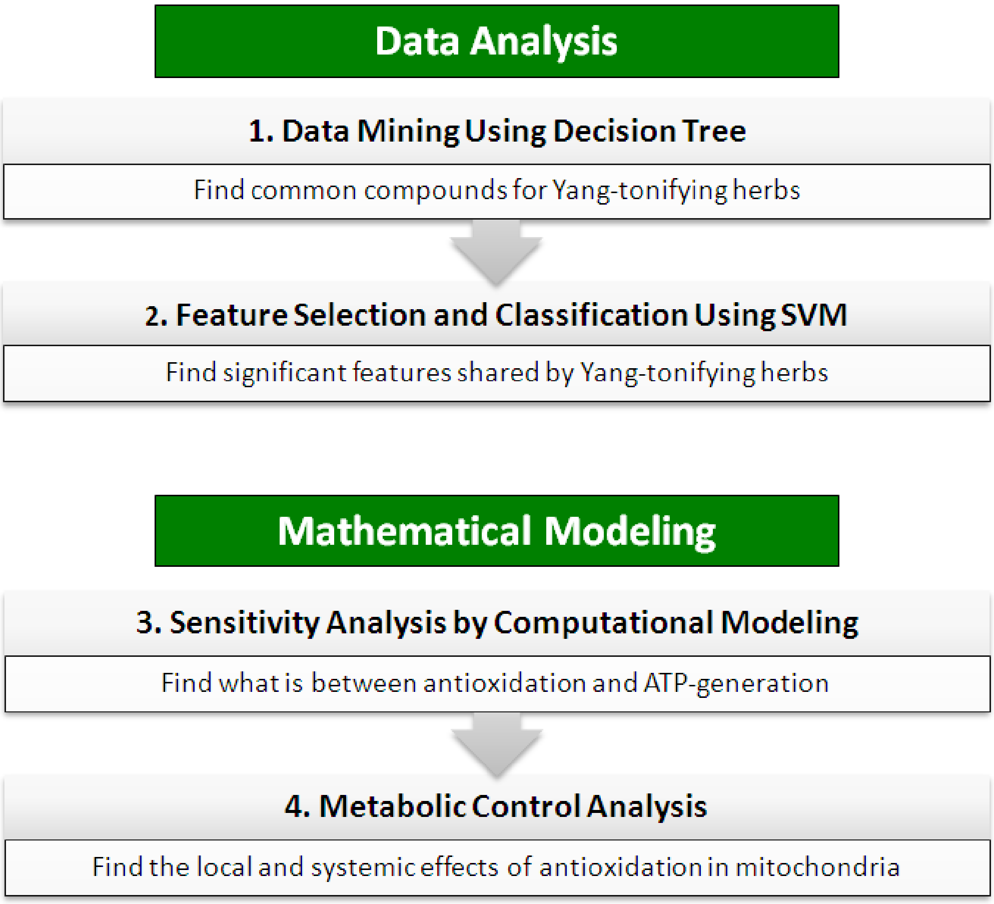

Figure 5. Scheme of analysis on the role of antioxidant activity in Yang-invigorating Chinese tonifying herbs.

The methods employed in this study are divided into two main parts: data analysis and mathematical modeling. The procedure is summarized in **Figure 5**.

2.1 Data Mining of Common Compounds Using Decision Tree

2.1.1 ID3 Decision Tree Algorithm

Decision tree is the classification method used to find common compounds in Yang-tonifying herbs. The structure of a decision tree is like a flow chart, where each internal node represents a test on an attribute, each branch the test outcome, and leaf nodes are the classes or class distributions (Han and Kamber, 2001). An example is the maximization of pay-off in investment decisions, as shown in **Figure 6**.

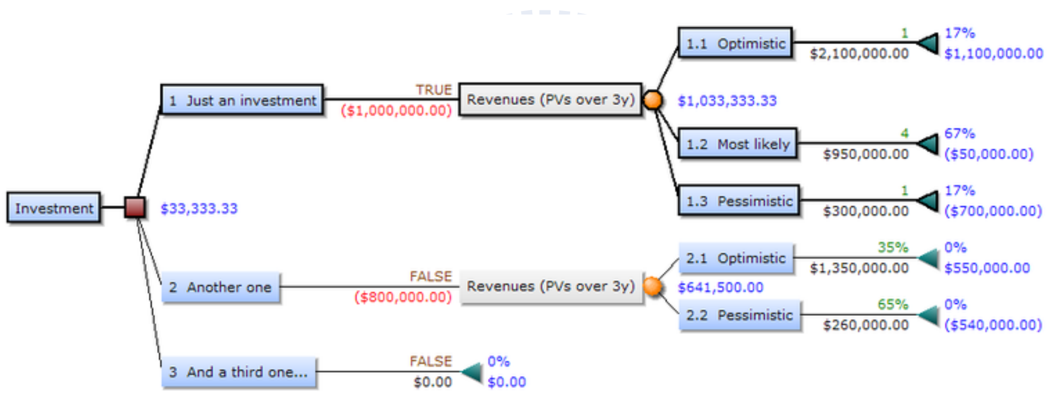

Figure 6. An example of decision tree. A public-domain image.

ID3 decision tree (Quinlan, 1986) is a well-known decision tree algorithm. Its basic strategy can be summarized as follows:

1. Take all unused attributes and calculate their entropies concerning test samples.
2. Choose an attribute for which the entropy is maximum.
3. Create a node that contains the attribute.

The algorithm of ID3 is shown in **Figure 7**.

Algorithm: Generate_decision_tree (ID3). Generate a decision tree from the training data.

Input: The training samples, *samples*; the set of candidate attributes, *attribute-list*.

Output: A decision tree.

Proecdure:

Create a node *N*.

if samples are all of the same class, *C* **then**

    return N as a leaf node labled with the class *C;*

if *attribute-list* is empty **then**

    return *N* as a leaf node labeled with the most common class in the *samples*// majority voting

select *test-attribute*, the attribute among attribute-list with the highest information gain;

label node *N* with *test-attribute*

for each known value a_i of the *test-attribute* // partition the samples

    grow a branch from node N for the condition *test-attribute* = a_i

    let s_i be the set of samples in samples for which *test-attribute* = a_i // a partition

    if s_i is empty **then**

        attach a leaf labeled with the most common class in samples

    else attach the node returned by Generate_decision_tree(s_i, *attribute-list-test-attribute);*

Figure 7. ID3 decision tree algorithm (Han and Kamber, 2001)

2.1.2 Data collection and preprocessing

Traditional Chinese Medicine Database System (2007) was accessed for the presence of chemical species in the Chinese tonifying herbs. A large list of chemical compounds associated with 65 Chinese tonifying herbs was collected (**Appendix A**).

The list was then condensed to the compounds present in a total of 40 Chinese tonifying herbs consisting of 9 Yin-, 12 Yang-, 10 Qi- and 9 Blood-tonifying herbs (**Table 1**), of which the compound data appeared fuller and more credible. Data duplicates and errors, mainly typing errors and confused use of full-form with half-form characters, were manually corrected. In cases of data ambiguities, TCM pharmacopoeia were consulted.

Table 1. Forty Chinese tonifying herbs of which the chemical compounds were collected and analyzed for association with the category of tonifying actions.

No.	Category	Herbal Name	Chinese Name	No.	Category	Herbal Name	Chinese Name
1	Yin	Fructus Ligustri	女貞子	**21**	Yang	Semen Cuscutae	菟絲子
2	Yin	Herba Dendrobii	石斛	**22**	Qi	Radix Astragali	黃耆
3	Yin	Herba Ecliptae	墨旱蓮	**23**	Qi	Radix Codonopsis	黨參
4	Yin	Radix Asparagi	天門冬	**24**	Qi	Radix Fici	五指毛桃
5	Yin	Radix Ophiopogonis	麥門冬	**25**	Qi	Radix Glycyrrhizae	甘草
6	Yin	Radix Oryzae	糯稻根	**26**	Qi	Radix Pseudostellariae	太子參
7	Yin	Radix Rehmanniae	幹地黃	**27**	Qi	Fructus Ziziphi	大棗
8	Yin	Semen Prinsepiae	蕤仁	**28**	Qi	Radix Panacis quinquefolii	西洋參
9	Yin	Rhizoma Polygonati	玉竹	**29**	Qi	Rhizoma Atractylodis	白朮
10	Yang	Cortex Eucommiae	杜仲	**30**	Qi	Rhizoma Dioscoreae	山藥
11	Yang	Fructus Psoraleae	補骨脂	**31**	Qi	Radix Ginseng	人參
12	Yang	Herba Cistanches	肉蓯蓉	**32**	Blood	Fructus Mori	桑椹子
13	Yang	Herba Cynomorii	鎖陽	**33**	Blood	Radix Angelicae	當歸
14	Yang	Herba Epimedii	淫羊藿	**34**	Blood	Radix Polygoni	何首烏
15	Yang	Radix Dipsaci	續斷	**35**	Blood	Ramulus Visci	槲寄生
16	Yang	Radix Morindae	巴戟天	**36**	Blood	Fructus Lycii	枸杞子
17	Yang	Rhizoma Cibotii	狗脊	**37**	Blood	Radix Rehmanniae Peraparata	熟地黃
18	Yang	Rhizoma Curculiginis	仙茅	**38**	Blood	Semen Sesami	黑芝麻
19	Yang	Rhizoma Drynariae	骨碎補	**39**	Blood	Testa Dolichoris	扁豆衣
20	Yang	Semen Allii	韭子	**40**	Blood	Rhizoma Polygonati	黃精

2.1.3 Classification

ID3 decision tree, an unsupervised learning method, was used as the classifier to find the compounds common in Yang-tonifying herbs. The classification was implemented in Weka, a data mining software in Java (Witten and Frank, 2005). Leave-one-out cross-validation was used (k set to be equal to data size in k-fold cross-validation).

2.2 Data Mining of Useful Features Using Support Vector Machine

2.2.1 Support vector machines

Support vector machines (SVMs) are a set of related supervised learning methods used for classification and regression. They are used in a variety of applications such as text classification, facial expression recognition, gene analysis and many others. In SVMs, a special kind of rule called a linear classifier is first constructed, and then classifiers are produced with theoretical guarantees of good predictive performance, i.e., the quality of classification on unseen data. The theoretical foundation of SVMs is given by statistical learning theory. (Fradkin and Muchnik, 2000)

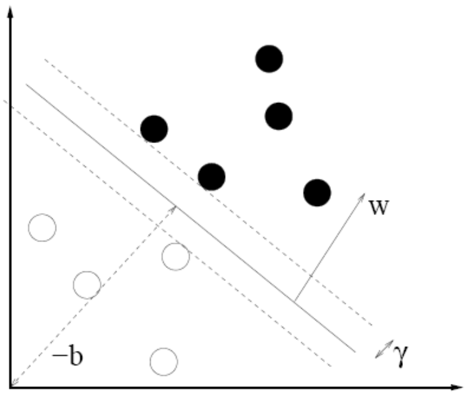

Figure 8. Definition of the margin in SVM learning method (Fradkin and Muchnik, 2006). White and black dots represent data from different classes.

A number of good reviews of SVMs with theoretical and mathematical details being freely available, a brief description of SVM is as follows (Fradkin and Muchnik, 2006):

First, w defines the separating hyperplane and γ the size of the margin (**Figure 8**).

A hyperplane

$$\langle w^*, x\rangle + b^* = 0;\ \|w^*\| = 1 \tag{1}$$

is called γ-margin separating hyperplane if

$$y_i(\langle w^*, x\rangle + b^*) \geq \gamma \tag{2}$$

for all (x_i, y_i) in set *S*. Here γ (clearly γ > 0) is the margin. Any separating hyperplane can be converted into this form.

Second, if the two classes are separable, maximize the margin. Since the probability of classification error is inversely proportional to the margin size, it is desired that the largest margin be found for a classifier which still correctly separates the training data.

The maximal-margin separating hyperplane can be found by solving the following optimization problem:

$$\text{Minimize}_{w,b}\ \langle w, w\rangle \tag{3}$$

subject to:

$$y_i(\langle w, x_i\rangle + b) \geq 1, \forall i = 1, \ldots, l \tag{4}$$

2.2.2 Data collection

Antioxidant activity and related data of Chinese tonifying herbs were collected from literature focused on numerous medicinal plants (Liu et al., 2001, Cai et al., 2006, Wong et al., 2006, Lee et al., 2003, Katalinic et al., 2006, Liao et al., 2007). Sources of raw data from literature are listed in **Table 2**.

Table 2. Sources of raw data that are subject to data preprocessing and analysis.

Data source	Data type	Number of entries
Liao et al., 2007	ORAC (mmol TE/g)	45
Yim and Ko, 2002	Yield (%`) of methanol extract; DPPH radical scavenging IC50 (mg/ml); Glutathione regeneration capacity (arbitrary unit); Immunomodulatory index *in vitro*; Immunomodulatory index *ex vivo*	36
Ko et al., 2006	ATP generation (% control)	37
Ko et al., 2006	Mitochondrial electron transport (% control)	12
Ko and Leung, 2007	ATP generation (% control)	19
Szeto and Benzie, 2006	DNA protection, ORAC value, DNA damage (% after H_2O_2 treatment compared to cells without treatment)	25
Wong et al., 2006	Total phenolic content of methanol extracts (GAE/g dry weight of plant material), total antioxidant power (µmol Fe(II)/g)	30

2.2.3 Data preprocessing

Discarding features with too few available entries led to a total of 8 features, including DPPH radical scavenging IC50 (mg/ml), glutathione regeneration capacity (arbitrary unit), immunomodulatory index *in vitro*, immunomodulatory index *ex vivo*, ATP generation (% control), mitochondrial electron transport (% control), total antioxidant power and total phenolic content. Data duplicates were removed and errors corrected by cross-checking the references.

Table 3 shows the original data of total phenolic content of Chinese tonifying herbs, sorted in descending order. The total amount of phenolics in Chinese medicinal plants (Wong et al., 2006) is generally higher in Yang- than in Yin-tonifying herbs, with one exception being *Radix Rehmanniae*. Unit of total phenolic content was expressed in gallic acid equivalents(GAE)/g dry weight of plant material. Latin bionomials were used to represent different medicinal plants.

Table 3. Original data of total phenolic content sorted in descending order.

Yang-tonifying herbs are colored red and Yin-tonifying herbs colored blue.

Category	Herbal Name	中藥名	Total phenolic content (GAE/g
Blood	Radix Polygoni	何首烏	24.2
Yang	Fructus Psoraleae	補骨脂	20.5
Yang	Radix Dipsaci	續斷	18.5
Yang	Herba Epimedii	淫羊藿	16.8
Yin	Radix Rehmanniae	幹地黃	15.8
Qi	Radix Glycyrrhizae	甘草	14.5
Yang	Herba Cistanches	肉蓯蓉	13
Yang	Herba Cynomorii	鎖陽	12.3
Blood	Rhizoma Polygonati	黃精	10.3
Blood	Fructus Lycii	枸杞子	8.42
Yang	Semen Cuscutae	菟絲子	6.69
Yang	Cortex Eucommiae	杜仲	4.99
Blood	Radix Angelicae	當歸	4.79
Yang	Rhizoma Curculiginis	仙茅	4.59
Qi	Radix Astragali	黃耆	3.87
Yang	Radix Morindae	巴戟天	3.71
Yin	Herba Dendrobii	石斛	2.97
Qi	Rhizoma Atractylodis	白朮	2.84
Yin	Radix Asparagi	天門冬	2.32
Qi	Rhizoma Dioscoreae	山藥	1.44
Yin	Rhizoma Polygonati	玉竹	1.39
Yin	Radix Ophiopogonis	麥門冬	1.31

Table 4 shows the original data of total antioxidant power in Chinese medicinal plants (Wong et al., 2006). As can be seen, the total antioxidant power is generally higher in Yang- than in Yin-tonifying herbs, with two exceptions being the Yin-tonifying *Radix Rehmanniae* and the Yang-tonifying *Radix Morindae*. Unit of total antioxidant power was expressed in μmol Fe(II)/g dry weight of plant material.

Table 4. Original data of total antioxidant power sorted in descending order. Yang-tonifying herbs are colored red and Yin-tonifying herbs colored light blue.

Category	Herbal Name	中藥名	Total antioxidant power (μmol Fe(II)/g dry weight of plant material)
Blood	Radix Polygoni	何首烏	302
Yang	Radix Dipsaci	續斷	95.6
Yang	Herba Epimedii	淫羊藿	81.8
Yang	Fructus Psoraleae	補骨脂	72.7
Yin	Radix Rehmanniae	幹地黃	67.2
Yang	Herba Cistanches	肉蓯蓉	62.8
Yang	Herba Cynomorii	鎖陽	51.7
Qi	Radix Glycyrrhizae	甘草	32.4
Blood	Rhizoma Polygonati	黃精	27.5
Blood	Radix Angelicae	當歸	27.3
Yang	Semen Cuscutae	菟絲子	21.7
Blood	Fructus Lycii	枸杞子	21.7
Yang	Cortex Eucommiae	杜仲	20.4
Yang	Rhizoma Curculiginis	仙茅	12.3
Yin	Radix Asparagi	天門冬	9.3
Yin	Herba Dendrobii	石斛	9.3
Qi	Radix Astragali	黃耆	9.1
Qi	Rhizoma Atractylodis	白朮	9
Yin	Radix Ophiopogonis	麥門冬	8.8
Yang	Radix Morindae	巴戟天	6.1
Qi	Rhizoma Dioscoreae	山藥	4.1
Yin	Rhizoma Polygonati	玉竹	3.6

Listed in **Table 5** are the glutathione regeneration capacities of 41 Chinese tonifying herbs (Yim and Ko, 2002). Data being also sorted in descending order, Yang- and Yin-tonifying herbs did not seem to differ much in GRC, which represents a measure of an *ex vivo* antioxidative effect.

2.2.4 Defining and Computing Derived Features

Since data of antioxidant power in both *in vitro* and *ex vivo* conditions and the amount of phenolics—the main source of antioxidants in medicinal plants—are available, a measure of unit antioxidant activity is calculable. Unit antioxidant activities will reflect effects the environment has on the antioxidant power.

The derived features are: (1) unit *in vitro* antioxidant ability, calculated from total antioxidant power divided by total phenolics; (2) unit *ex vivo* antioxidant ability, calculated from glutathione regeneration capacity divided by total phenolics; and (3) the "physiological factor," representing the relative change of antioxidant ability when the environment changes from *in vitro* to *ex vivo*, is defined to be the ratio of unit *ex vivo* over unit *in vitro* antioxidant ability just computed.

Following normalization of antioxidant activities and amount of phenolics for all the 40 herbs, the derived features were calculated for all entries with sufficient data. To preview their discrimination performance, the data were listed in descending order in **Table 6**, **Table 7**, and **Table 8**, with missing values left untreated until next step.

Among the three derived features, the Yang- and Yin-tonifying herbs form the clearest clusters when sorted unit *ex vivo* antioxidant activity, as in the case of original data of ATP generation capacity (**Table 9**).

Table 5. Original data of glutathione regeneration capacity sorted in descending order. Yang- and Yin-tonifying herbs are colored red and light blue respectively.

Category	Herbal Name	中藥名	Glutathione regeneration capacity (arbitrary unit)
Qi	Radix Glycyrrhizae	甘草	1707
Yang	Cortex Eucommiae	杜仲	1611
Blood	Semen Sesami	黑芝麻	1576
Qi	Radix Ginseng	人參	1555
Qi	Radix Astragali	黃耆	1550
Yang	Herba Epimedii	淫羊藿	1491
Yang	Fructus Psoraleae	補骨脂	1491
Yin	Fructus Ligustri	女貞子	1482
Yang	Radix Dipsaci	續斷	1433
Yin	Herba Ecliptae	墨旱蓮	1368
Blood	Radix Polygoni	何首烏	1350
Qi	Radix Codonopsis	黨參	1348
Qi	Fructus Ziziphi	大棗	1318
Blood	Testa Dolichoris	扁豆衣	1245
Qi	Radix Panacis quinquefolii	西洋參	1225
Qi	Rhizoma Atractylodis	白朮	1205
Yin	Herba Dendrobii	石斛	1190
Blood	Fructus Mori	桑椹子	1184
Blood	Radix Rehmanniae Peraparata	熟地黃	1179
Blood	Fructus Lycii	枸杞子	1167
Qi	Rhizoma Dioscoreae	山藥	1148
Yang	Rhizoma Cibotii	狗脊	1129
Qi	Radix Pseudostellariae	太子參	1125
Yin	Radix Asparagi	天門冬	1121
Yin	Radix Ophiopogonis	麥門冬	1106
Yang	Radix Morindae	巴戟天	1089
Yin	Semen Prinsepiae	蕤仁	1057
Yang	Herba Cistanches	肉蓯蓉	1035
Yang	Semen Cuscutae	菟絲子	1018
Yang	Rhizoma Drynariae	骨碎補	1015
Blood	Rhizoma Polygonati	黃精	993
Qi	Radix Fici	五指毛桃	982
Blood	Ramulus Visci	槲寄生	973
Yin	Rhizoma Polygonati	玉竹	969
Blood	Radix Angelicae	當歸	721
Yin	Radix Oryzae	糯稻根	674

Table 6. Unit *in vitro* antioxidant activity list in descending order.

No.	Category	Herbal Name	中藥名	Unit *in vitro* activity (arbitrary unit)
20	Blood	Radix Polygoni	何首烏	1
18	Yin	Radix Ophiopogonis	麥門冬	0.538294323
10	Blood	Radix Angelicae	當歸	0.45670478
14	Yang	Radix Dipsaci	續斷	0.414089851
9	Yang	Herba Epimedii	淫羊藿	0.390168716
5	Yang	Herba Cistanches	肉蓯蓉	0.387101375
26	Yin	Radix Rehmanniae	幹地黃	0.340816498
6	Yang	Herba Cynomorii	鎖陽	0.336816885
1	Yang	Cortex Eucommiae	杜仲	0.327595589
11	Yin	Radix Asparagi	天門冬	0.321220598
4	Yang	Fructus Psoraleae	補骨脂	0.284177031
34	Yang	Semen Cuscutae	菟絲子	0.259921401
28	Qi	Rhizoma Atractylodis	白朮	0.253940864
7	Yin	Herba Dendrobii	石斛	0.250919794
31	Qi	Rhizoma Dioscoreae	山藥	0.228154893
30	Yang	Rhizoma Curculiginis	仙茅	0.214734017
39	Blood	Rhizoma Polygonati	黃精	0.213945863
40	Yin	Rhizoma Polygonati	玉竹	0.207537281
23	Blood	Fructus Lycii	枸杞子	0.206517123
12	Qi	Radix Astragali	黃耆	0.188425142
16	Qi	Radix Glycyrrhizae	甘草	0.179054579
17	Yang	Radix Morindae	巴戟天	0.131754164

Table 7. Unit *ex vivo* antioxidant activity listed in descending order.

No.	Category	Herbal Name	中藥名	Unit *ex vivo* activity (arbitrary unit)
18	Yin	Radix Ophiopogonis	麥門冬	11.96921522
31	Qi	Rhizoma Dioscoreae	山藥	11.30215453
40	Yin	Rhizoma Polygonati	玉竹	9.883046111
11	Yin	Radix Asparagi	天門冬	6.850140396
28	Qi	Rhizoma Atractylodis	白朮	6.015206647
7	Yin	Herba Dendrobii	石斛	5.680314175
12	Qi	Radix Astragali	黃耆	5.678094001
1	Yang	Cortex Eucommiae	杜仲	4.576957078
17	Yang	Radix Morindae	巴戟天	4.161365047
34	Yang	Semen Cuscutae	菟絲子	2.157265038
10	Blood	Radix Angelicae	當歸	2.133937012
23	Blood	Fructus Lycii	枸杞子	1.964900709
16	Qi	Radix Glycyrrhizae	甘草	1.668965517
39	Blood	Rhizoma Polygonati	黃精	1.366765062
9	Yang	Herba Epimedii	淫羊藿	1.258201523
5	Yang	Herba Cistanches	肉蓯蓉	1.128700825
14	Yang	Radix Dipsaci	續斷	1.098136449
4	Yang	Fructus Psoraleae	補骨脂	1.031111492
20	Blood	Radix Polygoni	何首烏	0.79086116

Table 8. Physiological factor listed in descending order.

No.	Category	Herbal Name	中藥名	Physiological factor (arbitrary unit)
31	Qi	Rhizoma Dioscoreae	山藥	49.53719977
40	Yin	Rhizoma Polygonati	玉竹	47.62058192
17	Yang	Radix Morindae	巴戟天	31.58431531
12	Qi	Radix Astragali	黃耆	30.1344818
28	Qi	Rhizoma Atractylodis	白朮	23.68743084
7	Yin	Herba Dendrobii	石斛	22.63796763
18	Yin	Radix Ophiopogonis	麥門冬	22.23544762
11	Yin	Radix Asparagi	天門冬	21.32534598
1	Yang	Cortex Eucommiae	杜仲	13.97136359
23	Blood	Fructus Lycii	枸杞子	9.51446875
16	Qi	Radix Glycyrrhizae	甘草	9.320987654
34	Yang	Semen Cuscutae	菟絲子	8.299682252
39	Blood	Rhizoma Polygonati	黃精	6.388368749
10	Blood	Radix Angelicae	當歸	4.672464813
4	Yang	Fructus Psoraleae	補骨脂	3.6284125
9	Yang	Herba Epimedii	淫羊藿	3.224762699
5	Yang	Herba Cistanches	肉蓯蓉	2.915775805
14	Yang	Radix Dipsaci	續斷	2.651927946
20	Blood	Radix Polygoni	何首烏	0.79086116

2.2.5 Filling in missing values

After data cleaning, the 6 features collected from literature plus the 3 derived features led to a final list of 9 features, which are summarized in **Table 10**. To fill in the missing values, either attribute mean or attribute median was used in the classification, producing two sets of results. Finally, a total of 21 herbs composed of 12 Yang-tonifying herbs and 9 Yin-tonifying herbs with 11 features were prepared for classification. Data with both kinds of filled missing value are shown in **Table 11** and **Table 12**).

Table 9. Original data of ATP generation capacity by each Chinese tonifying herb (% control).

No.	Category	Herbal Name	中藥名	ATP generation (% control)
16	Qi	Radix Glycyrrhizae	甘草	285
6	Yang	Herba Cynomorii	鎖陽	230
34	Yang	Semen Cuscutae	菟絲子	222
5	Yang	Herba Cistanches	肉蓯蓉	191
4	Yang	Fructus Psoraleae	補骨脂	175
1	Yang	Cortex Eucommiae	杜仲	157
32	Yang	Rhizoma Drynariae	骨碎補	154
30	Yang	Rhizoma Curculiginis	仙茅	149
17	Yang	Radix Morindae	巴戟天	142
33	Yang	Semen Allii	韭子	133
9	Yang	Herba Epimedii	淫羊藿	130
3	Blood	Fructus Mori	桑椹子	129
10	Blood	Radix Angelicae	當歸	126
14	Yang	Radix Dipsaci	續斷	120
23	Blood	Fructus Lycii	枸杞子	118
26	Yin	Radix Rehmanniae	幹地黃	117
20	Blood	Radix Polygoni	何首烏	114
12	Qi	Radix Astragali	黃耆(黃芪)	110
22	Blood	Ramulus Visci	槲寄生	106
38	Blood	Testa Dolichoris	扁豆衣	105
40	Yin	Rhizoma Polygonati	玉竹	102
18	Yin	Radix Ophiopogonis	麥門冬	102
2	Yin	Fructus Ligustri	女貞子	101
36	Blood	Semen Sesami	黑芝麻	100
11	Yin	Radix Asparagi	天門冬	98.2
35	Yin	Semen Prinsepiae	蕤仁	95.5
25	Qi	Radix Panacis quinquefolii	西洋參	93.5
21	Qi	Radix Pseudostellariae	太子參	88.3
24	Qi	Fructus Ziziphi	大棗	85.1
19	Yin	Radix Oryzae	糯稻根	85
31	Qi	Rhizoma Dioscoreae	山藥	84.2
28	Qi	Rhizoma Atractylodis	白朮	84.2
7	Yin	Herba Dendrobii	石斛	82.7
13	Qi	Radix Codonopsis	黨參	81.7
15	Qi	Radix Fici	五指毛桃	80.6
8	Yin	Herba Ecliptae	墨旱蓮	80.3

Table 10. Description of the total 9 features to be classified by SVM.

Feature	Biological Meaning	Brief Description of Measurement Method	Source	Reference
1. Glutathione regeneration capacity (arbitrary unit)	*Ex vivo* antioxidant activity	A mouse model of hepatic glutathione regeneration capacity is used. The prepared hepatic tissue homogenate from treatment and control groups is challenged with tBHP at 0.1 mM, and the time-dependent change in reduced glutathione (GSH) content is monitored.	Experimental	Yim and Ko, 2002
2. Immunomodulatory index *in vitro*	*In vitro* immunomodulatory activity	Murine splenocytes were cultured in medium, in the presence or absence of Con A, with or without herbal extracts.	Experimental	Yim and Ko, 2002
3. Immunomodulatory index *ex vivo*	*Ex vivo* immunomodulatory activity	Female Balb/c mice are randomly divided into groups of 3-5 animals an treated with the herbal extracts in the same way as in the *ex vivo* antioxidant activity assay.	Experimental	Yim and Ko, 2002
4. ATP generation (% control)	Myocardial ATP-generation capacity, an indirect measure of mitochondrial oxidative phosphorylation	Nucleus-free myocardial homogenate is harvested from adult male Balb/c mice in treatment and control groups as described in the reference. The ATP level is measured and estimated from the standard curve after incubating the homogenate with ADP solution for 10 min. at 37 ℃.	Experimental	Ko et al., 2006 Ko and Leung, 2007
5. Total antioxidant power	Antioxidant power per unit dry weight of plant material	Ferric-reducing antioxidant power assay was performed as described in the reference. After a 4-min reaction with FRAP reagent, absorbance of the mixture at 593 nm was recorded. Results were expressed in μmol Fe(II)/g dry weight of plant material.	Experimental	Wong et al., 2006
6. Total phenolic content		Folin-Ciocalteu method as described in reference was used to estimate total phenolics. After incubation with Folin-Ciocalteu reagent, absorbance at 765 nm was recorded.	Experimental	Wong et al., 2006
7. Unit *in vitro* activity	*In vitro* antioxidant activity per unit phenolic content	Total antioxidant power / Total phenolic content	Computational	
8. Unit *ex vivo* activity	Ex vitro antioxidant activity per unit phenolic content	Glutathione regeneration capacity / Total phenolic content	Computational	
9. Physiological factor	The factor influencing antioxidant activity from an *in vitro* to an *ex vivo* environment	Unit *ex vivo* activity / unit *in vitro* activity	Computational	

Table 11. Dataset for SVM classification with attribute means used to fill in missing values. All original data were normalized.

No.	Category	Herbal Name	Chinese name	Raw features (normalized): Glutathione regeneration capacity	Raw features (normalized): Immuno-modulatory index *in vitro*	Raw features (normalized): Immuno-modulatory index *ex vivo*	Raw features (normalized): ATP generation	Raw features (normalized): Total antioxidant power	Raw features (normalized): Total phenolic content	Derived features: Unit *in vitro* activity	Derived features: Unit *ex vivo* activity	Derived features: Phys. factor
1	Yin	Fructus Ligustri	女貞子	0.8682	0.5242	1.0000	0.3544	0.0650	0.1966	0.3308	3.3398	10.0969
2	Yin	Herba Dendrobii	石斛	0.6971	0.7697	0.8833	0.2902	0.0308	0.1227	0.2509	5.6803	22.6380
3	Yin	Herba Ecliptae	墨旱蓮	0.8014	0.5000	0.7056	0.2818	0.0650	0.1966	0.3308	3.3398	10.0969
4	Yin	Radix Asparagi	天門冬	0.6567	0.2121	0.6889	0.3446	0.0308	0.0959	0.3212	6.8501	21.3254
5	Yin	Radix Ophiopogonis	麥門冬	0.6479	0.5000	0.8000	0.3579	0.0291	0.0541	0.5383	11.9692	22.2355
6	Yin	Radix Oryzae	糯稻根	0.3948	0.2364	0.5389	0.2983	0.0650	0.1966	0.3308	3.3398	10.0969
7	Yin	Radix Rehmanniae	幹地黃	0.6566	0.4614	0.7576	0.4105	0.2225	0.6529	0.3408	3.3398	10.0969
8	Yin	Semen Prinsepiae	蕤仁	0.6192	0.5152	0.7722	0.3351	0.0650	0.1966	0.3308	3.3398	10.0969
9	Yin	Rhizoma Polygonati	玉竹	0.5677	0.4333	0.6722	0.3579	0.0119	0.0574	0.2075	9.8831	47.6206
10	Yang	Cortex Eucommiae	杜仲	0.9438	0.1394	0.5778	0.5509	0.0676	0.2062	0.3276	4.5770	13.9714
11	Yang	Fructus Psoraleae	補骨脂	0.8735	0.4303	0.6833	0.6140	0.2407	0.8471	0.2842	1.0311	3.6284
12	Yang	Herba Cistanches	肉蓯蓉	0.6063	0.2273	0.5278	0.6702	0.2080	0.5372	0.3871	1.1287	2.9158
13	Yang	Herba Cynomorii	鎖陽	0.7363	0.3310	0.6167	0.8070	0.1712	0.5083	0.3368	1.5866	4.7078
14	Yang	Herba Epimedii	淫羊藿	0.8735	0.1727	0.5444	0.4561	0.2709	0.6942	0.3902	1.2582	3.2248
15	Yang	Radix Dipsaci	續斷	0.8395	0.1273	0.5667	0.4211	0.3166	0.7645	0.4141	1.0981	2.6519
16	Yang	Radix Morindae	巴戟天	0.6380	0.6546	0.7278	0.4983	0.0202	0.1533	0.1318	4.1614	31.5843
17	Yang	Rhizoma Cibotii	狗脊	0.6614	0.0485	0.5389	0.5751	0.1564	0.4641	0.3370	1.5866	4.7078
18	Yang	Rhizoma Curculiginis	仙茅	0.7363	0.3310	0.6167	0.5228	0.0407	0.1897	0.2147	1.5866	4.7078
19	Yang	Rhizoma Drynariae	骨碎補	0.5946	0.1788	0.5444	0.5404	0.1564	0.4641	0.3370	1.5866	4.7078
20	Yang	Semen Allii	韭子	0.7363	0.3310	0.6167	0.4667	0.1564	0.4641	0.3370	1.5866	4.7078
21	Yang	Semen Cuscutae	菟絲子	0.5964	1.0000	0.8389	0.7790	0.0719	0.2765	0.2599	2.1573	8.2997

Table 12. Dataset for SVM classification with attribute medians used to fill in missing values. All original data were normalized.

No.	Category	Herbal Name	Chinese name	Raw features (normalized)						Derived features		
				Glutathione regeneration capacity	Immuno-modulatory index *in vitro*	Immuno-modulatory index *ex vivo*	ATP generation	Total antioxidant power	Total phenolic content	Unit *in vitro* activity	Unit *ex vivo* activity	Phys. factor
1	Yin	Fructus Ligustri	女貞子	0.8682	0.5242	1.0000	0.3544	*0.0308*	*0.0959*	*0.3212*	*9.0561*	*28.1928*
2	Yin	Herba Dendrobii	石斛	0.6971	0.7697	0.8833	0.2902	0.0308	0.1227	0.2509	5.6803	22.6380
3	Yin	Herba Ecliptae	墨旱蓮	0.8014	0.5000	0.7056	0.2818	*0.0308*	*0.0959*	*0.3212*	*8.3595*	*26.0242*
4	Yin	Radix Asparagi	天門冬	0.6567	0.2121	0.6889	0.3446	0.0308	0.0959	0.3212	6.8501	21.3254
5	Yin	Radix Ophiopogonis	麥門冬	0.6479	0.5000	0.8000	0.3579	0.0291	0.0541	0.5383	11.9692	22.2355
6	Yin	Radix Oryzae	糯稻根	0.3948	0.2364	0.5389	0.2983	*0.0308*	*0.0959*	*0.3212*	*4.1186*	*12.8218*
7	*Yin*	Radix Rehmanniae	幹地黃	*0.6912*	*0.5000*	*0.7389*	0.4105	0.2225	0.6529	0.3408	*1.0587*	*3.1062*
8	*Yin*	Semen Prinsepiae	蕤仁	0.6192	*0.5152*	*0.7722*	0.3351	*0.0308*	*0.0959*	*0.3212*	*6.4591*	*20.1078*
9	*Yin*	Rhizoma Polygonati	玉竹	0.5677	*0.4333*	*0.6722*	0.3579	0.0119	0.0574	0.2075	9.8831	47.6206
10	Yang	Cortex Eucommiae	杜仲	0.9438	0.1394	0.5778	0.5509	0.0676	0.2062	0.3276	4.5770	13.9714
11	Yang	Fructus Psoraleae	補骨脂	0.8735	0.4303	0.6833	0.6140	0.2407	0.8471	0.2842	1.0311	3.6284
12	Yang	Herba Cistanches	肉蓯蓉	0.6063	0.2273	0.5278	0.6702	0.2080	0.5372	0.3871	1.1287	2.9158
13	Yang	Herba Cynomorii	鎖陽	*0.6614*	*0.1788*	*0.5667*	0.8070	0.1712	0.5083	0.3368	*1.3013*	*3.8635*
14	Yang	Herba Epimedii	淫羊藿	0.8735	0.1727	0.5444	0.4561	0.2709	0.6942	0.3902	1.2582	3.2248
15	Yang	Radix Dipsaci	續斷	0.8395	0.1273	0.5667	0.4211	0.3166	0.7645	0.4141	1.0981	2.6519
16	Yang	Radix Morindae	巴戟天	0.6380	0.6546	0.7278	0.4983	0.0202	0.1533	0.1318	4.1614	31.5843
17	*Yang*	Rhizoma Cibotii	狗脊	0.6614	*0.0485*	*0.5389*	*0.5404*	*0.1712*	*0.5083*	*0.3368*	*1.3013*	*3.8635*
18	*Yang*	Rhizoma Curculiginis	仙茅	*0.6614*	*0.1788*	*0.5667*	0.5228	0.0407	0.1897	0.2147	*3.4871*	*16.2391*
19	*Yang*	Rhizoma Drynariae	骨碎補	0.5946	*0.1788*	*0.5444*	0.5404	*0.1712*	*0.5083*	*0.3368*	*1.1699*	*3.4734*
20	*Yang*	Semen Allii	韭子	*0.6614*	*0.1788*	*0.5667*	0.4667	*0.1712*	*0.5083*	*0.3368*	*1.3013*	*3.8635*
21	*Yang*	Semen Cuscutae	菟絲子	0.5964	*1.0000*	*0.8389*	0.7790	0.0719	0.2765	0.2599	2.1573	8.2997

2.2.6 Implementation

Data entries of Yang-tonifying herbs were used as the positive dataset and Yin-tonifying herbs as the negative dataset. Leave-one-out cross-validation was used. The performance of classifiers using features in different combinations was compared to disclose the ability of the various features to differentiate Yang- from Yin-tonifying herbs.

LIBSVM (Chang and Lin, 2001) is an integrated software for support vector classification, (C-SVC, nu-SVC), regression (epsilon-SVR, nu-SVR) and distribution estimation (one-class SVM). It also supports multi-class classification. The LIBSVM package was implemented in Weka, a data mining software in Java (Witten and Frank, 2005).

2.3 Sensitivity Analysis by Computational Modeling

2.3.1 Scope of the Model

To simulate the effects of oxidation and antioxidation, employed in the present study is a validated mathematical model of oxidative phosphorylation, tricarboxylic acid cycle and ion transport, mitochondrial ROS generation and scavenging system in cardiac myocytes (Cortassa et al., 2004, Cortassa et al., 2003) The diagrams of the original and expanded models are in **Figure 9** and **Figure 10**.

The expanded model is able to qualitatively and semiquantitatively reproduce experimental data concerning mitochondrial bioenergetics, Ca^{2+} dynamics, respiratory control (Cortassa et al., 2003), as well as the experimentally observed oscillations in mitochondrial membrane potential ($\Delta\Psi_m$), NADH and ROS production (Cortassa et al., 2004). The main reactive oxygen species (ROS) associated with the system of mitochondrial energetics include hydrogen peroxide (H_2O_2) and superoxide anions in either mitochondrial matrix ($O_2^{\cdot -}{}_m$) or cytoplasm (intermembrane space) ($O_2^{\cdot -}{}_i$).

Effects of antioxidant activities were simulated by instantly lowered concentrations of reactive oxygen species; rate of ATP production of ATP synthase reflects mitochondrial ATP generation capacity.

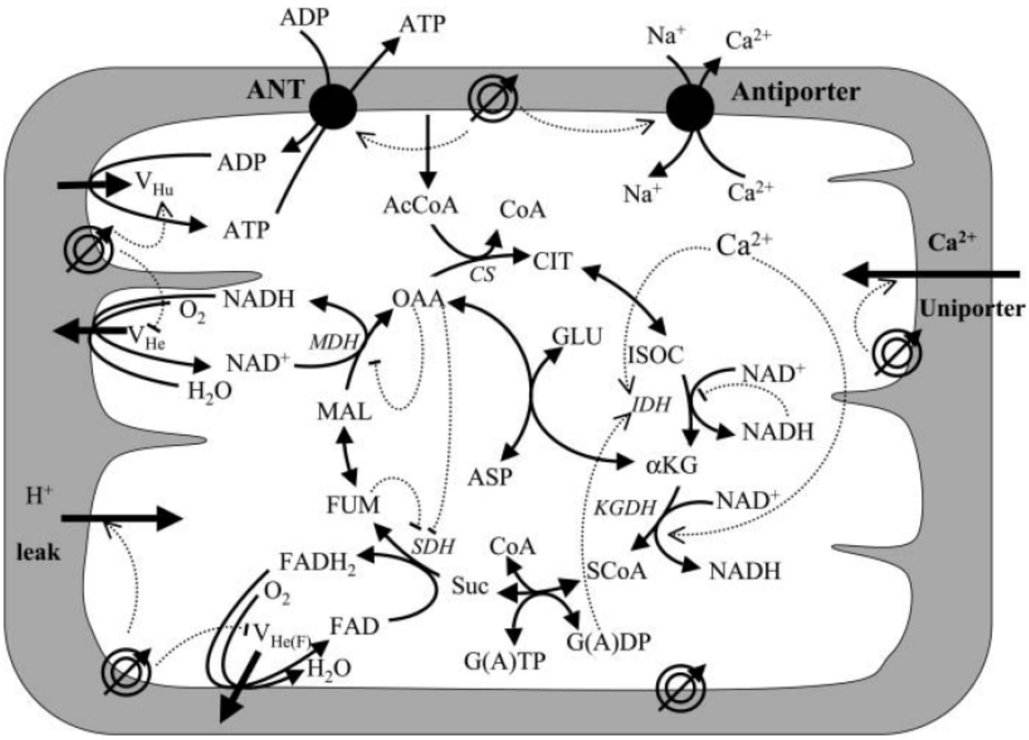

Figure 9. Diagram of Cortassa's previous model of mitochondrial energetics and calcium dynamics, before extension with ROS metabolism (Cortassa et al., 2003).

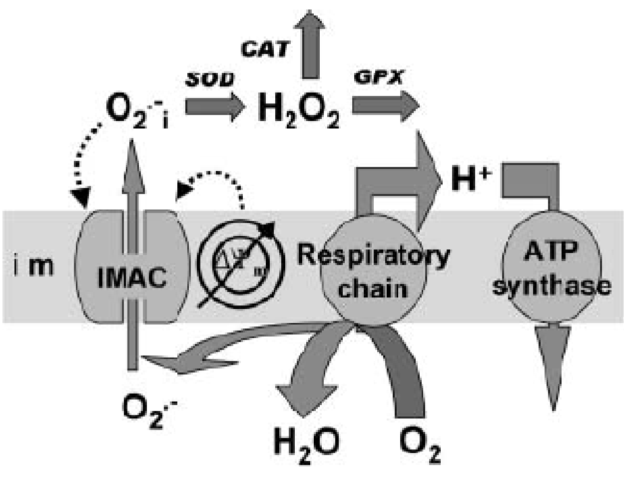

Figure 10. Diagram of Cortassa's model of mitochondrial metabolism extended with ROS production, transport and scavenging (Cortassa et al., 2004).

2.3.2 Sensitivity Analysis: Perturbation Studies

Sensitivity analysis is "the study of how the variation (uncertainty) in the output of a mathematical model can be apportioned, qualitatively or quantitatively, to different sources of variation in the input of a model (Cacuci, 2005)." In order to see whether ATP generation is causally related to mitochondrial antioxidant status, these two variables are set to be the output and input respectively.

The inputs in the present sensitivity analysis are: initial concentrations of hydrogen peroxide ($[H_2O_2]$), superoxide anions in mitochondrial matrix ($[O_2^{\cdot -}{}_m]$) and in cytoplasm (intermembrane space) ($[O_2^{\cdot -}{}_i]$), which were modified by one variable at a time, two variables at a time, and all three variables at a time. The output variables being monitored are (1) the rate of production of $O_2^{\cdot -}{}_i$, or V_{SO2m}; (2) the concentration of $O_2^{\cdot -}{}_i$; (3) the rate of production of ATP, or V_{ATPase} ; (4) the concentration of $O_2^{\cdot -}{}_m$; and (5) the concentration of H_2O_2. The basic elements of a sensitivity analysis, inputs and outputs, are summarized in **Table 13**.

Table 13. Summary of inputs and outputs in the sensitivity analysis performed.

Varied Inputs	Monitored Outputs
1. the concentration of $O_2^{-}{}_i$ at 0s	1. the rate of production of $O_2^{-}{}_m$ at 0s
2. the concentration of $O_2^{-}{}_m$ at 0s	2. the rate of production of ATP at 0s
3. the concentration of H_2O_2 at 0s	3. the rate of production of $O_2^{-}{}_m$ at various time points
4. the concentration of $O_2^{-}{}_i$ at 0s; the concentration of $O_2^{-}{}_m$ at 0s	4. the rate of production of ATP at various time points
5. the concentration of $O_2^{-}{}_m$ at 0s; the concentration of H_2O_2 at 0s	
6. the concentration of $O_2^{-}{}_i$ at 0s; the concentration of H_2O_2 at 0s	
7. the concentration of $O_2^{-}{}_i$ at 0s; the concentration of $O_2^{-}{}_m$ at 0s; the concentration of H_2O_2 at 0s	

The perturbation range was set to be -90% to +1000% of the value of the perturbed variable at reference point, covering a wide 1090% so that any observable trend in the outputs such as an asymptotic line or asymptotic surface could be obvious.

2.3.3 Implementation

All variables and parameters at the reference point for perturbation studies are from the original publication of the model (Cortassa et al., 2004), with corrections by referring to model codes requested from the author. The mathematical model was implemented in MATLAB® (Version 7.0.1.24704 (R14) Service Pack 1, The MathWorks, Inc., Natick, MA).

2.4 Metabolic Control Analysis

2.4.1 Rationale

Metabolic control analysis (Kacser and Burns, 1973, Heinrich and Rapoport, 1974) is a useful mathematical approach to quantitatively analyze how control of a pathway is shared among the contributing enzymes and modulators. Almost all original results of MCA are based on three main concepts: flux control coefficient (FCC), concentration control coefficient (CCC) and the elasticity (Torres and Voit, 2002).

The flux control coefficient of an enzyme, E_i, is a system property describing its effect on the steady-state flux J:

$$C_i^J = \frac{E_i}{J} \cdot \frac{\delta J}{\delta E_i} = \frac{\partial \ln J}{\partial \ln E_i} \tag{5}$$

Likewise, the concentration control coefficient of an enzyme $E_i$describes the effect of a change in enzyme E_i on the steady-state concentration of metabolite S_j:

$$C_i^{S_j} = \frac{E_i}{S_j} \cdot \frac{\delta S_j}{\delta E_i} = \frac{\partial \ln S_j}{\partial \ln E_i} \tag{6}$$

The above two control coefficients both characterize systemic properties of an enzyme, in which a slight local perturbation is related to a global system response. A crucial property uncovered by the MCA formalism is that the summation of all FCCs (all steps) of a pathway is equal to unity:

$$\sum_i C_{v_i}^J = 1$$

(7)

Moreover, the sum of all CCCs for a given reference metabolite concentration is equal to zero:

$$\sum_i C_{v_i}^{[M]} = 0$$

(8)

The summations above represent sums of all steps in the metabolic system. MCA was once well-described as being “not really a theory, but rather a formal model that allows the expression of parameters that describe, in quantitative terms, the global behavior of an enzyme system (Ricard, 1999).” Hence MCA is well-suited here to study the global effects of all antioxidation-related metabolites and enzymes on the steady-state of the mitochondrial energetics system.

On the other hand, the elasticity is a local property that relates a perturbation in metabolite S_j to the subsequent change in one particular reaction rate:

$$\varepsilon_{S_j}^{v_i} = \frac{S_j}{v_i} \cdot \frac{\delta v_i}{\delta S_j} = \frac{\partial \ln v_i}{\partial \ln S_j}$$

(9)

Elasticity is used here to study the local influence of antioxidation on ATP synthesis.

2.4.2 Implementation

MCA in the present study was performed by using COPASI 4.5 (Build 30) (Hoops et al., 2006), a simulator of biochemical systems. All initial concentrations of metabolites, parameter values and reaction kinetics were set according to Cortassa’s mitochondrial energetics model expanded with ROS metabolism (Cortassa et al., 2004), with corrections and tunings according to model codes requested from the author.

CHAPTER 3 RESULTS

3.1 Finding Common Compounds of Yang-tonifying Herbs by Decision Tree

As has been recognized as one pharmacological basis of the actions of Yang-tonifying herbs, ATP-generation capacity is shown by results of ID3 decision tree (**Table 14**) to be a crucial feature to distinguish Yang-tonifying herbs from other tonifying herbs. When ATP-generation is removed from the features, sensitivity of the classifier becomes as low as 20% for all four kinds of Chinese tonifying herbs, 31.6% for Yin- and Yang-tonifying herbs, and 51.4% for Yin and Yang families. The data of chemical compound names did not appear to be informative in distinguishing Yang-tonifying herbs from all Chinese tonifying herbs, Yang-tonifying from Yin-tonifying herbs, or herbs under the Yang family from those under the Yin family.

Table 14. Results of ID3 decision tree learning in order to find common compounds in Yang-tonifying herbs.

Features	Class	Sen.	Spe.	Pre.	Recall	F-measure	ROC Area
Chemical compounds plus ATP-generation capacity	Yin, Yang, Qi, and Blood	0.486	0.838	0.438	0.486	0.455	0.662
	Yin- and Yang-tonifying herbs	0.947	0.962	0.953	0.947	0.948	0.955
	Yin and Yang families	0.657	0.676	0.677	0.657	0.658	0.667
Chemical compounds only	Yin, Yang, Qi, and Blood	0.200	0.727	0.206	0.200	0.201	0.463
	Yin- and Yang-tonifying herbs	0.316	0.332	0.332	0.316	0.316	0.324
	Yin and Yang families	0.514	0.502	0.518	0.514	0.516	0.508

However, the specificity for all Chinese tonifying herbs after removal of the ATP-generation feature is still as high 72.7%, suggesting that the compounds list is still usable in rejecting false claims of tonifying actions.

In **Appendix B** are the full reports from ID3 decision tree algorithm

3.2 Finding Significant Features Shared by Yang-tonifying Herbs by SVM

Results of the supervised learning method SVM are shown in **Table 15**.

For the data normalized with respect to maximum values in all the four Chinese tonifying herbs, various combinations of the 6 original features produced a sensitivity of 57.1%, a specificity of 42.9%, and a precision 32.7%. After the derived features of unit *in vitro* and *ex vivo* activity were taken into consideration, the classifier produced sensitivities from 66.7% to 90.5%, specificities from 66.7% to 92.9%, and precisions from 67.3% to 92.2%. If only the derived features were considered, the classifier gave sensitivities from 71.4% to 90.5%, specificities from 73.0% to 92.9%, and precisions from 73.0% to 92.2%. The numbers clearly showed better classification results from derived features over the original features.

Moreover, considering unit *in vitro* antioxidant activity with unit *ex vivo* antioxidant activity only, without any other features, could have high accuracies over 90%; whereas the inclusion of physiological factor never made the classification accuracy to 80%, suggesting the physiological factor to be the least important among the three derived features.

Table 15. Results of SVM classification using different combinations numerical features.

No.	Filling missing value	GRC	I.I. *in vitro*	I.I. *ex vivo*	ATP generation	Total antioxidant power	Total phenolic content	Unit *in vitro* activity	Unit *ex vivo* activity	Phys. factor	Sen	Spe	Pre	Recall	F-measure	ROC Area
1		o	o	o	o	o	o				0.571	0.429	0.327	0.571	0.416	0.500
2		o				o	o				0.571	0.429	0.327	0.571	0.416	0.500
3	attribute	o				o	o	o	o		0.905	0.929	0.922	0.905	0.905	0.917
4	means	o				o	o	o	o	o	0.762	0.766	0.768	0.762	0.763	0.764
5								o	o		0.905	0.929	0.922	0.905	0.905	0.917
6								o	o	o	0.762	0.766	0.768	0.762	0.763	0.764
7		o	o	o	o	o	o				0.571	0.429	0.327	0.571	0.416	0.500
8		o				o	o				0.571	0.429	0.327	0.571	0.416	0.500
9	attribute	o				o	o	o	o		0.857	0.837	0.859	0.857	0.856	0.847
10	medians	o				o	o	o	o	o	0.667	0.667	0.673	0.667	0.668	0.667
11								o	o		0.857	0.837	0.859	0.857	0.856	0.847
12								o	o	o	0.714	0.730	0.730	0.714	0.716	0.722

3.3 Sensitivity Analysis by Computational Modeling of the Mitochondrial System

3.3.1 Perturbations of $[H_2O_2]$, $[O_2^{\cdot-}]_i$ and $[O_2^{\cdot-}]_m$ respectively

V_{ATPase} at 0s is unaffected by change in $[H_2O_2]$ (**Figure 11** and **Figure 12**). V_{ATPase} plunges fast in the first 10s of simulation time, levels off thereafter and appears intact under the perturbation of $[H_2O_2]$ (**Figure 13**). It is because the amplitude of change is small and the its value stays between $\pm$ 4×10^{-6} % (**Figure 14**).

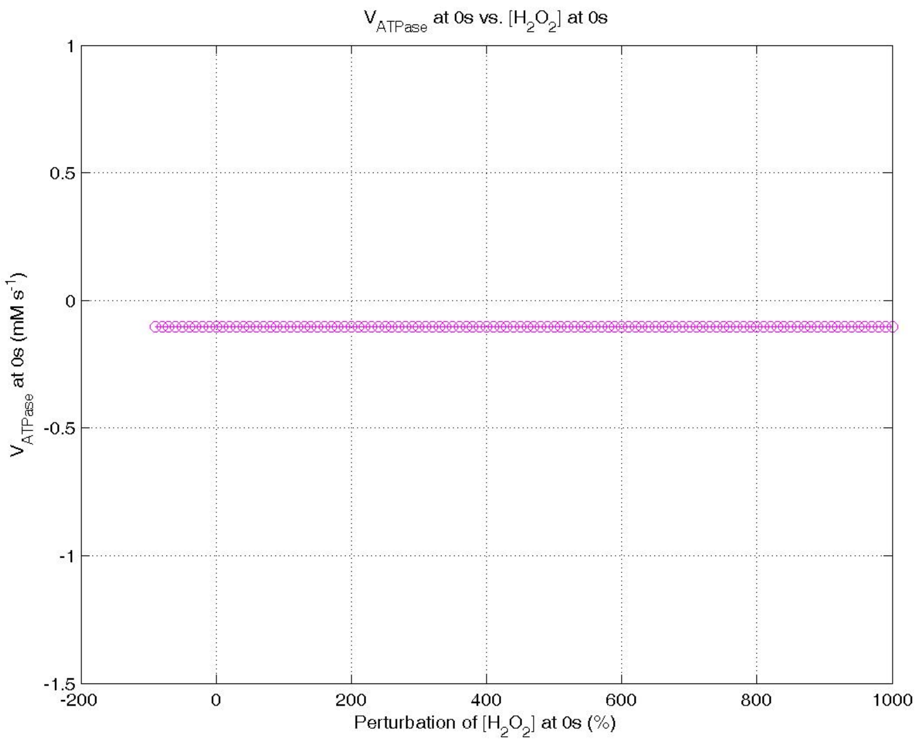

Figure 11. V_{ATPase} at 0s vs. $[H_2O_2]$ at 0s.

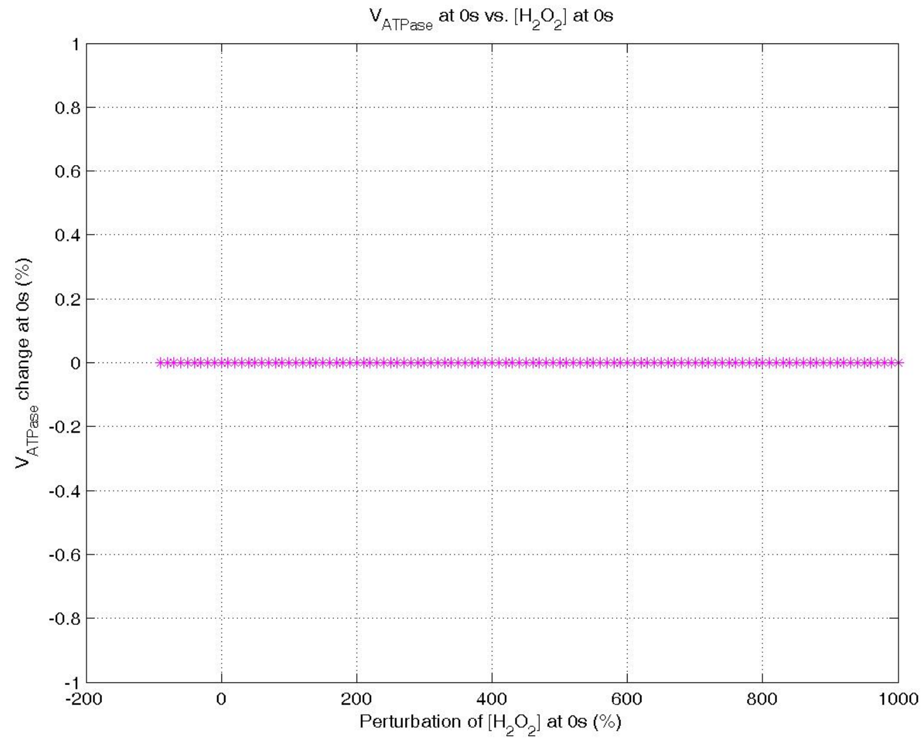

Figure 12. V_{ATPase} (% change) at 0s vs. $[H_2O_2]$ at 0s.

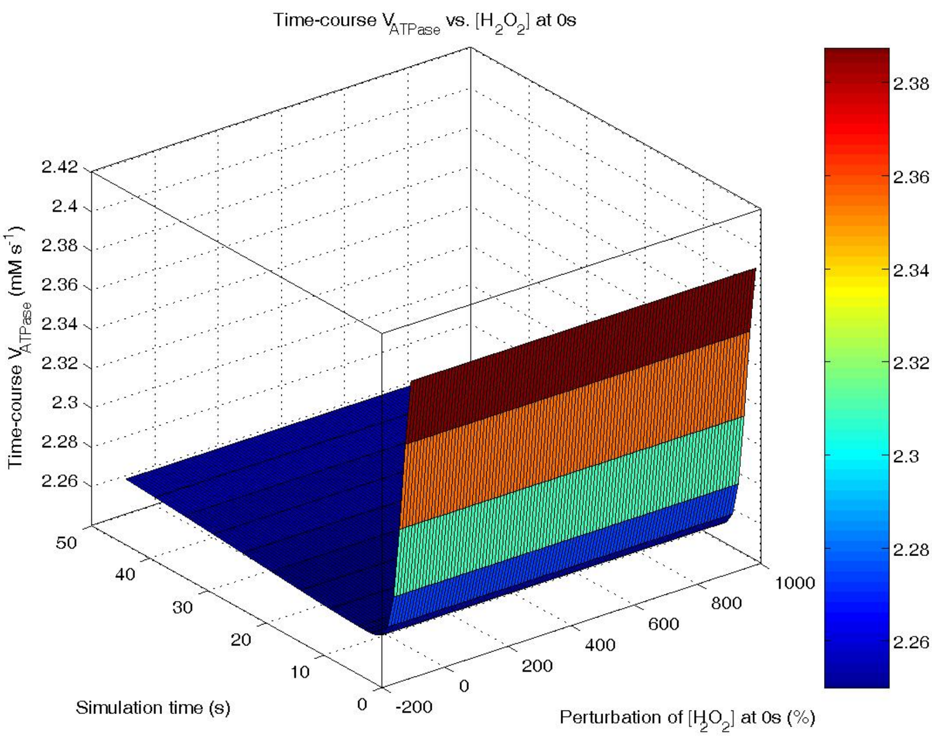

Figure 13. Time-course V_{ATPase} vs. $[H_2O_2]$ at 0s.

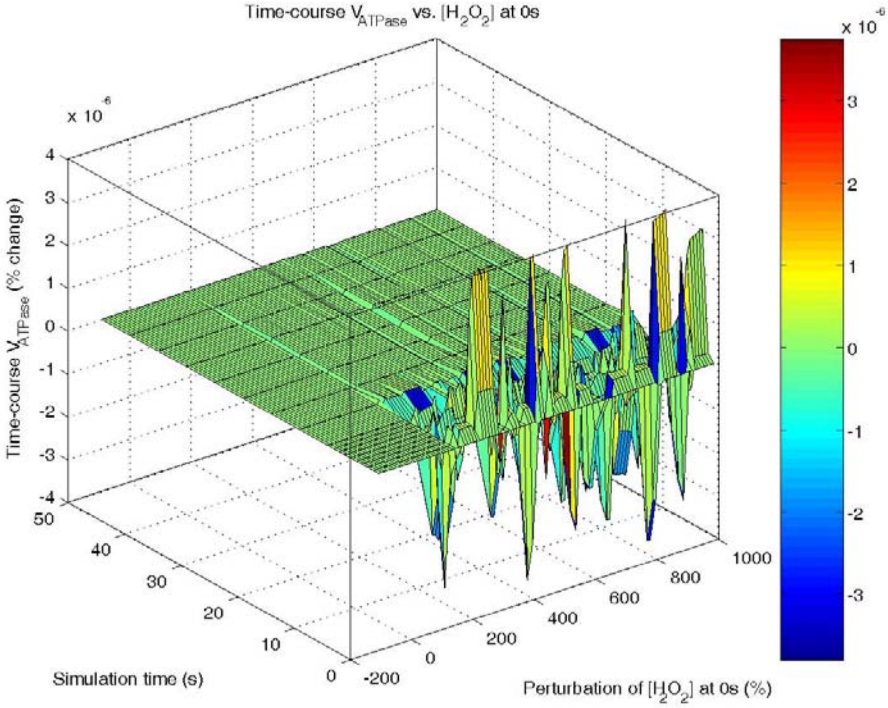

Figure 14. Time-course V_{ATPase} (% change) vs. $[H_2O_2]$ at 0s

Under various extents of $[O_2^{\cdot-}]_I$ perturbation, the time-course V_{ATPase} looks unaffected (**Figure 15**) but the amplitude (**Figure 16**) is around 10^{-2} %, which is four orders of magnitude higher compared with that from $[H_2O_2]$ perturbations.

The time-course V_{ATPase} still appears largely unaffected to perturbations in $[O_2^{\cdot-}]_m$ (**Figure 17**). V_{ATPase} actually inversely responds to perturbations in $[O_2^{\cdot-}]_m$ within the 2×10^{-7} to 5×10^{-7}% range, exhibiting a trend opposite to that under $[O_2^{\cdot-}]_i$ perturbations (**Figure 18**).

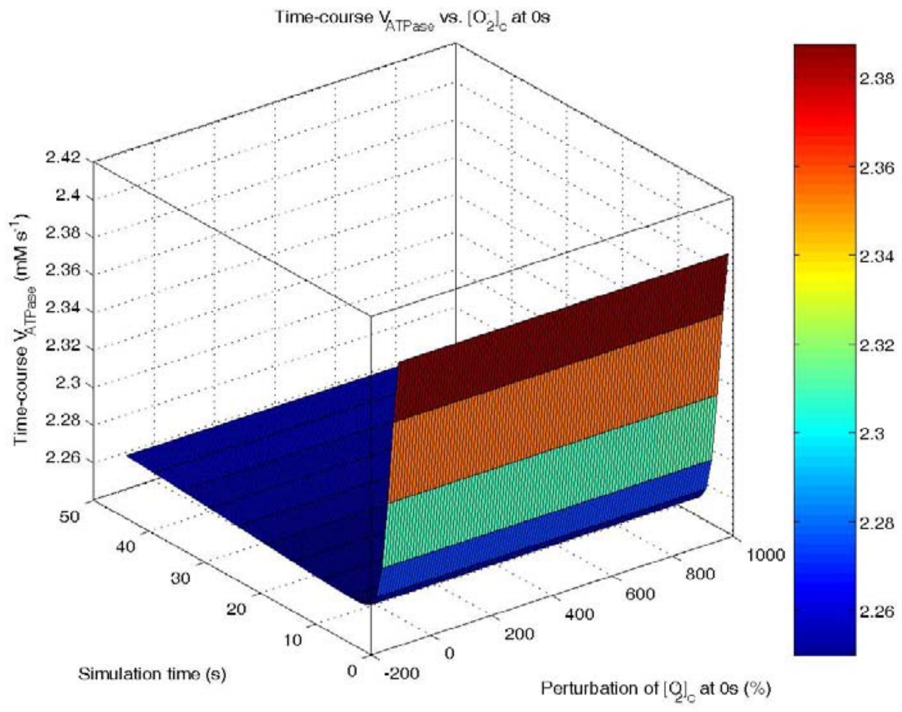

Figure 15. Time-course V_{ATPase} vs. $[O_2^{\cdot -}]_c$ at 0s

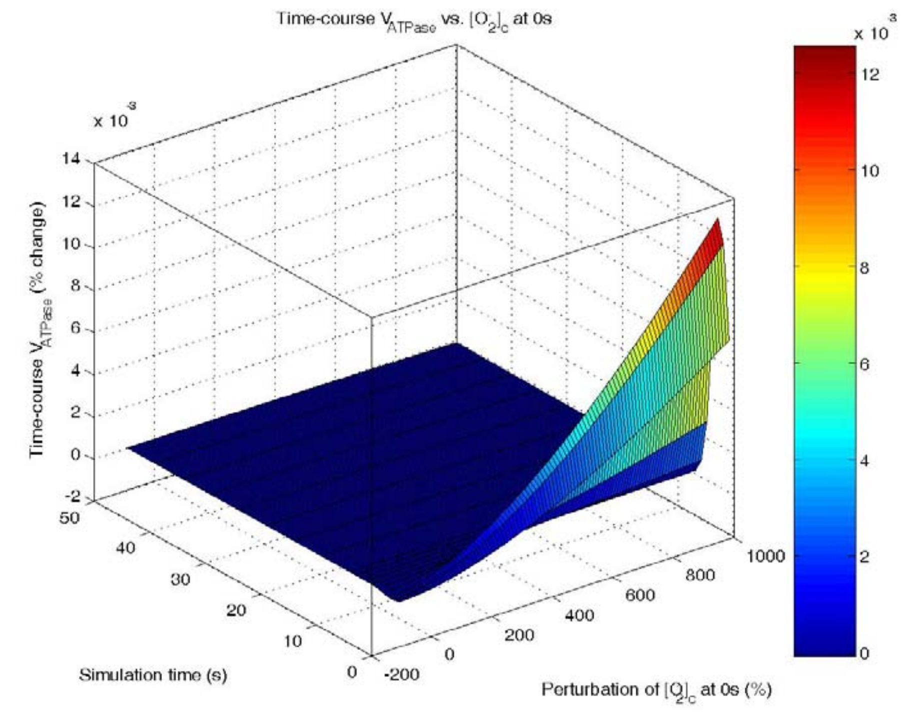

Figure 16. Time-course V_{ATPase} (% change) vs. $[O_2^{\cdot -}]_c$ at 0s

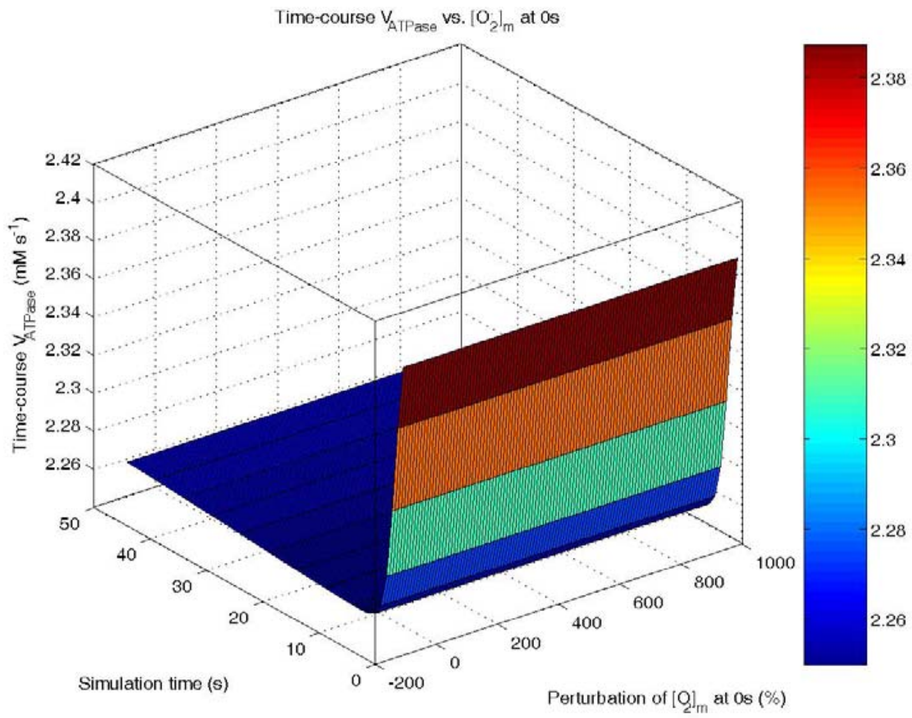

Figure 17. Time V_{ATPase} vs. $[O_2^{\cdot-}]_m$ at 0s

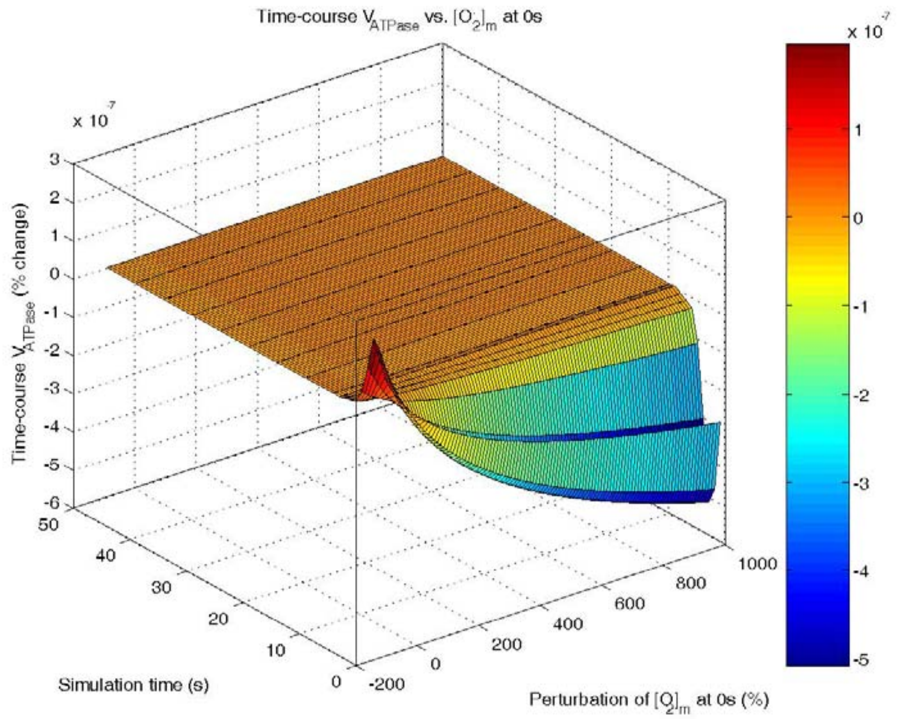

Figure 18. Time V_{ATPase} (% change) vs. $[O_2^{\cdot-}]_m$ at 0s

3.3.2 Perturbation of two and three metabolites at a time

As can be seen in **Figure 19**, the surface of time-course V_{ATPase} plotted against simulation time and percent perturbation of $[H_2O_2]$ and $[O_2^{\cdot-}]_m$ displays an overlap shape of the perturbation results from $[H_2O_2]$ and $[O_2^{\cdot-}]_m$.. However, when $[H_2O_2]$ and $[O_2^{\cdot-}]_c$ or $[O_2^{\cdot-}]_m$ and $[O_2^{\cdot-}]_c$ are perturbed together, the surface shapes are dominated by single-variable perturbation in $[O_2^{\cdot-}]_c$ (**Figure 20** and **Figure 21**).

Since no other behavior than additive effects is observed for multi-variable perturbations, it suggests that each of these three reactive oxygen species is independent in, if any, soliciting changes in V_{ATPase} instantly or subsequently. Therefore, the variable under perturbation to which V_{ATPase} is more sensitive, i.e., the percent change is higher, will dominate in multi-variable perturbations.

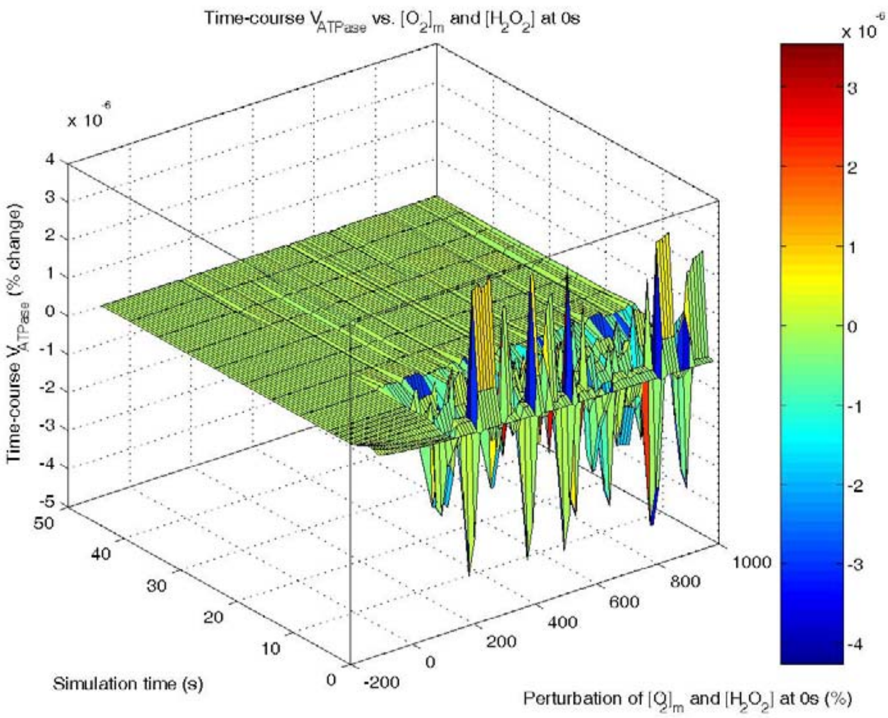

Figure 19. Time-course V_{ATPase} (% change) vs. $[O_2^{\cdot-}]_m$ and $[H_2O_2]$ at 0s.

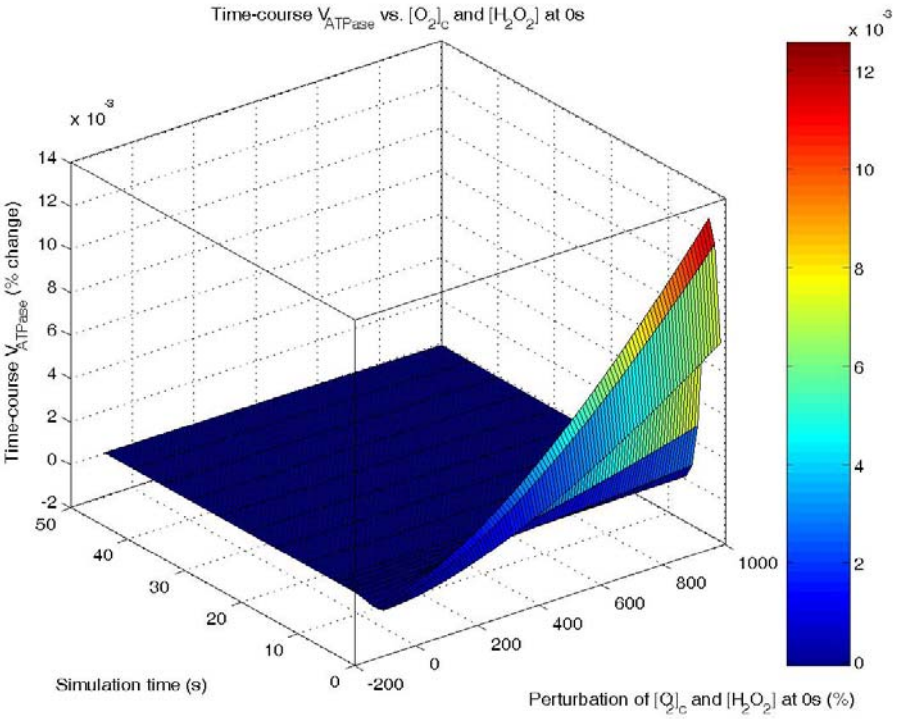

Figure 20. Time-course V_{ATPase} (% change) vs. $[O_2]_c$ and $[H_2O_2]$ at 0s.

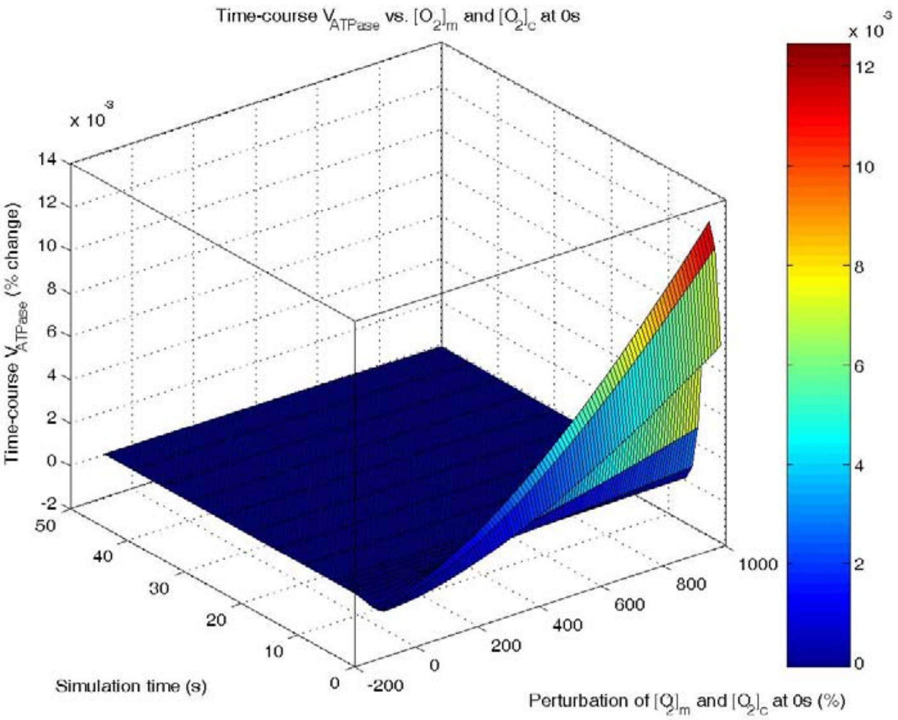

Figure 21. Time-course V_{ATPase} (% change) vs. $[O_2^{\cdot-}]_c$ and $[O_2^{\cdot-}]_m$ at 0s.

In terms of amplitude in the response of V_{ATPase}, perturbations in $[O_2^{\cdot -}]_i$ brings the greatest (10^{-3}–10^{-2}%), $[H_2O_2]$ brings smaller (10^{-6}–10^{-5}%), and $[O_2^{\cdot -}]_m$ brings the smallest change (10^{-7}–10^{-6}%). In terms of the relationship between metabolite perturbations and the response of V_{ATPase}, $[O_2^{\cdot -}]_i$ appears to be directly related, $[O_2^{\cdot -}]_m$ inversely related and $[H_2O_2]$ unrelated. A summary of their effects on V_{ATPase} is provided in **Table 16**.

Table 16. Summary of sensitivity analysis of ROS inputs on V_{ATPase} outputs.

Perturbed Metabolite (Perturbation Range = -90% to +1000%)	Order of Magnitude of Change in V_{ATPase} Output (%)	Relationship With Change of V_{ATPase} Output
$[O_2^{\cdot -}]_i$	10^{-3}–10^{-2}	Directly related
$[H_2O_2]$	10^{-6}–10^{-5}	Unrelated
$[O_2^{\cdot -}]_m$	10^{-7}–10^{-6}	Inversely related

3.4 Finding the Effects of Antioxidation on the Mitochondrial System by MCA

As shown in **Table 17**, the only variables that have non-zero elasticities for ATP synthesis are D_psi_m ($\Delta\Psi_m$, electric potential gradient across the mitochondrial membrane), $[ATP]_m$ and $[ADP]_m$. $\Delta\Psi_m$ has a positive elasticity on ATP synthesis, $[ATP]_m$ negative and $[ADP]_m$ positive. The elasticity of $\Delta\Psi_m$ on ATP synthesis is about 250 times the value of the elasticities of $[ATP]_m$ and $[ADP]_m$.

Table 18 shows the flux control coefficients. For ATP synthesis, the absolute values of all the FCCs fall in the range of 10^{-30} to 10^{-14}, indicating that, at the steady state found in the model, the flux of ATP synthesis is neither comparably sensitive to any particular reactions with non-zero FCCs nor absolutely sensitive to any of these reactions.

Concentration control coefficients are listed in **Table 19**. The enzymatic actions (reactions) that have positive CCCs on steady-state concentration of matrix ATP are oxidative phosphorylation, proton leakage, $FADH_2$ oxidation, $\Delta\Psi_m$ reduction by adenine nucleotide translocation, and $\Delta\Psi_m$ reduction by calcium uniporter; with negative CCCs on steady-state $[ATP]_m$, they are isocitrate dehydrogenase, Ca^{2+} uniporter, proton efflux driven by NADH oxidation, proton efflux drive by $FADH_2$ oxidation, proton uptake, and adenine nucleotide translocator. The enzyme or enzymatic process with the largest absolute values are $FADH_2$ oxidation and $\Delta\Psi_m$ reduction by adenine nucleotide translocation.

Table 17. Elasticities (scaled) from metabolic control analysis of the system under study.

	D_psi_m	NADH	GSH	ATP_m	H2O2	aKG	OAA	Ca2_m	SA_m	FUM	SA_i	Suc	MAL	SCoA	ADP_m
(CS)	0	0	0	0	0	0	0.904591	0	0	0	0	0	0	0	0
(IDH)	0	-0.7225	0	0	0	0	0	0.0312732	0	0	0	0	0	0	0.331225
(ACO)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(KGDH)	0	0	0	0	0	0.91684	0	0.0979054	0	0	0	0	0	0	0
(SL)	0	0	0	-0.000857223	0	0	0	0	0	0	0	-0.000857223	0	1.00086	1.00086
(SDH)	0	0	0	0	0	0	-0.000345784	0	0	-0.138594	0	0.768917	0	0	0
(FH)	0	0	0	0	0	0	0	0	0	1.98722	0	0	-0.987218	0	0
(MDH)	0	0	0	0	0	0	-0.019496	0	0	0	0	0	0.914842	0	0
(Ca2 uniporter)	3.51423	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(AAT)	0	0	0	0	0	-0.356657	1	0	0	0	0	0	0	0	0
(OxiPhos)	-5.45732	0.111896	0	0	0	0	0	0	0	0	0	0	0	0	0
(H_efflux)	0	0.111896	0	0	0	0	0	0	0	0	0	0	0	0	0
(H_efflux_FAD)	-3.91037e-07	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(H_uptake)	-0.00761001	0	0	0.997475	0	0	0	0	0	0	0	0	0	0	-0.997475
(ANT)	18.6656	0	0	5.30763	0	0	0	0	0	0	0	0	0	0	-5.30763
(V_HLeak)	1.18794	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(NaCa_antiporter)	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf
(ATP synthesis)	25.6419	0	0	-0.130016	0	0	0	0	0	0	0	0	0	0	0.130016
(V_He(F))	-2.62465e-07	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(D_psi_m(V_ANT))	18.6656	0	0	5.30763	0	0	0	0	0	0	0	0	0	0	-5.30763
(V_NaCa/C_mito)	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf
(-2V_uni/C_mito)	3.51423	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(V_C_ASP)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(V_ROS_Tr)	0.0177551	0	0	0	0	0	0	0	-0.00916499	0	-0.116565	0	0	0	0
(V_SOD)	0	0	0	0	0	0	0	0	0	0	0.999826	0	0	0	0
(V_CAT)	0	0	0	0	0.999999	0	0	0	0	0	0	0	0	0	0
(V_GPX)	0	0	8.25579e-08	0	1	0	0	0	0	0	0	0	0	0	0
(V_GR)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(V_shunt_O2)	-8.52688e-06	0.499923	0	0	0	0	0	0	0	0	0	0	0	0	0

Table 18. Flux control coefficients (scaled) from metabolic control analysis of the system under study.

	(CS)	(IDH)	(ACO)	(KGDH)	(SL)	(SDH)	(FH)	(MDH)	(Ca2 uniporter)	(AAT)	(OxiPhos)	(H_efflux)	(H_efflux_FAD)	(H_uptake)	(ANT)	(V_HLeak)	(NaCa_antiporter)
(CS)	1.11022e-16	-1.51097e-07	0	1.44688e-14	-3.14496e-14	-9.99351e-15	0	-1.65111e-14	-6.06968e-08	-6.91608e-17	3.47711e-07	-1.3472e-06	-4.11788e-06	-3.02953e-07	-3.15517e-06	6.30641e-07	-1.82331e-21
(IDH)	1.54528e-19	-1.76691e-07	0	-2.11316e-16	4.42182e-15	-5.58686e-15	0	-3.66078e-16	-7.09779e-08	9.27668e-20	4.06608e-07	-1.5754e-06	-4.81538e-06	-3.54268e-07	-3.68961e-06	7.37462e-07	-2.13224e-21
(ACO)	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(KGDH)	-7.98154e-19	-1.74772e-07	0	8.41684e-17	3.62415e-15	-5.36221e-15	0	-3.77971e-16	-7.02073e-08	-1.18785e-18	4.02193e-07	-1.55829e-06	-4.7631e-06	-3.50422e-07	-3.64955e-06	7.29456e-07	-2.10909e-21
(SL)	-3.70275e-18	-1.58287e-07	0	4.41673e-16	-4.63159e-15	9.27688e-15	1.07136e-17	2.76686e-16	-6.35848e-08	-1.05842e-18	3.64256e-07	-1.41131e-06	-4.31381e-06	-3.17368e-07	-3.3053e-06	6.60649e-07	-1.91014e-21
(SDH)	-2.26248e-19	-1.57652e-07	0	1.96711e-16	-6.23882e-15	7.00532e-15	-1.43396e-17	1.7416e-16	-6.33301e-08	-1.55696e-18	3.62796e-07	-1.40565e-06	-4.29653e-06	-3.16096e-07	-3.29205e-06	6.58002e-07	-1.90249e-21
(FH)	-3.50338e-18	-1.52575e-07	0	8.84896e-16	-8.61588e-15	1.29312e-14	0	2.24735e-16	-6.12905e-08	-1.40409e-18	3.51112e-07	-1.36038e-06	-4.15815e-06	-3.05916e-07	-3.18603e-06	6.3681e-07	-1.84122e-21
(MDH)	0	-1.50748e-07	0	1.97426e-16	-7.43364e-15	9.95545e-15	0	6.66134e-16	-6.05567e-08	4.84433e-19	3.46909e-07	-1.34409e-06	-4.10837e-06	-3.02254e-07	-3.14789e-06	6.29186e-07	-1.81918e-21
(Ca2 uniporter)	-4.48897e-17	8.95628e-15	0	-7.04988e-15	2.92318e-14	-3.41335e-14	0	9.30573e-15	1.11022e-15	7.18375e-18	-4.74378e-21	1.20308e-14	3.67734e-14	2.70543e-15	-1.48501e-15	-5.63175e-15	-4.51778e-26
(AAT)	0	-2.11984e-14	0	2.07535e-14	-3.90499e-14	-5.33251e-15	0	-2.79763e-15	-1.74342e-15	0	3.41022e-21	-1.88637e-14	-5.76588e-14	-4.24197e-15	1.73393e-14	8.83029e-15	8.6264e-26
(OxiPhos)	-6.41768e-17	-0.434548	0	-9.30618e-17	3.69485e-16	-2.3328e-15	0	-1.214e-15	-0.174561	1.06572e-17	1	-3.87449	-11.8428	-0.871278	-9.07411	1.81369	-5.24396e-15
(H_efflux)	1.97466e-18	0.168198	0	4.32707e-17	-6.84236e-16	8.78867e-16	0	7.02331e-17	0.00720449	-3.25337e-19	-6.82609e-08	1.11261	0.344219	0.0253242	0.271843	-0.0527161	1.52419e-16
(H_efflux_FAD)	1.19477e-18	-1.57652e-07	0	6.33347e-16	-4.29576e-15	1.53464e-14	0	3.6714e-16	-6.333e-08	-2.42955e-18	3.62796e-07	-1.40565e-06	0.999996	-3.16096e-07	-3.29205e-06	6.58001e-07	-1.90249e-21
(H_uptake)	-4.91465e-17	-0.438739	0	9.41265e-17	-1.24847e-15	1.11027e-15	0	-8.7744e-16	-0.132307	7.62068e-18	1.80019e-07	-2.90222	-8.87094	0.347363	-7.01656	1.35856	-3.92803e-15
(ANT)	-4.65705e-18	-1.99418e-07	0	9.05112e-16	-9.43421e-15	1.61399e-14	0	2.68454e-16	-8.01078e-08	-1.74835e-18	4.5891e-07	-1.77804e-06	-5.43478e-06	-3.99838e-07	-4.1642e-06	8.32322e-07	-2.4065e-21
(V_HLeak)	1.6303e-17	0.148547	0	3.35992e-17	-2.5969e-16	7.91515e-16	0	3.16498e-16	0.0447961	-2.70665e-18	-2.77567e-08	0.982623	3.0035	0.220968	2.30331	0.540023	1.32994e-15
(NaCa_antiporter)	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf
(ATP synthesis)	-2.46528e-20	-7.49708e-16	0	7.07166e-16	1.6465e-15	4.31056e-15	0	3.32511e-16	-1.46826e-16	-9.55488e-19	-3.18091e-23	-5.39087e-15	-1.64778e-14	-1.21228e-15	-7.85564e-15	2.52353e-15	3.96722e-27
(V_He(F))	1.19477e-18	-1.57652e-07	0	6.33347e-16	-4.29576e-15	1.53464e-14	0	3.6714e-16	-6.333e-08	-2.42955e-18	3.62796e-07	-1.40565e-06	-4.29653e-06	-3.16096e-07	-3.29205e-06	6.58001e-07	-1.90249e-21
(D_psi_m(V_ANT))	-4.65704e-18	-1.69523e-07	0	9.05112e-16	-9.43421e-15	1.61399e-14	0	2.68454e-16	-7.10923e-08	-1.74836e-18	4.5891e-07	-1.58029e-06	-4.83032e-06	-3.55367e-07	-1	7.3975e-07	-2.13884e-21
(V_NaCa/C_mito)	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf
(-2V_uni/C_mito)	-4.48897e-17	3.92827e-08	0	-7.04988e-15	2.92318e-14	-3.41335e-14	0	9.30573e-15	-1	7.18375e-18	-7.34015e-15	2.59851e-07	7.94263e-07	5.84341e-08	6.09102e-07	-1.21639e-07	3.51653e-22
(V_C_ASP)	-2.13035e-16	0	0	3.68353e-16	-1.51157e-14	1.79953e-14	-1.37878e-17	4.4101e-16	5.43044e-17	1.26607e-16	0	-8.41515e-17	-2.57218e-16	-1.89236e-17	5.37995e-15	3.93923e-17	6.72384e-28
(V_ROS_Tr)	6.08816e-20	0.00518592	0	7.81961e-19	-2.11973e-17	2.93617e-17	0	1.75017e-18	0.000222128	-8.91532e-21	-2.10463e-09	0.0034721	0.0106129	0.00078079	0.00838139	-0.00162533	4.69934e-18
(V_SOD)	6.08799e-20	0.00518593	0	5.14322e-18	-4.17804e-17	7.49371e-17	0	-4.25919e-19	0.000222128	-9.86482e-21	-2.10464e-09	0.00347211	0.0106129	0.000780791	0.00838141	-0.00162533	4.69935e-18
(V_CAT)	6.08808e-20	0.005186	0	4.74417e-18	-4.28172e-17	7.5003e-17	0	-7.1742e-19	0.000222131	-8.86206e-21	-2.10467e-09	0.00347216	0.010613	0.000780803	0.00838153	-0.00162536	4.69942e-18
(V_GPX)	6.08808e-20	0.00518601	0	4.74418e-18	-4.28173e-17	7.50031e-17	0	-7.17421e-19	0.000222132	-8.86207e-21	-2.10467e-09	0.00347216	0.010613	0.000780804	0.00838154	-0.00162536	4.69943e-18
(V_GR)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(V_shunt_O2)	8.85083e-18	0.753911	0	1.93951e-16	-3.06694e-15	3.93932e-15	0	3.14802e-16	0.0322922	-1.45823e-18	-3.05964e-07	0.504762	1.54286	0.113509	1.21846	-0.236285	6.83174e-16

Table 18. Continued.

	(ATP synthesis)	(V_He(F))	(D_psi_m(V_ANT))	(V_NaCa/C_mito)	(-2V_uni/C_mito)	(V_C_ASP)	(V_ROS_Tr)	(V_SOD)	(V_CAT)	(V_GPX)	(V_GR)	(V_shunt_O2)
(CS)	0	4.11788e-06	3.21202e-06	1.82338e-21	5.86272e-08	0	0	0	0	0	0	0
(IDH)	-8.51702e-17	4.81538e-06	3.75609e-06	2.13224e-21	6.85578e-08	0	0	0	0	0	0	0
(ACO)	0	0	0	0	0	0	0	0	0	0	0	0
(KGDH)	-6.44776e-17	4.7631e-06	3.71531e-06	2.10909e-21	6.78135e-08	0	0	0	0	0	0	0
(SL)	8.80342e-16	4.31381e-06	3.36486e-06	1.91014e-21	6.14168e-08	0	0	0	0	0	0	0
(SDH)	1.48066e-15	4.29653e-06	3.35138e-06	1.90249e-21	6.11707e-08	0	0	0	0	0	0	0
(FH)	-1.74682e-16	4.15816e-06	3.24344e-06	1.84122e-21	5.92007e-08	0	0	0	0	0	0	0
(MDH)	1.6187e-16	4.10837e-06	3.20461e-06	1.81918e-21	5.84919e-08	0	0	0	0	0	0	0
(Ca2 uniporter)	1.50519e-15	9.39214e-15	-2.8684e-14	-1.62832e-29	-5.23552e-16	0	0	0	0	0	0	0
(AAT)	0	1.65168e-14	4.4975e-14	2.55312e-29	8.20903e-16	0	0	0	0	0	0	0
(OxiPhos)	0	11.8428	9.23763	5.24396e-15	0.168609	0	0	0	0	0	0	0
(H_efflux)	0	-0.344219	-0.268497	-1.52419e-16	-0.00490073	0	0	0	0	0	0	0
(H_efflux_FAD)	0	-0.999996	3.35137e-06	1.90249e-21	6.11707e-08	0	0	0	0	0	0	0
(H_uptake)	2.64927e-16	8.87094	6.91951	3.92803e-15	0.126298	0	0	0	0	0	0	0
(ANT)	1.2401e-15	5.43478e-06	4.23924e-06	2.40651e-21	7.73764e-08	0	0	0	0	0	0	0
(V_HLeak)	0	-3.0035	-2.34279	-1.32994e-15	-0.0427615	0	0	0	0	0	0	0
(NaCa_antiporter)	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf
(ATP synthesis)	1.08922e-15	-3.97472e-15	1.2853e-14	7.29633e-30	2.34599e-16	0	0	0	0	0	0	0
(V_He(F))	0	4.29653e-06	3.35137e-06	1.90249e-21	6.11707e-08	0	0	0	0	0	0	0
(D_psi_m(V_ANT))	1.2401e-15	4.83032e-06	1	2.13885e-21	6.87704e-08	0	0	0	0	0	0	0
(V_NaCa/C_mito)	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf	inf
(-2V_uni/C_mito)	1.50519e-15	-7.94264e-07	-6.19541e-07	-3.51698e-22	1	0	0	0	0	0	0	0
(V_C_ASP)	1.91728e-16	-1.02366e-14	2.00635e-16	1.13896e-31	3.66208e-18	0	0	0	0	0	0	0
(V_ROS_Tr)	7.55459e-21	-0.0106129	-0.00827824	-4.69934e-18	-0.000151098	0	9.96418e-17	1.38778e-17	-1.05622e-17	-2.92013e-21	0	0.00687869
(V_SOD)	1.23769e-17	-0.0106129	-0.00827825	-4.69935e-18	-0.000151098	0	1.05078e-15	1.11022e-16	-1.31308e-16	-3.6303e-20	0	0.0068787
(V_CAT)	1.25955e-17	-0.010613	-0.00827837	-4.69942e-18	-0.0001511	0	1.03246e-15	1.47494e-16	0.000276395	-0.000276395	0	0.0068788
(V_GPX)	1.25955e-17	-0.010613	-0.00827838	-4.69943e-18	-0.000151101	0	1.03246e-15	1.47494e-16	-0.999725	0.999724	0	0.00687881
(V_GR)	0	0	0	0	0	0	0	0	0	0	0	0
(V_shunt_O2)	0	-1.54286	-1.20346	-6.83174e-16	-0.0219661	0	0	0	0	0	0	1

Table 19. Concentration control coefficients (scaled) from metabolic control analysis of the system under study.

		(IDH)	(ACO)	(KGDH)	(SL)	(SDH)	(FH)	(MDH)	(Ca2 uniporter)	(AAT)	(OxiPhos)	(H_efflux)	(H_efflux_FAD)	(H_uptake)	(ANT)	(V_HLeak)	(NaCa_antiporter)
D_psi_m	1.79116e-300	0.125222	0	2.83234e-17	-2.18913e-16	6.67232e-16	0	2.66802e-16	0.0377622	-2.28165e-18	-2.33983e-08	0.828332	2.53189	0.186271	1.94165	-0.387752	1.12111e-15
NAD	-1.07423e-17	-0.915015	0	-2.35397e-16	3.74275e-15	-4.80165e-15	0	-3.82075e-16	-0.0391931	1.76987e-18	3.71346e-07	-0.612634	-1.87258	-0.137766	-1.47885	0.286781	-8.29174e-16
GSH	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
aKG	-4.61595e-18	0.0294905	0	-1.09086	5.14654e-15	-7.29077e-15	0	0	-0.0507294	-6.85814e-19	4.22314e-07	-0.101204	-0.309342	-0.0227584	-0.234896	0.0473749	-1.36976e-16
ATP_m	-1.31238e-17	-0.117153	0	2.52573e-17	-3.34654e-16	2.98667e-16	0	-2.34259e-16	-0.0353289	2.03465e-18	4.81316e-08	-0.774955	-2.36873	-0.174268	-1.87371	0.362765	-1.04887e-15
H2O2	6.08808e-20	0.00518601	0	4.74418e-18	-4.28173e-17	7.50031e-17	0	-7.17421e-19	0.000222132	-8.86207e-21	-2.10467e-09	0.00347216	0.010613	0.000780804	0.00838154	-0.00162536	4.69943e-18
OAA	-1.10542	-1.67026e-07	0	1.59941e-14	-3.47651e-14	-1.10471e-14	0	-1.82518e-14	-6.70956e-08	-7.64519e-17	3.84368e-07	-1.48923e-06	-4.55199e-06	-3.34891e-07	-3.48779e-06	6.97125e-07	-2.01553e-21
FADH2	1.86518e-24	-2.46115e-13	0	9.88735e-22	-6.70624e-21	2.39577e-20	0	5.73152e-22	-9.88662e-14	-3.79283e-24	5.66371e-13	-2.1944e-12	-6.70742e-12	-4.93466e-13	-5.13931e-12	1.02722e-12	-2.97002e-27
Ca2_i	-5.86456e-17	-0.275508	0	-4.52386e-15	1.89811e-14	-2.30695e-14	0	5.30216e-15	-0.715937	9.56625e-18	5.14799e-08	-1.82246	-5.57054	-0.409826	-4.27192	0.853114	-2.46662e-15
SA_m	1.56446e-17	-0.423382	0	-1.03585e-16	2.48503e-15	-3.04831e-15	0	2.62021e-16	0.0362852	-2.73093e-18	2.17884e-07	0.967057	2.95592	0.217467	2.23718	-0.452691	1.30887e-15
MAL	-0.0235467	0.0539936	0	5.70386e-16	-9.087e-15	1.09302e-14	0	-1.09309	0.00231266	-1.20342e-18	3.65476e-07	0.0361492	0.110494	0.00812906	0.0872614	-0.0169218	4.89264e-17
ASP	-2.13035e-16	0	0	3.68353e-16	-1.51157e-14	1.79953e-14	-1.37878e-17	4.4101e-16	5.43044e-17	1.26607e-16	0	-8.41515e-17	-2.57218e-16	-1.89236e-17	5.37995e-15	3.93923e-17	6.72384e-28
SA_i	6.08905e-20	0.00518683	0	5.14412e-18	-4.17877e-17	7.49502e-17	0	-4.25993e-19	0.000222167	-9.86654e-21	-2.10501e-09	0.00347271	0.0106147	0.000780927	0.00838287	-0.00162562	4.70017e-18
Suc	-0.00260551	0.00483462	0	3.94355e-16	-9.72454e-15	-1.30053	-0.090701	-0.0978803	0.000206999	-2.29436e-18	5.36572e-07	0.00323502	0.00988818	0.000727476	0.00780923	-0.00151435	4.37846e-18
FUM	-0.0116978	0.0268235	0	7.28649e-16	-8.84993e-15	1.19371e-14	-0.503207	-0.543038	0.00114888	-1.3044e-18	3.58248e-07	0.017958	0.0548905	0.0040383	0.0433492	-0.00840632	2.43053e-17
Pi	-3.27579e-15	-29.8366	0	0	6.54014e-14	-1.15569e-13	0	-6.04312e-14	-8.99758	5.34416e-16	5.67338e-06	-197.366	-603.271	-44.3828	-462.849	92.3893	-2.67127e-13
Na_m	-2.63913e-17	-0.217407	0	2.17168e-15	5.06866e-16	-1.10589e-15	0	-4.40099e-16	-0.381768	-7.68048e-18	4.06235e-08	-1.43813	-4.3958	-0.3234	-3.37104	0.673204	-0.333334
SCoA	-2.23181e-06	-0.32172	0	5.10993e-16	-0.999143	-0.001114	-7.76921e-05	-8.38417e-05	-0.0970196	4.52805e-18	4.96582e-07	-2.12817	-6.50498	-0.478573	-5.14555	0.99622	-2.88039e-15
GLU	1.10542	0.0104962	0	-0.388252	-2.45303e-15	3.11967e-15	0	1.54542e-14	-0.0180552	-1	-2.34061e-07	-0.0360184	-0.110094	-0.00809966	-0.0835989	0.0168606	-4.87494e-17
NADH	6.96217e-18	0.593027	0	1.52562e-16	-2.39201e-15	3.07815e-15	0	2.47625e-16	0.0254013	-1.14706e-18	-2.40672e-07	0.397052	1.21363	0.0892872	0.958454	-0.185865	5.37394e-16
ADP_m	-2.73604e-18	3.61027e-07	0	-1.45038e-15	9.83738e-15	-3.51436e-14	0	-8.40757e-16	1.45027e-07	5.56371e-18	-8.3081e-07	3.21897e-06	9.83913e-06	7.23867e-07	7.53886e-06	-1.50684e-06	4.35673e-21
Ca2_m	2.63913e-17	0.217407	0	-2.17168e-15	-5.06866e-16	1.10589e-15	0	4.40099e-16	0.381768	7.68048e-18	-4.06235e-08	1.43813	4.3958	0.3234	3.37104	-0.673204	0.333334
FAD	4.05396e-17	0.190449	0	3.12718e-15	-1.30778e-14	1.59417e-14	0	-3.6652e-15	0.494901	-6.6128e-18	-3.55862e-08	1.2598	3.85072	0.283298	2.95303	-0.589727	1.70509e-15
GSSG	3.60292e-17	0.321623	0	-6.93395e-17	9.18735e-16	-8.19939e-16	0	6.43118e-16	0.0969894	-5.58578e-18	-1.32137e-07	2.12751	6.50296	0.478424	5.14395	-0.99591	2.87949e-15

Table 19. Continued.

	(ATP synthesis)	(V_He(F))	(D_psi_m(V_ANT))	(V_NaCa/C_mito)	(-2V_uni/C_mito)	(V_C_ASP)	(V_ROS_Tr)	(V_SOD)	(V_CAT)	(V_GPX)	(V_GR)	(V_shunt_O2)
D_psi_m	0	-2.53189	-1.97492	-1.12111e-15	-0.0360471	0	0	0	0	0	0	0
NAD	0	1.87258	1.46065	8.29174e-16	0.0266604	0	0	0	0	0	0	0
GSH	0	0	0	0	0	0	0	0	0	0	-7.32101e-05	0
aKG	0	0.309342	0.241293	1.36976e-16	0.00440418	0	0	0	0	0	0	0
ATP_m	7.09104e-17	2.36873	1.84766	1.04887e-15	0.0337243	0	0	0	0	0	0	0
H2O2	1.25955e-17	-0.010613	-0.00827838	-4.69943e-18	-0.000151101	0	1.03246e-15	1.47494e-16	-0.999725	-0.000276395	0	0.00687881
OAA	0	4.55199e-06	3.55064e-06	2.01561e-21	6.48079e-08	0	0	0	0	0	0	0
FADH2	0	-1.56112e-06	5.23192e-12	2.97003e-27	9.54953e-14	0	0	0	0	0	0	0
Ca2_i	9.52564e-16	5.57054	4.34513	2.46662e-15	0.0793092	0	0	0	0	0	0	0
SA_m	-1.58628e-16	-2.95592	-2.30567	-1.30887e-15	-0.0420841	0	109.45	12.7496	2.83016e-15	7.82458e-19	0	-0.840574
MAL	1.76938e-16	-0.110494	-0.0861874	-4.89264e-17	-0.00157313	0	0	0	0	0	0	0
ASP	1.91728e-16	-1.02366e-14	2.00635e-16	1.13896e-31	3.66208e-18	-1	0	0	0	0	0	0
SA_i	1.23791e-17	-0.0106147	-0.00827969	-4.70017e-18	-0.000151124	0	1.05096e-15	-1.00017	-1.31331e-16	-3.63093e-20	0	0.0068799
Suc	1.92564e-15	-0.00988819	-0.00771298	-4.37846e-18	-0.000140781	0	0	0	0	0	0	0
FUM	0	-0.0548905	-0.0428156	-2.43053e-17	-0.000781489	0	0	0	0	0	0	0
Pi	-9.26905	603.271	470.563	2.67127e-13	8.58892	0	0	0	0	0	0	0
Na_m	1.48709e-16	4.3958	3.42881	1.94645e-15	0.062584	0	0	0	0	0	0	0
SCoA	1.07597e-15	6.50498	5.07401	2.88039e-15	0.0926131	0	0	0	0	0	0	0
GLU	0	0.110094	0.0858757	4.87494e-17	0.00156744	0	0	0	0	0	0	0
NADH	0	-1.21363	-0.946658	-5.37394e-16	-0.0172788	0	0	0	0	0	0	0
ADP_m	0	2.29001	-7.67471e-06	-4.35674e-21	-1.40082e-07	0	0	0	0	0	0	0
Ca2_m	-1.48709e-16	-4.3958	-3.42881	-1.94645e-15	-0.062584	0	0	0	0	0	0	0
FAD	-6.58473e-16	-3.85072	-3.00363	-1.70509e-15	-0.0548236	0	0	0	0	0	0	0
GSSG	-1.94673e-16	-6.50296	-5.07244	-2.87949e-15	-0.0925843	0	0	0	0	0	0	0

CHAPTER 4 DISCUSSION

4.1 Absence of Common Active Compounds Responsible for Yang-tonifying Actions

The absence of common active compounds responsible for Yang-tonifying actions can have the following explanations: (1) Insufficient or inconsistent data of chemical compounds prevented a rigorous search for such a compound or compounds; (2) Yang-tonifying action cannot be fully explained only by substances in the herbs without referring to a living environment; (3) The concept hierarchy of data mining placed at the compounds level might be too low to find a biochemically functional entity of Yang-tonifying actions. To search on higher levels, e.g., compound genres, might be a solution to the first reason discussed above, if it were indeed the case.

Since the specificity of the classifier for Yin-, Yang-, Qi- and Blood-tonifying herbs is as high as 72.7% despite the low sensitivity, knowledge of the chemical content of Chinese tonifying herbs may still have potential for rejecting Chinese herbal products of dubious origins. Assays of active compounds for quality of herbs are already widely used in the quality control of commercial herbal products.

4.2 New Insights from Data Analysis

4.2.1 Derived Features Are Useful for Analyzing Chinese Tonifying Herbs

Published biochemical data of Chinese tonifying herbs remain relatively scarce, and the attributes of a medicinal most available for bioinformatic analysis are glutathione regeneration capacity, total antioxidant power and total phenolic content. These features were shown in SVM classification results to be incapable of characterizing the Yang-tonifying herbs.

As demonstrated in the data (**Table 11**, **Table 12**), the inclusion of unit *in vitro* and unit *ex vivo* antioxidant activities significantly improved the performance of classification: sensitivities by about 30%, specificities by 40-50% and precision by 50-60%. The only requirement of the calculation of these features is that the data of GRC, total antioxidant power and total phenolic content are available. For purposes of quality assessment, calculating these two derived features can be set as a standard analytic operation in studying Chinese tonifying herbs or even any kind of medicinal plants. The table of features characterizing Chinese tonifying herbs is therefore expanded (shown in **Table 20**).

Table 20. The biochemical features that characterize Yin- and Yang-tonifying herbs.

Feature	Method	Discrimination
Mitochondrial ATP-generation	Experimental (Ko et al., 2006, Ko and Leung, 2007)	Higher in Yang-tonifying herbs
Immunomodulatory activity	Experimental (Yim and Ko, 2002)	Higher in Yin-tonifying herbs
Unit *ex vivo* antioxidant activity	Experimental and Computational	Higher in Yin-tonifying herbs; lower in Yang-tonifying herbs

The usefulness of the two derived features can be further tested after more source data, and hence training data, on Chinese tonifying herbs are made available. Since not all antioxidant power is conferred by phenolic compounds, being just an approximate measure of the total amount of antioxidants, it is reasonable that the calculated unit antioxidant activities will somewhat deviate from reality.

4.2.2 Rethinking of Modern TCM Investigations

Solving the counter-intuitive problem of antioxidative power (a Yin property) existing in Yang-tonifying herbs (expected to stimulate and promote) is one of the main goals in this study. Yet on the issue of studying TCM in a modern, biochemical and somewhat reductionist way, the failure to find common active compounds and the success of defining derived features for Yang-tonifying herbs should arouse some discussions.

As was mentioned in Introduction, the mutually opposing Yin-Yang actions were once equated with the antioxidation-oxidation pair in one study (Ou et al., 2003). However, in an earlier study (Yim and Ko, 2002), Yang-invigorating herbs examined were actually found to be more potent in their antioxidant activities than those of the other tonifying herbs. This inconsistency was later suggested to be due to different selection criteria for herbal study subjects (Ko et al., 2004), namely the criterion based on the general Yin or Yang "property" was adopted by Ou *et al.* (Ou et al., 2003) whereas the herbal Yin or Yang "action" employed by Yim and Ko (Yim and Ko, 2002).

The reason why unit *in vitro* and unit *ex vivo* antioxidant activities (the latter being more discriminative than the former, as can be seen in **Table 7**) improved the classifier, should be that the intracellular environment has some effects on antioxidation by the herbs. Meanwhile, the poor contribution of physiological factor, another derived feature defined in this study, excluded that possibility that the essence Yang- or Yin-tonifying herbs could lie in the "change" of unit antioxidant activity from a lifeless to a living environment (**Figure 22**). Therefore, in addition to the recognized ATP generation capacity, possession of lower unit *ex vivo* antioxidant activities can be regarded as an essence of herbal species being Yang-tonifying, whereas higher values as Yin-tonifying herbs.

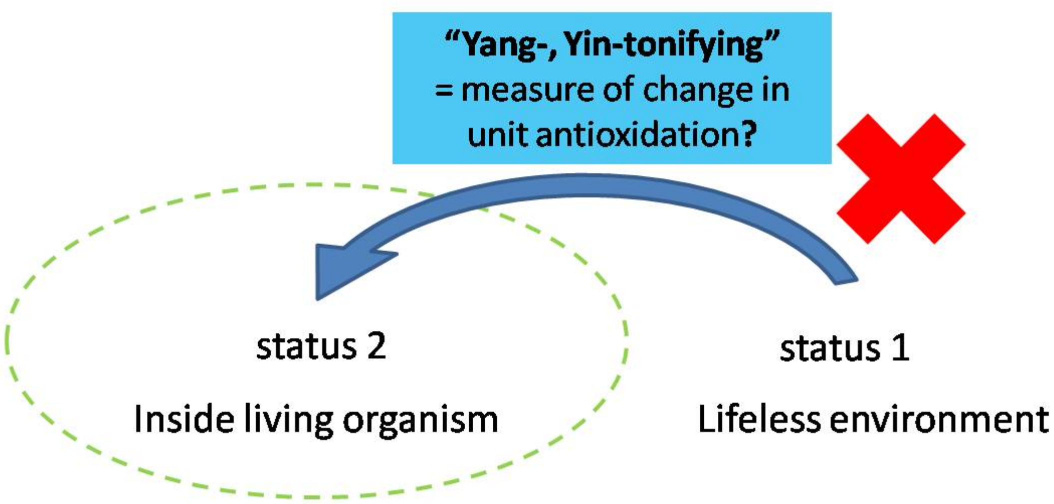

Figure 22. The excluded possibility of Yang- and Yin-tonifying to stand for a measure of change in unit antioxidation.

Since any sort of pharmacological action must involve interaction with the intracellular and extracellular environment, the fuller the environmental context is considered, the more an *in silico* approach is supposed to reflect reality. TCM is a medicine that is built up through countless *in vivo* observations and experiments. Such an idea is drawn in **Figure 23**. Therefore, modern investigations into TCM should bear much fruit only if a more systems than reductionist approach is employed.

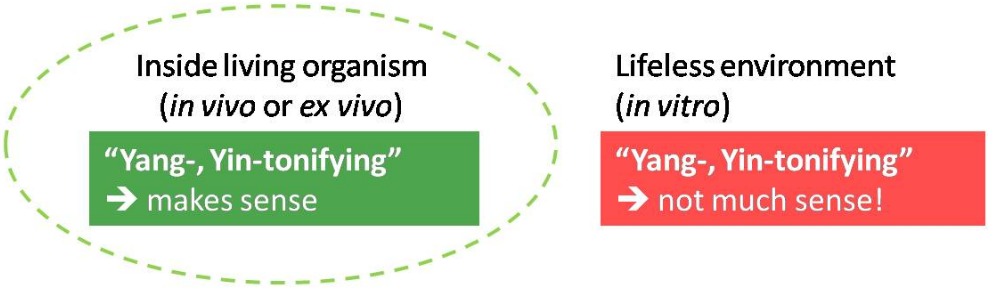

Figure 23. The ideas of Yang- and Yin-tonifying should be considered in a system of living organism to make its sense in TCM.

4.3 Limited Influence Over ATP Generation By Antioxidation

Since the model system does not distinguish between Yang- and Yin-tonifying herbs, the relationship between antioxidation should hold right in either group of tonifying herbs. Moreover, the level of antioxidation in a cell is measured in glutathione regeneration capacity (**Table 5**), and not much difference exists between the Yang- and Yin-tonifying herbs.

The large difference between the orders of magnitude in the data of enhanced ATP generation by Yang-tonifying herbs, from 20% to 130% (**Table 9**), and in the data from sensitivity analysis of ATP-generation on oxidation, from 10^{-7} % to 10^{-6} % (**Table 16**), suggests that antioxidation does not play a primary role in stimulating ATP generation, as mentioned in a previous report, where the data was not shown (Ko et al., 2006). Nonetheless, if antioxidation targeted at ROS were to influence V_{ATPase}, the most likely intermediate species should be matrix superoxide anions.

4.4 Control Over ATP Synthesis Is Evenly Distributed In Mitochondria

As can be seen from **Table 17**, $\Delta\Psi_m$ has the largest number (fourteen) of non-zero elasticities on reactions in the model. Provided that (1) antioxidation has limited influence over ATP generation, (2) mitochondrial membrane potential has high and almost monopolistic control over ATP synthesis (elasticity(ATP synthesis, $\Delta\Psi_m$) = 25.2508, 250 times the values of the other control parameters) and (3) proton fluxes have high FCCs and CCCs over steady-state matrix ATP concentration, the membrane potential should be a good subject for future studies for the mechanism of Yang-tonifying actions. Moreover, since antioxidation targeted against ROS does not significantly stimulate ATP generation, it is likely that the Yang-tonifying herbs changes $\Delta\Psi_m$ or $\Delta\Psi_m$-related variables to achieve the Yang-tonifying action.

The FCCs and CCCs of matrix ATP concentration in **Table 18** are generally low and even. Since control coefficients are systemic properties, the results might indicate the control over ATP synthesis is relatively evenly distributed to many metabolites and enzymatic processes across the mitochondria, preventing any unexpected perturbation in the mitochondrial system from compromising the main purpose of mitochondria—manufacturing ATPs. In other words, the mitochondrial system is robust in terms of ATP generation.

CHAPTER 5 CONCLUSION

5.1 Summary of Procedures and Results

1. Common active common chemical compounds were searched in Yang-tonifying herbs but none was found.

2. By using support vector machine, the representativeness of collected and derived biochemical features was tested in Yang-tonifying herbs and novel features were found.

3. By mathematical modeling, sensitivity analysis of ATP generation to antioxidation performed and a low sensitivity was reported, rejecting a direct causal relationship between them.

4. Results from metabolic control analysis suggested that control over ATP synthesis is evenly distributed across mitochondria, though mitochondrial membrane potential has the largest control.

5.2 Goals Achieved and Major Contributions

1. To determine the causal relationship between antioxidation and mitochondrial ATP generation: Antioxidation was not found to effectively influence mitochondrial ATP generation, steady-state ATP concentration in intermembrane space and mitochondrial matrix. Rather, the control over ATP generation in mitochondria appears to be distributed evenly across the whole mitochondrial system.

2. To discover the mechanism behind different antioxidant potentials and

ATP generation capacities between Yang- and Yin-tonifying herbs: The derived features of unit *in vitro* and unit *ex vivo* antioxidant activity were shown to significantly improve the discrimination performance in classifiers and can serve as a novel standard feature to characterize Yin- and Yang-tonifying herbs. Besides, role of intracellular effects was underscored. Unit *ex vivo* antioxidant activity was found to be higher in Yin-tonifying herbs than in Yang-tonifying herbs. Due to intracellular effects on antioxidation, future studies must involve wet-lab works, presumably focused on membrane potentials.

3. To propose a rationale for Yang- and Yin-tonifying herbs being categorized as such in TCM literature: First, no single chemical compounds were found to associate with the categorization of tonifying herbs, excluding the possibility of "Yang-tonifying compounds." Second, the lower unit *ex vivo* antioxidant activities suggested that Yang-tonifying actions contain but are not specialized for antioxidation. Therefore, Yang- and Yin-tonifying herbs are supposed to be categorized as such Chinese pharmacopoeia for thousands of years not because of their Yang- or Yin-tonifying "properties," but of their Yang- or Yin-tonifying "actions" within a living system. For researchers of modern investigations in TCM, this also serves as a reminder that TCM theories are not applicable and practical unless the system of consideration is full enough with physiological contexts.

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APPENDIX A List of Chemical Compounds Found in 65 Chinese Herbs

No.	Herbal Name	Chinese Name	Chemical Compounds
1	**Cortex Eucommiae**	杜仲	(+)-syringaresinol, syringaresinol-O-beta-D-glucopyranoside, syringylglycerol-beta-syringaresinol ether 4",4"'-di-O-beta-Dglucopyranoside, pinoresinol, epipinoresinol, pinoresinol-O-beta-D-glucopyranoside, pinoresinol-di-O-beta-D-glucopyranoside, l-hydroxypinoresinol, 1-hydroxypinol-4'-O-beta-D-glucopyranoside, 1-hydroxypinoresinol-4"-O-beta-D-glucopyranside, l-hydroxypinoresinol-4',4"-di-O-beta-D-glucopyranoside, dihydrodehydrodiconiferylalcohol, threo-dihydroxydehydro diconiferyl alcohol, erytho-dihydroxy-dehyrodiconiferyl alcohol, dehydrodiconiferyl alcohol-4,r'-di-O-beta-D-glucopyranoside, olivil, olivil-4'-O-beta-D-glucopyranoside, olivil-4"-O-beta-D-glucopyranoside, olivil-4',4"-di-O-beta-D-glucopyranoside, cycloolivil, medioresinol, eucommin, medioresinol-4-O-beta-D-glucopyranoside, medioresinol-di-O-beta-D-glucopyranoside, hedyotol C-4",4"-di-O-beta-D-glucopyranoside, liriodendrin, citrusin B, aucubin, ulmoside, aucubigenin-1-beta-isomaltosde, genipin, geniposide, geniposidicacid, ajugoside, harpagide acetate, reptoside, eucommiol, eucommioside I, threo¡Ðguaiacylglycerol, erythro-guaiacyl glycerol, erythro-guaiacyl glycerol-beta-coniferyl aldehydeether, threo-guaiacylglycerol-beta-coniferylaldehyde ether, caffeic acid, chlorogenic acid, methyl chlorogenate, vanillic acid, betulin, betulic acid, ursolic acid, beta-sitosterol, dancosterol, phenylalanine, lysine, tryptophan, methionine, threonine, valine, leucine, isoleucine, glutamic acid, cysteine, histidine, ulmoprenol, kaempferol, tartaric acid, galactitol, n-triacontanol, n-nonacosane, guttapercha
2	**Fructus Ligustri**	女貞子	oleanolic acid, acetyloleanolic acid, ursolic acid, acetylursolic acid, p-hydroxyphenethyl alcohol, 3,4-dihydroxyphenethyl alcohol, beta-sitosterol, mannitol, eriodictyol, taxifolin, quercetin, ligustroside, p-hydroxy ligustroside, nuezhenide, oleuropein, 10-hydroxy oleuropein, p-hydroxyphen-ethyl-beta-D-glucoside, 3,4-dihydroxyphenethyl-beta-D-glucoside, methyl-alpha-D-galactopyranoside, acteoside, neonuezhenide, ligustrosidic acid, oleuropeinic acid, GI-3, rhamnoside, arabinose, glucose, fucose, phosphatidyl choline, potassium, calcium, magnesium, sodium, zinc, iron, manganese, copper, nickel, chronium, silver, ligustrin, 8-epikingiside
3	**Fructus Mori**	桑椹子	tannic acid, malic acid, vitamin B1, vitamin B2, carotene, linoleic acid, oleic acid, palmitic acid, stearic acid, caprylic acid, pelargonic acid, capric acid, myristic acid, linolenic acid, cineole, geraniol, linalyl acetat, linalool, camphor, alpha-pinene, limonene, phosphatidyl choline, lysophosphatidy choline, phosphatidyl ethanolamine, phosphatidic acid,

			phosphatidyl inositol, diphosphatidyl glycerol, cyanidin, chrysanthemin
4	**Fructus Psoraleae**	補骨脂	psoralen, isopsorasen, angelicin, xanthotoxin, 8-methoxypsoralen, psoralidin, isopsoralidin, bakuchicin, psoralidin2',3'-oxide, corylidin, bavacoumestan A, bavacoumestan B, sophoracoumestan A, astragalin, bavachin, corylifolin, islbavachin, bavachinin, corylifolinin, isobavachalcone, bavachalcone, bavachromene, neobavachalcone, isoneobavachalcone, bakuchalcone, bavachromanol, corylin, flavone, corylinal, psoralenol, bakuchiol, corylifonol, isocorylifonol, p-hydroxy-benzoic acid, stigmasterol, beta-sitosterol-D-glucoside, triacontane, trypsin inhibitor , potassium, manganese, calcium, iron, copper, zinc, arsenium, antimony, rubidium, strontium, selenium, palmitic acid, oleic acid, linoleic acid, stearic acid, linolenic acid, lignoceric acid
5	**Herba Cistanches**	肉蓯蓉	cistanoside A, cistanoside B, cistanoside C, cistanoside H, acteoside, 2-acetylacteoside, echinacoside, liriodendrin, 8-epiloganic acid, daucosterol, betaine, beta-sitosterol, mannitol, N,N-dimethylglycinemethyl ester, phenylalanine, valine, leucine, isoleucine, lysine, serine, succinic acid, triacontanol, polysaccharides
6	**Herba Cynomorii**	鎖陽	cynoterpene, acetylursolic acid, ursolic acid, palmitic acid, olic acid, inoleic acid, beta-sitosterol, campesterol, beta-sitosterol palmitate, daucosterol, tannic acid, aspartic acid, proline, serine, alanine ,
7	**Herba Dendrobii**	石斛	dendrobine, nobilonine, 6-hydroxydendrobine, dendramine, dendroxine, 6-hydroxydendroxine, 4-hydroxydendroxine, dendrine, 3-hydroxy-2-oxydendrobine, N-methyldendrobinium, N-isopentenyldendrobinium, dendrobine N-oxide, N-isopentenyl-6-hydroxydendroxinium, nobilomethylene, denbinobin, beta-sitosterol, daucosterol, shihunine, shihunidin, dendrophenol, hygrine, dendrochrysine, cis-p-hydroxycinnamic acid, trans-p-hydroxycinnamic acid, aduncin, crepidine, crepidamine, dendrocrepine, isodendrocrepine, isocrepidamine, densifloroside, dendroflorin, dengibsin, psoralen, scopoletin methylether, oleanolic acid
8	**Herba Ecliptae**	墨旱蓮	saponins, tannic acid, vitamin A, ecliptine, a-Terthienylmethanol, 2-buta-1,3-diynyl]-5-(but-3-en-l-ynyl)thiophene, 2-(buta-1,3-diynyl)-5-(4-chloro-3-hydroxybut-1-ynyl)thiophene, 5-(3-buten-1-ynyl)-2,2'-bithiennyl-5'-methylacetate, Wedelolactone, nicotine, alpha-terthienylmethanol, alpha-formyl-alpha-terthienel, demethylwedelolactone, demethylwedelolactoneglucoside, phytosterol A, beta-amyrin, luteolin-7-O-glucoside
9	**Herba Epimedii**	淫羊藿	icariin, icariside I, potassium, calcium, saponins, bitter substances, tannic acid, ceryl alcohol, triacontane, phytosterol, oleic acid, linoleic acid, palmitic acid, quercetin, quercetin-3-O-beta-D-glucoside, icaritin-3-O-a-rhamnoside, anhydroicaritin-3-O-a-rhamnoside, sagittatoside A, sagittatoside B, sagittatoside C, epimedin A, epimedin B, epimedin C, sagittatin A, sagittatin B, icariside A1, icariside B2, icariside B6, icariside B9, icariside D3, icariside E6, icariside E7, icariside H1, icarisidin B1, icariol A1, icariol A2, dilignol, 5,5'-dimethoxydilignol, dilignol rhamnosid, 5'-methoxydilignol rhamnoside, l,2-bis-(4-hydroxy-3-methoxyphenyl)-propane-1,3-diol, 5-methoxy-¡]¡Ð¡^-solaritiresinol, olivil, (+)-syringaresinol-O-beta-D-glucopy-glucopyranoside, symplocosigenin-O-beta-D-glucopyra-noside, dihydrodehydrodiconiferylalcohol, Phenethyl glucoside, (z)-3-hexenyl

			glucoside, blumenolC gfu-coside, wushanicariin, baohuoside I, baohuoside II, baohuoside VI, rouhuoside, quercetin-3-galactoside, quercetin-3-rhamnoside, epimedoside A, icaritin, 8-prenylkaempferol-4'-methoxy-3-[xylosyl(1->4)rhamnoside]-7-glucoside, Epmedin A1, Epmedin B1, quercetin, epimedokoreanodide I, epimedokoreanodide II, n-nonacosane, n-hentriacotane, campesterol, beta-sitosterol, beta-sitosterol-3-glucoside, 2''-Orhamnosylikarisoside A, ikarisioside A, baohuoside II, hyperosde, baohuosu, tricin, kaemPfero-3-dirhamnoside
10	**Radix Angelicae**	當歸	n-butylidenephthalide, n-valerophenone-o-carboxylic acid, delta2,4-dihydrophthalicanhydride, terpenes, sucrose, vitamin B12, vitamin A, arabigalactan, glucose, fructose, Ligustilide, Cnidilide, Isocnidilide, p-cymene, Butylphthalide, Sedanolide, Butylalcohol, ethanoic acid, calcium, copper, zinc, potassium, iron, ligustilide, folinic acid, citrovorum factor, nicotinic acid, biotin, ferulic acid, succinic acid, uracil, adenine, scopoletin, umbelliferone, vanillic acid, choline, falcarinol, falcarinolone, falcarindiol, b-pinene, camphene, P-cymene, b-phellandrene, myrcene, b-ocimene-X, allo-ocimene, 6-n-butyl-cycloheptadiene-1,4,2-methyl-dodecane-5-one, acetophenone, b-bisabolene, isoacroraene, acoradiene, chamigrene, a-cedrene, n-butyl-tetrahydrophthalide, n-butyl-phthalide, n-butylidene-phthialide, ligustilide, d-2,4-dihydrohpthalic anhydride, dodecanol, bergapten, P-methyl-benzolcohol, 5-methoxyl-2,3-dicresol, phenol, O-cresol, P-cresol, guaiacol, 2,3-dieresol, P-ehtyl phenol, O-eethyl phenol, 4-ethyl resorcinol, 2,4-dihydroacetophenone, carvacrol, isoeugenol, vanillin, phthalic anhydride, azelaic acid, sebacie acid, anisic acid, myristic acid, camphoric acid, dimethyl phthalate, dimethyl aelate, dimethyl sebacate, dimehtyl anisae, dimethyl myristate, dimethyl camphorate, n-valerophenone-o-carboxylic acid, ferulic acid, succinic acid, nicotinic acid, vanillic acid, n-tetracosanoic acid, palmitic acid, calcium, zinc, phosphorus, selenium, uracil, adenine, choline, stigmasterol, sitosterol, stigmaterol-D-glucoside, tetradecanol-1, scopletin, 6-methoxyl-7-hydroxycoumarin, angelicide and brefelclin A
11	**Radix Asparagi**	天門冬	Asp-IV, Asp-V, Asp-VI, Asp-VII, methylprotodioscin, pseudoprotodioscin, 3-O-alpha-L-rhamnopyranosyl(1->4)-beta-D-GLUCOPYRANOSYL-26-O-(beta-D-glucopyranosyl)-(25R)-furosta-5,20-beta,26-diol, yamogenin, diosgenin, sarsasapogenin, smilagenin, glucose, rhamnose, oligosaccharide I, oligosaccharide II, oligosaccharide III, oligosaccharide VII, sucrose, 5-methoxymethylfurfural, beta-sitosterol, citrulline, asparagine, glycine, alanine, valine, methionine, leucine, isoleucine, phenylalanine, tyrosine, aspartic acid, glutamic acid, arginine, histidine, lysine, asparagus-polysaccharide A, asparagus-polysaccharide B, asparagus-polysaccharide C, asparagus-polysaccharide D, asparagine, citrulline, serine, threonine, proline, clyccine , beta-sitosterol, smilagenin, 5-methoxymethylfurfural, rhamnose
12	**Radix Astragali**	黃耆	astragaloside I, astragaloside II, astragaloside III, astragaloside IV, astragaloside V, astragaloside VI, astragaloside VII, astragaloside VIII, daucosterol, beta-sitosterol, palmitic acid, astragalus saponin A, astragalus saponin B, astragalus saponin C, 2',4'-dihydroxy-5,6-dimethoxyisoflavane, kumataknin, choline, betaine, folic acid, calycosin, formononetin,

			L-3-hydroxy-9-methoxpterocarpan, soyasaponin I, astragaloside I, astragaloside II, astragaloside III, astragaloside IV, astrglalan I, astrglalan II, astrglalan III, formononetin, calycosin, daikon, Astragaloside, iron, manganese, zinc, rubidium, linoleic acid, linoleic acid, betaine
13	**Radix Codonopsis**	黨參	fructose, inulin, CP1, CP2, CP3, CP4, syringin, n-hexyl?beta-D-glucopyranoside, ethyl?alpha-D-fructofuranoside, tangshenoside, choline, perlolyrine, n-butyl allophanate, pyroglutamic acid N-furctoside, nicotinic acid, 5-hydroxy-2-pyridine methanol, lysine, threonine, valine, methionine, isoleucine, leucine, phenylalanine, aspartic acid, histidine, serine, glucamic acid, glycine, alanine, cystine, tyrosine, arginine, proline, taraxerol, taraxerl acettate, frideelin, alpha-spinasterol, alpha-spinasteryl-beta-D-glucoside, stigmast-7-en-3beta-ol, delta7-sitgmas-tenyl-beta-D-glucoside, stigmasterol, stigmasetyl-beta-D-glucoside, stigmasta-7,22-dien-3-one, stigmasta-5,22-dien-3-one, syringaldehyde, vanillic acid, 2-furan carboxylic acid, atractylenolide II, atractylenolide III, 5-hydroxymethl-2-furaldehyde, 5-metyoxymethy-2-furaldehyde, methylpalmitate, iron, copper, cobalt, manganese, zinc, nickel, selenium, aluminum, vanadium, fluorine, alpha-pinene, nona-2,4-dienal, borenol, xi-guaiene, alpha-curcumene, palmitic acid, methyl11,14-eicosadenoate, O-methoxyphenoxyphenol, (E)-2-hexenyl-beta-sophoroside, (E)-2-hexenyl-alpha-L-arabinopyranosyl(1->6)-beta-D-glucopyranoside, hexyl-beta-gentiobioside, hexyl-beta-soporoside, (6R,7R)-E,E-tetradeca-4,12-dien-8,10-diyne-1,6,7-triol-6-O-beta-D-glucopyranoside, codonolactone, codopiloic acid
14	**Radix Dipsaci**	續斷	sweroside, loganin, cantleyoside, akebiasaponin D,3-O-alpha-L-arabinopyranosylhederagenin-28-O-beta-D-glucopyranosyl (1->6)-beta-D-glucopyranoside, 3-O(4-O-acetyl)-alpha-L-arabinopyranosylhederagnin-28-O-beta-D-glucopyranosyl(1->6)-beta-D-glucopyranoside, 3-O-alpha-L-arabinopyranosyloleanolic acid-28-O-beta-D-glucopy-ranosyl(1->6)-beta-D-glucopyranoside, 3-O-beta-D-glucopyranosyl(1->3)-alpha-L-rhamnopyranosyl(1->2)-alpha-L-ara-binopyranosylhederagenin-28-O-beta-D-glucopyranosyl(1->6)-beta-D-glucopyranoside, 3-O-alpha-L-rhamnopyranosyl(1->3)-beta-D-glucopyranosyl(1->3)-alpha-L-rhamnopyranosyl(1->2)alpha-L-arabinopyranosylhederagenin-28-Obeta-D-glucopyranosyl(1->6)-beta -D-glucopyranoside, 3-O-[beta-D-xylopyranosyl(1->4)-beta-D-glucopyranosyl(1->4)][alpha-L-rhamnopyranosyl(1->3)-beta-D-glu-copyranosyl(1->3)-alpha-L-rhamnopyranosyl(1->2)-alpha-L-arabino pyran-nosylhederagein, 3-O-[beta-D-xylopyranosyl(1->4)-beta-D-glucopyranosyl(1->4)][alpha-L-rha-mnopyranosyl(1->3)-beta-D-glucopyranosyl(1->3)-alpha-L-rhamnopy-ranosyl(1->2)-alpha-L-arabin opyranosylhedagenin-28-O-beta-D-glu-copyranosyl(1->6)-beta-D-glucopyranoside], 3-O-[beta-D-xylopyranosyl(1->4)-beta-D-glucopyranosyl(1->4)][alpha-L-rhamnopy-ranosyl(1->3)]-beta-D-}gluopyranosyl(1->3)-alpha-L-rhamnopyranosyl(1->2)-alpha-L-arabin opyranosylhederagenin-28-O-beta-D-glucopyranoside, 3-O-alpha-L-ara-binopyranosylhederagenin, 3-O-alpha-L-arabinopyranosylhederagenin-28-O-beta-D-glucopyranoside,

			3-O-[beta-D-glucopyranosyl(1->4)][alpha-L-rhamnopyransoy(1->3)]-beta-D-glucopyranosyl(1->3)-alpha-L-rhamnopyranosyl(1->2)-alpha-L-arbinopyranosylenederagenin, 3-O-[beta-D-glucopyra-nosyl(1->3)]-beta-D-glucopyranosyl(1->3)-alpha-L-rhamnopyranosyl(1->2)-alpha-L-arabinopyranosylhedera-genin-28-O-beta-D-glucopyranosyl(1->6)-beta-D-glucopyranoside, 3-O-[beta-D-xylopyranosyl(1->4)-beta-D-glu-copyranosyl(1->4)][alpha-L-rhamnopranosyl(1->3)]-beta-D-glucopyransoyl(1->3)-alpha-L-rhamnopyranosyl(1->2)-alpha-L-arabinopyranosyleanolic acid-28-O-beta-D-glucopyranosyl(1->6)-beta-D-glucopyranoside, 3-O-[beta-D-xylopyranosyl(1->4)-beta-D-glucopyranosyl(1->4)][alpha-L-rhamnopyranosyl(1->3)]-beta-D-glucacetopyranosyl(1->3)-alpha-L-rhamnopyranosyl(->2)-alpha-D-arabinopyranosylhederagenin, asperosaponin F, 3-O-[beta-D-xylopyranosyl(1->4-beta-D-glucopyranosyl)(1->4)][alpha-L-rhamnopyranosyl(1->3)]-beta-D-galactopyranosyl(1->3)-alpha-L-rhamnopyranosyl(1->2)-alpha-L-arabinopyranosylhederagenin-28-O-beta-D-glucopyranosyl(1->6)-beta-D-glucopyranoside, asperosaponin H1, carvotanacetone, 2,4,6-tri-tert-butylphenol, 3-ethyl-5-methlphenol, 2,4-dimethylphenol, 4-methylphenol, 3-methylphenol, 2-ethyl-4-methylphenol, 2,6-bis(1,1-dimethylethyl)-4-methylpehnol, phenol, alpha,alpha,alpha,4-trimethyl-3-cyclohexene-methanol, 4-methyl-1-(1-methylethyl)-3-cylohexene-1-ol, 4-(3-methyl-2-butenyl)-4-cyclohexene-1,3-dione, dibenzofuran, phenanthrene, 1,2-dimethoxybenzene, ethylpropionate, hederagenin, beta-sitosterol, darcosterol, sucrose, titanium
15	**Radix Fici**	五指毛桃	coumarin, palmitic acid, oleic Acid, linoleic acid, ethyl acetate, Isopsoralen, bergapten
16	**Radix Glycyrrhizae**	甘草	Triterpenoid Saponins, glycyrrhizin, uralsaponin A, uralsaponin B, licoricesaponin A3, licoricesaponin B2, licoricesaponin C2, licoricesaponin D3, licoricesaponin E2, licoricesaponin F3, licoricesaponin G2, licoricesaponin H2, licoricesaponin J2, licoricesaponin K2, liquiritigenin, liquiritin, isoliquiritigenin, isoliquiritin, neoliquiritin, neoisoliquiritin, licoricidin, licoricone, formononetin, 5-O-methyllicoricidin, liquiritigenin-4'-qpiofur-anosyl(1->2)glucopyranoside, apioliquiritin, liquiritigenin-7,4'-diglucoside, vicenin?¢º, ononin, isolicoflanonol, isoliquiritigenin-4'-apiofuranosyl(1->2)glucopyranoside, licurazid, apioisoliquiritin, glycycoum-arim, glycyrol, isoglycyrol, glycyrin, neoglycyrol, licopyranocoumarin, licocoumarione, 5,6,7,8-tetrahydro-4-methylquinoline, 5,6,7,8-tetrahydro-2,4-dimethylquinoline, 3-methyl-6,7,8-trihydropyrrolo[1,2-]pyrimidin-3-one, licobenzofuran, liconeolignan, beta-sitosterol, n-tricosane, n-hexacosane, n-heptacosane, glucan GBW, glycyrrigan UA¡BUB¡BUC, polysaccharide GR-2a¡BGR-2¢ºb¡BGR-2¢ºC, Glycyrrhiza polysaccharide(GPS), Glycyrrhizic acid, 18-beta-glycyrrhetic acid, 18alpha-hydroxyglycyrrhetic acid, 24-hydroxyglycyrrhetic acid, 24-hydroxy-11-deoxyglycyrrhetic acid, 11-deoxyglycyrrhetic acid, 3beta-hydroxyolean-11,13(18)-dien-30-oic acid, glycyrrhetol, glabrolide, isoglabrolide, deoxyglabrolide, 21alpha-hydroxyisoglabrolide, liquoric acid, liquiritoside, liquiritogenin, isoliquiritoside, isoliquiritogenin, licuraside, licurazid,

			neolicuraside¡Aisoliquiritigenin-4-apiofuranosyl(1->2)glucopyranoside, glabranin, glabrol, glabridin, glabrone, glabreene, glyzaglabrin, glazarin, flavone, flavone, pinocembrin, prunetin, formononetin, liqcoumarin, pectin, glyasperin A, glyasperin B, glyasperin C, glyasperin D, kumata kenin, topazolin, flavone, flavone, flavanone, 3'(gamma,gamma-dimethylallyl)-kievitone, licoriisoflavan¡^A, 1-methyoxyficifolinol, isoglycycoumarin, glyeurysaponin, glycyroside, choerospondin, flavone, schaftoside, isoviosanthin, medicarpin-3-O-glucoside, beta-sitosterol, daucosterolphloretic acid, glyyyunnanpro-sapogenin D, glyyunnansapogenin A, glyyunnansapogenin B, glyyunnansapogenin C, glyyunnansapogenin E, glyyunnansapogenin F, glyyunnansapogenin G, glyyunnansapogenin H, macedonic acid, flavone, 7-methoxy-4'-hydroxyflavonol, yunganoside A1, yunganoside B1, yunganoside C1, yunganoside D1, yunganoside E2, yunganoside F2, hypaphorine
17	**Radix Morindae**	巴戟天	rubiadin, rubiadin-1-methyl ether, physcion, 2-hydroxy-3-hydrox-ymethylanthraquinone, 1-hydroxyanthraquinone, 1-hydroxy-2-methyl anthraquinone, 1,6-dihydroxy-2,4-dimethoxyan-thraquinone, 1,6-dihydroxy-2-methoxyanthraquinone, 2-methylanthraqui-none, monotropein, asperuloside tetraacetate, glucose, mannose, beta-sitosterol, palmitic acid, vitamin C, nonadecane, 24-ethyl cholesterol, zinc, manganese, iron, chronium
18	**Radix Ophiopogonis**	麥門冬	ruscogenin, ophiopogonin B , ophiopogonin D, (23S,24S,25S)-23,24-dihydroxyruscogenin-1-O-[alpha-L-rhamnopyranosyl(1->2)][beta-D-xylopyranosyl(1->3)]-alpha-L-arabinopyranoside-24-O-beta-D-fucopyranoside, (23S,24S,25S)-23,24-dihydroxyruscogenin-1-O-[alpha-L-2,3,4-tri-O-acetylrhamnopyranosyl(1->2)][beta-D-xylopyranosyl(1->3)]-alpha-L-arabinopyranoside-24-O-beta-D-fucopyranoside, (23S,24S,25S)-23,24-dihydroxyruscogenin-1-O-[alpha-L-4-O-acetylrhamnopyranosyl(1->2)][beta-D-xylopyranosyl(1->3)]-alpha-L-arabinopyranoside-24-O-beta-D-fucopyranoside, diosgenin, diosgenin-3-O-[alpha-L-rhamnopyranosyl(1->2)]-(3-O-acetyl)-beta-D-xylopyranosyl(1->3)-beta-D-glucopyranoside, diosgenin-3-O-[(2-O-acetyl)-alpha-L-rhamnopyranosyl(1->2)]-beta-D-xylopyranosyl(1->3)-beta-D-glucopyranoside, ophiogenin, ophioge-nin-3-O-alpha-L-rhamnopyranosyl(1->2)-beta-D-glucopyranoside, borneol-2-O-beta-D-glucopyranoside, borneol-2-O-beta-D-apiofuranosyl(1->6)-beta-D-glucopyranoside, borneol-2-O-alpha-L-arabinofuranosyl-(1->6)-beta-D-glucopyranoside, homoisoflavonoid, methylophiopogonanone A, methylophiopogonanone B, ophiopogonanone A, ophiopogonanone B, 6-aldehydo-7-O-methylisoophiopogonanone A, 6-aldehydo-7-O-methylisoophiopogonanone B, 6-aldehydoisoophiopogonone A, 6-aldehydoisoophiopogonone B, ophiopogone A, desmethylisoophiopogonone B, 5,7,2'-trihydroxy-6-methyl-3-(3',4'-methylenedioxybenzyl)chromone, 5,7,2'-trihydroxy-8-methyl-3-(3',4'-methylenedioxybenzyl)chromone, 5-hydroxy-7,8-dimethoxy-6-methyl-3-(3',4'-dihydroxybenzyl)chromanone, ruscogenin-1-O-sulfate, calcium bornyl sulfate, glycerol,

			N-[beta-hydroxy-beta-(4-hydroxy)phenyl]ethyl-4-hydroxy cinnamide, beta-sitosterol, stigmasterol, beta-sitosterol-3-O-beta-D-glucopyranoside, longifolene, patchoulene, cyperene, guaiol, alpha-humulene, camphor, linalool, terpinen-4-ol, jasmololone, potassium, sodium, calcium, magnesium, iron, copper, nickel, manganese, chromium, lead, cobalt, barium, zinc, beta-sitosteryl-beta-D-glucopyranoside, stigmasteryl-beta-D-glucopyranoside, campesteryl-beta-D-glucopyranoside, (25S)-ruscogenin?1-O-beta-D-fucopyranosido-3-O-alpha-L-rhamnopyranoside, (25S)-ruscogenin 1-O-beta-D-xylopyranosido-3-O-alpha-L-rhamnopyranoside, (25S)-ruscogenin 1-O-[(2-O-acetyl)-alpha-L-rhamnopyranosyl(1->2)][beta-D-xylopyranosyl(1->3)]-beta-D-fucopyranoside, (25S)-rucosgenin 1-O-[(3-O-acetyl)-alpha-L-rhamnopyranosyl(1->2)][beta-D-xylopyranosyl(1->3)]-beta-D-glucopyranoside, yamogenin3-O-[alpha-L-rhamnopyranosyl(1->2)][beta-D-xylopyranosyl(1->3)]-beta-D-glucopyranoside, (25S)-ruscogenin 1-O-alpha-L-rhamnopyranosyl(1->2)-beta-D-xylopyranoside, 1-n-butyl-beta-D-fructopyranoside, L-pyroglutamic acid, adenosine
19	**Radix Oryzae**	糯稻根	isoleucine, leucine, valine, methionine, threonine, lysine, Aspartic acid, serine, tyrosine, glycine, tricin
20	**Radix Polygoni**	何首烏	emodin, chrysophanol, physcion, rhein, chrysophanol anthrone, resveratrol, piceid, 2,3,5,4'-tetrahydroxystilbene-2-O-beta-D-glucopyranoside, 2,3,5,4'-tetrahydroxystilbene-2-O-beta-D-glucoPyranoside-2''-O-monogalloyl ester, 2,3,5,4'-tetrahydroxystilbene-2-O-beta-D-glucopyrano-side-3''-monogalloyl ester, gallic acid, catechin, epicatechin, 3-O-galloyl(-)-epicatechin, 3-O-galloyl-procyanidin, 3,3'-di-O-galloyl-Procyanidin B-2, beta-sitosterol, lecithin
21	**Radix Pseudostellariae**	太子參	palmitic acid, linoleic acid, glycerol 1-monolinolate, 3'-furfuryl pyrrole-2-carboxylate, behenic acid, 2-minaline, beta-sitosterol, manganese, heterophyllin A, heterophyllin B
22	**Ramulus Visci**	槲寄生	rhamnazin, rhamnzin-3-O-beta-D-glucoside, isorhamnetin-3-O-beta-D-gluco-side, isorhamnetin-7-O-beta-D-glucoside, 3-methyleriodictyol, 3'-methylerlodi ctyol-7-O-beta-D-glucoside, viscumneoside I, viscumneoside II, viscumneoside III, viscumneoside IV, viscumneoside V, viscumneoside VI, viscumneoside VII, beta-amyranol, beta-acetylamyranol, beta-amyrandiol, lupeol, oleanolic acid, betulic acid, beta-amyrin palmitate, beta-amyrin acetate, beta-sitosterol, daucosterol, syringin, syringenin-O-beta-D-apio-furanosyl(1->2)-beta-D-glu-copyranosideliriodendrin, butan-2,3-diol-3-O-monoglucoside, meso-inositol, palmitic acid, succinic acid, ferulic? acid, caffeic acid, protocatechuic acid
23	**Fructus Lycii**	枸杞子	atropine, gyoscyamine, cryptosxanthin, scopoletin, carotene, thiamine, riboflavin, nicotinic acid, vitamin C, aspartate, proline, methionine, leucine, phenylalanine, serine, glycine, glutamic acid, cysteine, lysine, arginine, isoleucine, threonine, histidine, tyrosine, tryptophan, methionine, potassium, calcium, sodium, zinc, iron, copper, chromium, strontium, lead, nickel, cadmium, cobalt, magnesium, taurine, gamma-aminobutyric acid, betaine, zeaxanthin, physalien, leucine, valine, proline, alanine, tyrosine, glutamine, glycine,

			glutamic acid, sapartic acid, asparagine, histidine, tryptophan, safranal, 3-hydroxy-beta-ionone, 1,2-dehydrox-alpha-cyperene, solavetivone, carotene, thiamine, riboflavin, nicotinic acid, vitamin C3, cholesterol, cholest-7-enol, campesterol, 24-methylenecholesterol, isofucoterol, isofucosterol, stigmasterol, beta-sitosterol, 24-methylcholesta-5,24-dienol24-ethyl-cholesta-5,24-dienol, cholestanol, 24-methylcholestanol, 24-ehtylcholest-22-enol, 31-norcycloartanol, 31-norcycloartenol, cycloeucalenol, 31-norlanost-8-enol, 4alpha,14alpha24-trimethylcholesta-8-24-dienol, 24-methyl-31-norlanost-9(11)-enol, 4alpha-methylcholest-8-enol, 4-methylcholest-7-enol24-ethylolphenol, 4,24-methyllophenol, gramisterol, citrostadienol, alpha,24-dimethylcholesta-7,24-dienol, 4alpha-methyl-24-ethylcholesta-7,24-dienol, lanost-8-enol, cycloartanol, cycloartenol, lanosterol, beta-amyrin, lupeol, 24-methylenelanost-8-enol, 24-methylenecycloartanol, taurine, gamma-aminobutyric acid
24	**Fructus Ziziphi**	大棗	stepharine, N-nornuciferine, asmilobine, betulonic acid, oleanolic acid, maslinic acid, cratagolic acid, 3-O-trans-p-coumaroyl-maslinic acid, 3-O-cis-p-coumaroyl-maslinic acid, betulinic acid, alphitolic acid, 3-O-trans-p-coumaroyl alphi-tolic acid, 3-O-cis-P-coumaroylal-phitolic acid, zizyphus saponin I, zizyphus saponin II, zizyphus saponin III, jujuboside B, cyclic adenosine 3',5'-monophasphate (cAMP), cyclic guanosine 3',5'-monophosphate (cGMP), fructose, glucose, sucrose, oleic acid, sitosterol, stigmasterol, desmosterol, rutin, vitamin C, riboflavin, thiamine, carotene, nicotinic acid, tannic acid, coumarin derivatives, lipids, resins, malic acid, jujuboside A, jujuboside B, jujuboside B1, indole acetic acid, lysine, aspartic acid, asparagine, glycine, glutamic acid, alanine, proline, valine, leucine, selenium, zizybeoside I, zizybeoside II, zizyvoside I, zizyvoside II, roseoside, zizyphusin, daechu alkaloid A, nuciferine, co-claurine, nornuciferine, lysicamine, daechucy-clopeptide-1, daechuine S3, vomifliol 6, 6,8-di-C-glucosyl-2(S)-naringenin, 6,8-di-C-glucosyl-2(R)-naringenin, palmitoleic acid, vaccenic acid, oleic acid, zizyphus-arabinan, glycolipid, phospholipid
25	**Radix Panacis quinquefolii**	西洋參	octanol, hexanoic acid, undecane, pinocarveol, octanoic acid, dodecane, 3-phenylhexane, 1-phenylhexane, pulegone, 2-methoxy-4-(1-propenyl)-phenol, 1,3,5-triisopropylphene, beta-gurjunene, piperitene, beta-farnesene, alpha-curcumene, alpha-cedrene, 2, 6-diterbutyl-4-methylphenol, beta-bisabolene, beta-caryophyllene, 3-phenyldecane, hexadecane, 6-phenylundecane, 4-phenglundecane, 3-phenylundecane, 6-phenyldodecane, 5-phenyldodecane, 4-phenyldodecane, 3-phenyldodecane, 2-phenyldodecane, 5-phenyltridecane, 4-phenyltridecane, 3-cyclohexyldodecane, ginsenoside R0, ginsenoside Rb1, ginsenoside Rb2, ginsenoside Rb3, ginsenoside Rc, ginsenoside Rd, ginsenoside Re, ginsenoside Rf, ginsenoside Rg1, ginsenoside Rg2, ginsenoside Rg3, ginsenoside Rh1, ginsenoside RA0, quinquenoside R1, gypenoside X1, gypenoside F3, gypenoside F11, caproic acid, heptanoic acid, caprylic acid, nonanoic acid, palmitic acid, n-heptadecanoic acid, stearic acid, octadecenoic acid, linoleic acid, 9,12,15-octadecatrienoic acid, 8-methyl capric acid, oleanolic acid, plastochromanol-1, plastochromanol-2, plastochromanol-3, sucrose, panose, ginsengtrisaccharide, karusan A, karusan B, karusan C, karusan D, karusan E, Daucosterol, stigmasterol, stimast-3, 5-dien-7-one, Panaquilon, protopanaxadiol, protopanaxatriol, daucosterin, Oleanolic Acid, stigmast-5-en-3-ol, stigmast-3,5-diene-7-one, beta-farnesenehexadecane, beta-gurjunene, hexanoic acid, dodecane, (+)-Pulegone, longifolene, trans-Caryophyllene, 3-phenylundecane, 6-phenyldodecane, 4-phenyldodecane,

			3-phenyldodecane, 2-phenyldodecane, caproic acid, octanoic acid, Heptanoic Acid, nonanoic acid, pentadecanoic acid, hexadecanoic acid , heptadecanoic acid, octadecanoic acid, octadecadienoic acid, octadecadienoic acid, octadeca-9,12,15-trienoic acid, 8-methyldecanoic acid, ethyl alcohol, threonine, valine, methionine, isoleucine, leucine, lysine, phenylalanine, histidine, arginine, iron, chromium, copper, borium, manganese, strontium, zinc, calcium, potassium, magnesium, phosphorus, pseudoginsenoside-F11, , , ,
26	**Radix Rehmanniae**	幹地黃	leonuride, ajugol, aucubin, cotalpol, rehmannioside A, rehmannioside B, rehmannioside C, rehmannioside D, melittoside, rehmaglutin A, rehmaglutin B, rehmaglutin C, rehmaglutin D, acteoside, soacteoside, monometittoside, glutinoside, geniposide, ajugoside, 6-O-E-feruloyl ajugol, jioglutin D, jioglutin E, jioglutolide, 6,8-dihydroxyboschuialactone, cataepolgcnin, catalpolgenin-alpha-L-arabinofuranoside, jioglutoside, ggrardoside, mioporosidegenin, rehmaionoside A, rehmaionoside B, rehmaionoside C, rehmapicroside, purpureaside C, jionoside A1, jionoside B1, echinacoside, cistanoside A, cistanoside F, cerebroxide B1-b, 1-O-beta-D-glucopyranosyl-2-N-2'-hydroxypalmitoyl sphinga-4-trans,8-cis-dienine, stachyose, glucosamine, phosphoric acid, glucosamine, phosphoric acid, manganese, iron, copper, magnesium, aluminum, borium, strontium, zinc, benzoic acid, caprylic acid, phenyl acetic acid, pelargonic acid, capric acid, cinnamic acid, 3-methoxy-4-hydroxybenzoic acid, lauric acid, myristic acid, pentadecanoic acid, palmitoleic acid, palmitic acid, margaric acid, linoleic acid, stearic acid, nonadecanoic acid, arachidic acid, heneicosanoic acid, arachidic acid, heneicosanoic acid, behenic acid, linoleic acid, palmitic acid, succinic acid, beta-sitosterol, darcosterol, 5-hydroxymethylfurfural, (4-methyl-2-furanyl)-2-(5-methyl-5-ethenyl-2-tetrahydrofuranyl)-propan-1-one, 4-(1beta,2alpha,5alpha-trihydroxy-2beta,6,6,-trimethylcyclohexanyl)-3-buten-2-one, 5-¡]1beta,2alpha-dihydroxy-2beta-methyl-2-O-beta-quinovopyranosyl-6beta-hydroxymethyl)cyclohexanyl-2-methyl-2,4-pentadienoic acid, adenosine
27	**Radix Rehmanniae Peraparata**	熟地黃	leonuride, aucubin, catalpol, rehmannioside A, rehmannioside B, rehmannioside C, rehmannioside D, melittoside, tehmaglutin A, tehmaglutin D, glutinoside, jioglutin A, jioglutin B, jioglutin C, jioglutolide, jiolutin A, jiolutin B, jiolutin C, jioglutolide, jiofuran, rehmapicrogenin, trihydroxy-beta-ionone, 5-c-hydroxyaeginetic acid, succinic acid, 5-oxoproline, 5-hydroxymethylfuroic acid, uracil, uridine, linoleic acid, palmitic acid, stearic acid, arachidic acid, behenic acid, pentadecanoic acid, palmitoleic acid, myristic acid, nonadecanoic acid, heneicosanoic acid, margaric acid
28	**Rhizoma Atractylodis**	白朮	alpha-humulene, beta-humulene, beta-elemol, alpha-curcumene, alpha-tractlone, 3beta-acetoxyatractylone, selina-4(14),7(11)-diene-8-one, eudesmol, palmitic acid, hinesol, beta-selinene, atractylenolide I, atractylenolide II, atractylenolide III, 8beta-ethoxyatractylenolide II, 14-acetyl-12-senecioyl-2E,8Z,10E-atracetylentriol, 14-acetyl-12-senecioyl-2E,8E,10E-atracetylentriol, 12-senecioyl-2E,8Z,10E-atracetylentriol, 12-senecioyl-2E,8E,10E-atractylentriol, 12alpha-methyl butyryl-14-acetyl-2E,8Z,10E-atractylentriol, 12alpha-methylbutyryl-14-acetyl-2E,8E,10E-atractylentriol, 14alpha-methyl butyryl-2E,8Z,10E-atractylentriol, 14alpha-methyl butyryl-2E,8E,10E-atractylentriol, scopoletin, fructose, inulin, mannosan AM-3, aspartic acid, serine, glutamic acid, alanine, glycine, valine, isoleucine, leucine, tyrosine,

			phenylalanine, lysine, histidine, arginine, proline
29	**Rhizoma Cibotii**	狗脊	pterosin R, onitin, onitin-2'-O-beta-D-glucoside, onitin-2'-O-beta-D-allosideptaquiloside, pterosin Z
30	**Rhizoma Curculiginis**	仙茅	curculigoside A, curculigoside B, orcinol glucoside, corchioside A, curculigosaponin A, curculigosaponin B, curculigosaponin C, curculigosaponin D, curculigosaponin E, curculigosaponin F, curculigosaponin K, curculigosaponin L, curculigosaponin M, curculigine A, curculigine B, curculigine C, curculigenin A, curculigenin B, curculigenin C, curculigol, yuccagenin, 5,7-dimethoxymyricetin-3-O-alpha-L-xylopyranosyl(4->1)-O-beta-D-glucopyranoside, lycorine, N-acetyl-N-hydroxy-2-carbamic acid methylester, 3-acetyl-5-carbomethoxy-2H-3,4,5,6-tetrahydro-1-oxa-2,3,5,6-tetrazine, N,N,N',N'-tetramethylsuccinamide, cycloartenol, beta-sitosterol, stigmasterol, hentriacontanol, 3-methoxy-5-acetyl-31-tritriacontene, 21-hydroxytetracontan-20-one, 4-methylheptadecanoic acid, 27-hydroxytriacontan-6-one, 23-hydroxytriacontan-6-one, 4-acetyl-2-methoxy-5-methyltriacontane, 25-hydroxy-33-methylpentatriacontan-6-one
31	**Rhizoma Dioscoreae**	山藥	diosgenin, dopamine, batatasine hydrochloride, polyphenoloxidase, allantoin, abscisin II, glucoprotein, lysine, histidine, arginine, aspartic acid, threonine, serine, glutamic acid, proline, glycine, alanine, valine, leucine, isoleucine, tyrosine, phenylalanine, methionine, cystine, gamma-aminobutyric acid, mannose, glucose, galactose, barium, beryllium, cerium, cobalt, chromium, copper, lanthanum, lithium, manganese, niobiuim, nickel, phosphorus, strontium, thorium, titanium, vanadium, yttrium, ytterbium, zinc, zirconium, sodium oxide, potassium oxide, aluminum oxide, iron oxide, calcium oxide, magnesium oxide, catecholamine, cholesterol, ergosterol, campesterol, stigmasterol, beta-sitosterol, phytic acid, mannan Ia , mannan Ib, mannan Icbatatasin I, batatasin I, batatasin III, batatasin IV, batatasin V, cholestanol, (24R)-alpha-methyl cholestanol, (24S)-beta-methyl cholestanol, (24R)-alpha-ethyl cholestanol, (24S)-beta-methyl cholestanol, 24-methylenecholesterol, isfucosterol, clerosterol, 24-emthylene-25-methyl cholesterol, lathosterol, cholest-8(14)-enol, (24R)-alpha-methyl cholest-8(14)-enol, (24S)-beta-methyl cholest-8(14)-enol, (24R)-alpha-ethyl cholest-8(14)-enol, choline, dioscoran A, dioscoran B, dioscoran C, dioscoran D, dioscoran E, dioscoran F
32	**Rhizoma Drynariae**	骨碎補	naringin, hop-21-ene, fern-9(11)ene, fern-7-ene, filic-3-ene, beta-sitosterol, stigmasterol, campesterol, cycloardenyl acetate, cy-clomargenyl acetate, cyclolaudenylacetaet, 9,10-cycloanost-25-en-3beta-yl acetateneohop-13(18)-ene
33	**Semen Allii**	韭子	vitamin C, 1,2,3,4-tetrahydro-4-hydroxy-4-quinolin carboxylic acid, Tuberosine B, 7-hydroxy-2, 5-dimethyl 4-H-1-Benzopyran-4-one , Vernolic acid, 3-methoxy-4-hydroxybenzoic acid, p-Hydroxybenzoic acid, 3, 5-dimethoxy-4-hydroxybenzoic acid, Syringaresinol, tuberosine A, N-cis-feruloyl 3-methyldopanine, N-trans-feruloyl 3-methyldopanine, N-trans-coumaroyl tyramine, 3-formylindole, 3-Pyridine carboxylic acid, tabacin C, 1-O-alpha-L-rhamnose(22S)-cholest-5-en-1beta,3 beta,16beta,22-tetrahydroxyl-16-O-beta-D-¸²µå¿}?, daucosterol, adenine nucleoside, thymine nucleoside

34	**Semen Cuscutae**	菟絲子	quercetin, astragalin, hyperin, quercetin-3-O-beta-D-galactoside-7-O-beta-glucoside
35	**Semen Prinsepiae**	蕤仁	cyanogen, beta-sitosterol, Daucosterol, vanillic acid, protocatechuic acid, ursolic acid, Diploptene, balanophonin
36	**Semen Sesami**	黑芝麻	oleic Acid, linoleic acid, palmitic acid, stearic acid, arachidonic acid, lignoceric acid, sesamin, sesamolin, sesamol, vitamin E, phytosterol, lecithin, pedaliin, planteose, sesamose, phosphorus, potassium, cytochrome c, folic acid, nicotinic acid, sucrose, pentosans, calcium, linolenic acid
37	**Radix Ginseng**	人參	ginsenoside Rc , ginsenoside Ra1, ginsenoside Ra2, ginsenoside Ra3, ginsenoside Rba, ginsenoside Rb2, ginsenoside Rc, ginsenoside Rd, ginsenoside Rg, notoginsenoside R4, chikusetsuaponin IV, chikusetsuaponin IVa, panaxynol, ginsenyne, alpha pansinsene, beta pansinsene, beta farnesene, bicyclogermacrene, beta elemenegama elemene, alpha neodovene, beta neodovene, alpha humulene, beta humulene, caryophyllene , beta gurjunene, alpha gurjunene, alpha selinene, beta selinene, gama selinene, selin-4, alpha guaiene, gama cubebene , beta patchoulene, hepatadecanol-1, octanal, gama cadinene, trans beta farnesene, beta guaienebeta maaliene, cis caryophyllene, delta elemene, tetradecane, pentadecane, hexdecan, 2,6-ditertbutyl-4methly-phenol, heptadecane, delta cadinene, widdrol, beta bisablene, octadecane, abol, alpha elemenetridecan, eremophifene, gam patchoulene, cedrol, gama gurjunene, dodecane, alloaromadendrene, trans-caryophyllene, eicosane, alpha santalene, alpha muurodlene, palustalol, beta demene, alpha santalol, beta eubesmol, di-n-butyloxalate, eleutherosides, citric acid, isocitric acid, fumaric acid, oleic acid, linoleic acid, cis-butendicarboxylic acid, malic acid, pyuvic acid, succinic acid, tartaric acid, panax aid, salicyclic acid, vanillic acid, p-hydroxycinnamic acidtriglyceride, plmitin, palmitic acid, beta sitosterol, stigmasterol, daucosterol, sitosteryl-o-(6-O-fatty acyl)-glucpyranoside, choline, adenosine triphosphate, adenosine, vitamin B1 , vitamin B2, vitamin B12, vitamin C, nicotinic acid , folic acid, biotin, copper, zinc, iron, manganese, Gomisin N, gomisin A, Kaempferol and pansenoside, Sugars, fructose, glucose, arabinose , rhamnose, glucuronic acid, mannose, xylose, sucrose, maltose, raffinose, ginsengtrisaccharide A, ginsengtrisaccharide B, ginsengtrisaccharide C, ginsengtrisaccharide D, maltol, nonacosane, methoxy-5, nephyl-2(5H)-furanone, , , , , , , ,
38	**Testa Dolichoris**	扁豆衣	sucrose, glucose, maltodextrin, stachyose, raffinose, L-pipecolic acid, phytoagglutinin, phytin, calcium, phosphorus, iron, pantothenic acid, Dalbergioidin, Kievitone, Phaseollidin, Dimethylvestitol, Isovestitol, Laxifloran, Dolicholide, Dolichosterone, Homodolichosterone, Homodolicholide, Brassinolide, Castasterone
39	**Rhizoma Polygonati**	玉竹	odoratan, polygonatum fructan A, polygonatum fructan B, polygonatum fructan C, polygonatum fructan D, azetidine-2-carboxylic acid, polyspirostanol Poa, polyspirostanoside Pob, polyspirostanoside Poc, polyspirostanoside PO1, polyspirostanoside PO2, polyspirostanoside PO3, polyspirostanoside PO4, polyspirostanoside PO5¡A, polyfuroside, polyfuroside Poc, polyfuroside Pod, polyfuroside PO6, polyfuroside PO7, polyfuroside PO8, polyfuroside PO9
40	**Rhizoma Polygonati**	黃精	26-O-beta-D-glucopyranosyl-22-O-methyl-25(S)-furost-5-ene-3beta,26-diol3-O-beta-lycotetraoside, sibiricoside-A, 26-O-beta-D-glucopyranosyl-22-O-methyl-25(S)-fruost-5-ene-3beta,14alpha,26-triol 3-O-beta-lycotetraoside, 14alpha-hydroxysibiricoside A, sibiricoside B, neoprazerigenin A

			3-O-beta-lycotetraoside, polygona-polysaccharose A, polygona-polysaccharose B, polygona-polysaccharose C
41	**Radix Glehniae**	北沙參	9-(1,1-dimethylallyl)-4-hydroxypsoralen, 7-O-(3,3-dimethylallyl)-scopoletin, psoralen, bergapten, xanthotoxin, isoimperatorin, imperatorin, bergaptin, 9-geranyloxypsoralen, cnidiline, xanthotoxol, alloisoimperatorin, marmesin, ostheol-7-O-beta-gentiobioside, GLP, phospholipid, lecithin, cephalin
42	**Radix Adenophorae**	南沙參	beta-sitosterol, beta-sitosterol-O-beta-D-glucopyranoside, taraxerone, octacosanoic acid
43	**Bulbus Lilii**	百合	26-O-beta-D-glucopyranosyl-nuatigenin-3-O-alpha-L-rhamnopyranosyl(1¡÷2)-O-[beta-D-glucopyranosyl-(1¡÷4)]beta-D-glucopyranoside, 27-O-(3-hydroxy-3-methylglutaroyl)isonarthogenin-3-O-alpha-L-rhamnopyranosyl-(1¡÷2)-O-[beta-D-glucopyranosyl-(1¡÷4)]-beta-D-glucopyranoside, solasodine-3P-alpha-L-rha-mnopyranosyl-(1¡÷2)-O-[beta-D-glucopyranosyl-(1¡÷4)]-beta-D-glucopyranoside, regaloside, 3,6'-O-diferuloylsucrose, 1-O-feruloylglycerol, 1-O-p-coumaroylglycerol, brownioside, deacylbrownioside, beta-1-solamargine, lilioside
44	**Radix Changii**	明黨參	1,7,7-trimethyl-bicycol[2.2.1, 1,2,4a,5,6,8a-hexahydro-4,7-dimethyl-1-(1-methylethyl)naphthalene, decahydro-1,6-bis-(methylene)-4-(1-methylethyl)naphthalene, methyl-6,9-octadecadiynoate, beta-pinene, nerolidol, nerylpropionate, dodecylacetate, 1-tetradecanolacetate, 2,3,4,5,6-hex-ahyldro-1H-inden-2-ol, 9,11-octadecadienic acid, 6-phenylnonanoic acid, palmitic acid, 2-hydroxy-1-hydroxymethyl-9,10-octadeca-dienoic acid, 2-methylexadecanoic acid, hexadecenoic acid, 5-benzocy-clooctenol, stearic acid, linoleic acid, phosphatidic acid, phosphatidylcholine, 9,11-octadecadienoic acid, 10-oc-tadecenoic acid, 15-methylhexadecanoic acid, octanoic acid, changium smyrnioides polysaccharide, rhamnose, arabinose, xylose, mannose, galactose, glucose, gamma-aminobutyric acid, aspartic acid, arginine, threonine, lysine, methionine, alanine, ornithine, glutamic acid, serine
45	**Fructus Mori**	桑椹	tannic acid, malic acid, vitamin, carotene, linoleic acid, oleic acid, palmitic acid, stearic acid, caprylic acid, pelargonic acid, capric acid, myristic acid, linolenic acid, cineole, geraniol, linalyl acetat, linalool, camphor, alpha-pinene, limonene, phosphatidyl choline, lysophosphatidy choline, phosphatidyl ethanolamine, phosphatidic acid, phosphatidyl inositol, diphosphatidyl glycerol, cyanidin, chrysanthemin
46	**Carapax Trionycis**	鱉甲	calcium, sodium, aluminum, potassium, magnesium, copper , zinc, phosphorus, manganese, collagen, trionyx sinesis polysaccharides, aspartic acid, threonine, glutamic acid, glycine, alanine, cystine, valine, methionine, isoleucine, leucine, tyrosine, phenylalanine, lysine, histidine, arginine, proline, serine
47	**Cornu Cervi Pantotrichum**	鹿茸	spermidine, spermine, putrescine, linoleic acid , linolenic acid , glycine, lysine, arginine, aspartic acid, glutamicacid, proine, alanine, leucine, cholesteryl cyristate, cholesteryl oleate, cndested edwhtate, cholesteryl stearate, p-hydroxybenzaldehyde, cholesterol, cholest-5-en-3betaol-one, cholest-5-en-3beta,7alpha-diol, cholest-5-en-3beta,7beta-diol, uracil, hypoxanthine, urea, uridine, nicotinic acid, creatinine, fatty acid, triglycerides, monoglyceride, lauric acid, myristic acid, palmitic acid, palmitoleic acid, linotic acid, esrone,

			sphingomyeline, ganglioside, estradiol, ceramide, cholesterol, creatinine, p-hydroxybenzaldehyde, p-hydroxybenzoic acid, uridine, lysophosphatidylcholine,LPC, pentadecanoic acid, heptadecanoic acid, stearic acid, tryptophane, histidine, toreonine, adenosine triphosphate, decanoic acid
48	**Placenta Hominis**	紫河車	interferon, beta-inhibitor, gonadotropin, lactogen, thyrotropin, estrone, estradiol, estriol, progesterone, testosterone, deoxycorticosterone, 11-dehydrocorticosterone, cortisone, 17-hydroxycorticosterone, tetrahydrocorticosterone, 4-pregnen-20,21-diol-3,11-dione, chorionic gonadotropin, adrenocorticotropic hormone, lysozyme, kininase, histaminase, oxytocinase, phospholipid, beta-endorphin
49	**Fructus Alpinae Oxyphyllae**	益智仁	zingiberene, zinginerol, 1-(4'-hydroxy-3'-methoxyphenyl)-7-phenyl-3-heptanone, yakuchinone-B, trans-1-(4'-hydroxy-3'-methoxyphenyl)-7-phenylhept-1-en-3-one, 4'-hydroxy-3'-methoxyphenyl, manganese, zinc, potassium, sodium, calcium, magnesium, phosphorus, copper
50	**Gecko**	蛤蚧	carnosine, choline, carnitine, guanine, cholesterol, glycine, proline, glutamic acid, phosphatidylethanolamine, sphingomyelin, phosphatidylcholine, phosphatidic acid, lysolecithin, linoleic acid, palmitic acid, oleic acid, linolenic acid, palmitoleic acid, stearic acid, arachidic acid, arachidonic acid
51	**Cordyceps**	冬蟲夏草	aspartic acid, glutamic acid, serine, histidine, glucine, threonine, arginine, tyrosine, alanine, TCMLIByptophane, methboine, valine, phenylalanine, isoleucine, leucine, ornithine, lysine, lenolic acid, beta-lenoleic acid, cordycepic acid, D-mannitol, nicotinic acid, nicotinic amide, ergosterol, uracil, adenine, adenine nucleoside, ergosterol peroxide, cholesteryl palmitate, galactomannan, D-galactose, D-mannose, hypoxantine nucleoside, thymine, guanine, hypoxanthine, adenosine
52	**Actinolitum**	陽起石	manganese, aluminum, titanium, chromium, nickel
53	**Fluoritum**	紫石英	calcium fluoride, calcium, fluorine, ferric oxide, cadmium, chromium, copper , manganese, nickel, lead, zinc, yttrium, cerium
54	**Hippocampus**	海馬	glutamic acid, aspartic acid, glycine, proline, alanine, leucine, calcium, phosphorus, sodium, potassium, magnesium, strontium, silicon, stearic acid, cholesterol, cholesterdiol, gamma-carotene, astaxanthin, astacene, melanin, arginine, tourine
55	**Herba Pimpinellae thellungianae**	羊紅膻	3-methoxy-5-(1'-ethoxy-2'-hydrox-ypropyl)-phenol, api-genin-7-O-glucuronide, luteolin-7-O-glucuronide, luteolin-7-methyl-glucurunate, luteolin-7-methyl-glucurunate, beta-sitosterol, gamma-sitosterol, apigenin-7-O-beta-D-glucoside, thellungianate
56	**Semen Lablab Album**	白扁豆	palmitic acid, linoleic acid, elaidic acid, oleic acid, stearic acid, arachidic acid, behenic acid, trigonelline, methionone, leucine, threonine, vitamin, carotene, sucrose, glucose, stachyose, maltose, raffinose, L-pipecolic acid, phytoagglutinin
57	**Radix et Rhizoma Acanthopanacis**	刺五加	3beta-[O-alpha-L-rhamnopyranosyl-(1¡÷4)-O-alpha-L-rhamnopyranosyl(1¡÷4)[O-alpha-L-rhamnopyranosyl(1¡÷2)]-O-beta-D-glucopyranosyl(1¡÷x)-O-beta-D-glucoronopyranosyl]-16alpha-hydroxy-13beta,28-epoxyoleanane, daucosterol, syringin, syringaresinod-di-O-beta-D-glucoside, syringaresinol-O-beta-D-glucoside, pinoresinol-di-O-beta-D-glucoside,

	Senticosi		medioresinol-di-O-beta-D-glucoside, 2,6-dimethoxybenzoquinone, ciwu-jianoside, hederasaponin B, 3-O-alpha-rhamnopyranosyl(1¡÷2)-arabinopyra-nosyl oleanolic acid, 3-O-alpha-arabinopyranosyl-30-norolean-12,20(29)-dien-28-oic acid, sinapaldehyde glu-coside, coniferaldehyde glucoside, coniferin, liriodemdrin, amygdlin, seasamin, coniferylaldehyde, vanillin, isofraxidin, syringaresinol, sy-ringic acid, vanillic acid, hydroxybenzoic acid, p-coumaric acid, ferulic acid, chlorogenic acid, caffeic acid, 1,5-di-O-caffeoylquinic acid, methyloleate, ethyloleate, 10,13-oc-tadecadienoic acid ethyl ester, 9,11-oc-tadecadienoic acid, hexadecatrienoic acid, myristic acid, palmitic acid, stearic acid, betulic acid, beta-sitosterol, isofraxidin-7-O-beta-D-glucoside, hyperin, 3,4-dihydroxy benzoic acid
58	**Rhodiola Rosea**	紅景天	tyrosol, salidroside, rhodioloside, caffeic acid, umbelliferone, tyrosol, gallic acid, ethyl ester, kaemoferol, beta-sitosterol, daucosterol, rhodioloside
59	**Sea Buckthorn (Hippophae rhamnoides L.)**	沙棘	isorhamnetin, isorham-netin-3-O-beta-D-glucoside, isorhamnetin-3-O-beta-rutinoside, rutin, astragalin, quercetin, kaempferol, vitamin, dehydroascorbic acid, folic acid, carotene, carotenoid, catechin, anthocyanin, palmitic acid, stearic acis, oleic acid, linoleic acid, linolenic acid, zeaxanthin, cryptoxanthin, carotene, sitosterol, beta-sitosterol-beta-D-glucoside, phosphatide, serotonin, glucofrangulin, isorha-mnetin, hemin
60	**Mel**	蜂蜜	glucose, fructose, peroxidase, acetylcholine, nicotinic acid, pantothenic acid, carotene, alpha-glycerophosphate dehydrogenase
61	**peony**	白芍	paeoniflorin, oxy-paeoniflorin, benzoylpaooniflorin, albi-florin, paeoniflorigenone, galloylpaeoniflorin, z-1s,5R-beta-pinen-10-yl-beta-vicianoside, lacioflorin, paeoni-lactone, beta-siiosierol, daucos-terol, 1,2,3,6-tetra-O-galloyl-beta-D-glucose, 1,2,3,4,6-penta-O-galloyl-beta-D-glucose, catechin, benzoic acid, paeonol
62	**Colla Corii Asini**	阿膠	potassium, sodium, calcium, magnesium, iron, copper, aluminum, manganese, zinc, chromium, platinum, tin, silver, bromine, strontium, barium, titanium, zirconium, molybdenum, glycine, proline, glutamic acid, alanine acid, arginine, aspartic acid, lysine, phenylalanine, serine, histidine, cysterne, valine, methionine, isoleucine, leucine, tyrosine, tryptophan, hydroxyroline, threonine
63	**Dried Longan Pulp**	龍眼肉	glucose, sucrose, tartartic acid, adenine, choline
64	**Fructus Broussoentiae Papyriferae**	楮實子	lenolic acid, lenoleic acid, saponins

APPENDIX B Reports of ID3 Decision Tree Classification

1. **Features:** Including ATP Generation Capacity; **Class:** Yin-, Yang-, Qi-, and Blood-tonic Herbs

```
1_hasATPGC_class_is_all_four_tonic_herbs.txt                          2009/6/30 上午 04:24

=== Run information ===

Scheme:     weka.classifiers.trees.Id3
Relation:   herb-weka.filters.unsupervised.attribute.Remove-R156-159-weka.filters.supervised.attribu
Instances:  35
Attributes: 155
            [list of attributes omitted]
Test mode:  35-fold cross-validation

=== Classifier model (full training set) ===

Id3


ATP_generation_(percent_control) = '(-inf-129.5]'
|  manganese = yes
|  |  adenosine = yes: Yin
|  |  adenosine = no: Qi
|  manganese = no
|  |  calcium = yes: Blood
|  |  calcium = no
|  |  |  palmitic_acid = yes
|  |  |  |  alanine = yes: Qi
|  |  |  |  alanine = no
|  |  |  |  |  bergapten = yes: Qi
|  |  |  |  |  bergapten = no: Blood
|  |  |  palmitic_acid = no
|  |  |  |  carotene = yes: Qi
|  |  |  |  carotene = no
|  |  |  |  |  lecithin = yes: Blood
|  |  |  |  |  lecithin = no
|  |  |  |  |  |  phenol = yes: Yang
|  |  |  |  |  |  phenol = no: Yin
ATP_generation_(percent_control) = '(129.5-inf)'
|  formononetin = yes: Qi
|  formononetin = no: Yang

Time taken to build model: 0.02 seconds

=== Stratified cross-validation ===
=== Summary ===

Correctly Classified Instances        17        48.5714 %
Incorrectly Classified Instances      18        51.4286 %
Kappa statistic                    0.3054
Mean absolute error                   0.2571
Root mean squared error               0.5071
Relative absolute error             67.3892 %
```

```
Root relative squared error          114.6467 %
Total Number of Instances             35

=== Detailed Accuracy By Class ===

             TP Rate   FP Rate   Precision   Recall  F-Measure   ROC Area  Class
               0.625     0.296     0.385     0.625     0.476      0.664    Yin
               0.909     0.042     0.909     0.909     0.909      0.934    Yang
               0.222     0.231     0.25      0.222     0.235      0.496    Qi
               0         0.107     0         0         0          0.446    Blood
Weighted Avg.    0.486     0.162     0.438     0.486     0.455      0.662

=== Confusion Matrix ===

  a  b  c  d   <-- classified as
  5  0  3  0 |  a = Yin
  1 10  0  0 |  b = Yang
  3  1  2  3 |  c = Qi
  4  0  3  0 |  d = Blood
```

4. **Features:** Including ATP Generation Capacity; **Class:** Yin and Yang-tonic Herbs

2_hasATPGC_class_is_Yin_and_Yang_tonic.txt 2009/6/30 上午 04:23

```
=== Run information ===

Scheme:       weka.classifiers.trees.Id3
Relation:     herb-weka.filters.unsupervised.attribute.Remove-R156-159-weka.filters.supervised.attribu
Instances:    19
Attributes:   155
              [list of attributes omitted]
Test mode:    19-fold cross-validation

=== Classifier model (full training set) ===

Id3


ATP_generation_(percent_control) = '(-inf-129.5]'
|  phenol = yes: Yang
|  phenol = no: Yin
ATP_generation_(percent_control) = '(129.5-inf)': Yang

Time taken to build model: 0 seconds

=== Stratified cross-validation ===
=== Summary ===

Correctly Classified Instances          18               94.7368 %
Incorrectly Classified Instances         1                5.2632 %
Kappa statistic                          0.8939
Mean absolute error                      0.0263
Root mean squared error                  0.1622
Relative absolute error                  9.4421 %
Root relative squared error             44.0883 %
Total Number of Instances               19

=== Detailed Accuracy By Class ===

               TP Rate   FP Rate   Precision   Recall  F-Measure   ROC Area  Class
                 1         0.091      0.889     1         0.941      0.955    Yin
                 0.909     0          1         0.909     0.952      0.955    Yang
                 0         0          0         0         0          ?        Qi
                 0         0          0         0         0          ?        Blood
Weighted Avg.    0.947     0.038      0.953     0.947     0.948      0.955

=== Confusion Matrix ===

  a  b  c  d   <-- classified as
  8  0  0  0 |  a = Yin
  1 10  0  0 |  b = Yang
  0  0  0  0 |  c = Qi
  0  0  0  0 |  d = Blood
```

4. **Features:** Including ATP Generation Capacity; **Class:** Yin and Yang Families (Yin family = Yin- and Blood-tonic herbs; Yang family = Yang- and Qi-tonic herbs)

3_hasATPGC_class_is_Yin_and_Yang_family.txt 2009/6/30 上午 04:23

```
=== Run information ===

Scheme:       weka.classifiers.trees.Id3
Relation:     herb-weka.filters.unsupervised.attribute.Remove-R156-159-weka.filters.supervised.attribu
Instances:    35
Attributes:   155
              [list of attributes omitted]
Test mode:    35-fold cross-validation

=== Classifier model (full training set) ===

Id3


ATP_generation_(percent_control) = '(-inf-129.5]'
|  alpha-curcumene = yes: Yang
|  alpha-curcumene = no
|  |  titanium = yes: Yang
|  |  titanium = no
|  |  |  linoleic_acid = yes
|  |  |  |  stearic_acid = yes: Yin
|  |  |  |  stearic_acid = no: Yang
|  |  |  linoleic_acid = no
|  |  |  |  malic_acid = yes: Yang
|  |  |  |  malic_acid = no: Yin
ATP_generation_(percent_control) = '(129.5-inf)': Yang

Time taken to build model: 0.02 seconds

=== Stratified cross-validation ===
=== Summary ===

Correctly Classified Instances          23               65.7143 %
Incorrectly Classified Instances        12               34.2857 %
Kappa statistic                          0.3226
Mean absolute error                      0.3429
Root mean squared error                  0.5855
Relative absolute error                 68.0315 %
Root relative squared error            115.1202 %
Total Number of Instances               35

=== Detailed Accuracy By Class ===

               TP Rate   FP Rate   Precision   Recall  F-Measure   ROC Area  Class
                 0.733     0.4        0.579     0.733     0.647      0.667    Yin
                 0.6       0.267      0.75      0.6       0.667      0.667    Yang
Weighted Avg.    0.657     0.324      0.677     0.657     0.658      0.667

```

```
=== Confusion Matrix ===

  a  b   <-- classified as
 11  4 |  a = Yin
  8 12 |  b = Yang


```

4. **Features:** Except ATP Generation Capacity;

Class: Yin-, Yang-, Qi- and Blood-tonic Herbs

4_noATPGC_class_is_all_four_tonic_herbs.txt 2009/6/30 上午 04:23

```
=== Run information ===

Scheme:      weka.classifiers.trees.Id3
Relation:    herb-weka.filters.unsupervised.attribute.Remove-R156-159-weka.filters.supervised.attribu
Instances:   35
Attributes:  154
             [list of attributes omitted]
Test mode:   35-fold cross-validation

=== Classifier model (full training set) ===

Id3


nicotinic_acid = yes
|  calcium = yes: Blood
|  calcium = no: Qi
nicotinic_acid = no
|  arginine = yes
|  |  asparagine = yes: Yin
|  |  asparagine = no: Qi
|  arginine = no
|  |  formononetin = yes: Qi
|  |  formononetin = no
|  |  |  linoleic_acid = yes
|  |  |  |  capric_acid = yes
|  |  |  |  |  3-methoxy-4-hydroxybenzoic_acid = yes: Yin
|  |  |  |  |  3-methoxy-4-hydroxybenzoic_acid = no: Blood
|  |  |  |  capric_acid = no
|  |  |  |  |  calcium = yes: Yang
|  |  |  |  |  calcium = no: Qi
|  |  |  linoleic_acid = no
|  |  |  |  ferulic_acid = yes: Blood
|  |  |  |  ferulic_acid = no
|  |  |  |  |  lecithin = yes: Blood
|  |  |  |  |  lecithin = no
|  |  |  |  |  |  phosphorus = yes: Blood
|  |  |  |  |  |  phosphorus = no
|  |  |  |  |  |  |  campesterol = yes: Yang
|  |  |  |  |  |  |  campesterol = no
|  |  |  |  |  |  |  |  liriodendrin = yes: Yang
|  |  |  |  |  |  |  |  liriodendrin = no
|  |  |  |  |  |  |  |  |  vitamin_C = yes: Yang
|  |  |  |  |  |  |  |  |  vitamin_C = no
|  |  |  |  |  |  |  |  |  |  astragalin = yes: Yang
|  |  |  |  |  |  |  |  |  |  astragalin = no
|  |  |  |  |  |  |  |  |  |  |  phenol = yes: Yang
|  |  |  |  |  |  |  |  |  |  |  phenol = no
```

```
| | | | | | | | | | | | | stigmasterol = yes
| | | | | | | | | | | | | | adenosine = yes: Yin
| | | | | | | | | | | | | | adenosine = no: Yang
| | | | | | | | | | | | | stigmasterol = no: Yin

Time taken to build model: 0.02 seconds

=== Stratified cross-validation ===
=== Summary ===

Correctly Classified Instances          7               20      %
Incorrectly Classified Instances       28               80      %
Kappa statistic                        -0.071
Mean absolute error                     0.4
Root mean squared error                 0.6325
Relative absolute error               104.8276 %
Root relative squared error           142.9896 %
Total Number of Instances              35

=== Detailed Accuracy By Class ===

               TP Rate   FP Rate   Precision   Recall  F-Measure   ROC Area  Class
                 0.25      0.333      0.182      0.25      0.211      0.458    Yin
                 0.182     0.333      0.2        0.182     0.19       0.424    Yang
                 0.222     0.192      0.286      0.222     0.25       0.515    Qi
                 0.143     0.214      0.143      0.143     0.143      0.464    Blood
Weighted Avg.    0.2       0.273      0.206      0.2       0.201      0.463

=== Confusion Matrix ===

 a b c d   <-- classified as
 2 3 1 2 | a = Yin
 5 2 2 2 | b = Yang
 1 4 2 2 | c = Qi
 3 1 2 1 | d = Blood
```

5. **Features:** Except ATP Generation Capacity;   **Class:** Yin- and Yang-tonic Herbs

```
=== Run information ===

Scheme:      weka.classifiers.trees.Id3
Relation:    herb-weka.filters.unsupervised.attribute.Remove-R156-159-weka.filters.supervised.attribu
Instances:   19
Attributes:  154
             [list of attributes omitted]
Test mode:   19-fold cross-validation

=== Classifier model (full training set) ===

Id3


adenosine = yes: Yin
adenosine = no
|  glycine = yes: Yin
|  glycine = no
|  |  palmitic_acid = yes: Yang
|  |  palmitic_acid = no
|  |  |  oleanolic_acid = yes: Yin
|  |  |  oleanolic_acid = no
|  |  |  |  protocatechuic_acid = yes: Yin
|  |  |  |  protocatechuic_acid = no
|  |  |  |  |  beta-sitosterol = yes: Yang
|  |  |  |  |  beta-sitosterol = no
|  |  |  |  |  |  3-methoxy-4-hydroxybenzoic_acid = yes: Yang
|  |  |  |  |  |  3-methoxy-4-hydroxybenzoic_acid = no
|  |  |  |  |  |  |  astragalin = yes: Yang
|  |  |  |  |  |  |  astragalin = no: Yin

Time taken to build model: 0 seconds

=== Stratified cross-validation ===
=== Summary ===

Correctly Classified Instances          6               31.5789 %
Incorrectly Classified Instances       13               68.4211 %
Kappa statistic                        -0.3351
Mean absolute error                     0.3421
Root mean squared error                 0.5849
Relative absolute error               122.7468 %
Root relative squared error           158.9625 %
Total Number of Instances              19

=== Detailed Accuracy By Class ===

               TP Rate   FP Rate   Precision   Recall  F-Measure   ROC Area  Class
                 0.375     0.727      0.273     0.375     0.316      0.324    Yin
                 0.273     0.625      0.375     0.273     0.316      0.324    Yang
                 0         0          0         0         0          ?        Qi
                 0         0          0         0         0          ?        Blood
Weighted Avg.    0.316     0.668      0.332     0.316     0.316      0.324

=== Confusion Matrix ===

 a b c d   <-- classified as
 3 5 0 0 | a = Yin
 8 3 0 0 | b = Yang
 0 0 0 0 | c = Qi
 0 0 0 0 | d = Blood
```

6. **Features:** Except ATP Generation Capacity;   **Class:** Yin and Yang Families
(Yin family = Yin- and Blood-tonic herbs; Yang family = Yang- and Qi-tonic herbs)

```
=== Run information ===

Scheme:      weka.classifiers.trees.Id3
Relation:    herb-weka.filters.unsupervised.attribute.Remove-R156-159-weka.filters.supervised.attribu
Instances:   35
Attributes:  154
             [list of attributes omitted]
Test mode:   35-fold cross-validation

=== Classifier model (full training set) ===

Id3


myristic_acid = yes: Yin
myristic_acid = no
|  lead = yes: Yin
|  lead = no
|  |  manganese = yes: Yang
|  |  manganese = no
|  |  |  campesterol = yes: Yang
|  |  |  campesterol = no
|  |  |  |  calcium = yes: Yin
|  |  |  |  calcium = no
|  |  |  |  |  protocatechuic_acid = yes: Yin
|  |  |  |  |  protocatechuic_acid = no
|  |  |  |  |  |  diosgenin = yes: Yin
|  |  |  |  |  |  diosgenin = no
|  |  |  |  |  |  |  glutamic_acid = yes: Yang
|  |  |  |  |  |  |  glutamic_acid = no
|  |  |  |  |  |  |  |  aspartic_acid = yes: Yin
|  |  |  |  |  |  |  |  aspartic_acid = no
|  |  |  |  |  |  |  |  |  lecithin = yes: Yin
|  |  |  |  |  |  |  |  |  lecithin = no
|  |  |  |  |  |  |  |  |  |  oleanolic_acid = yes: Yin
|  |  |  |  |  |  |  |  |  |  oleanolic_acid = no
|  |  |  |  |  |  |  |  |  |  |  saponins = yes: Yin
|  |  |  |  |  |  |  |  |  |  |  saponins = no
|  |  |  |  |  |  |  |  |  |  |  |  beta-sitosterol = yes: Yang
|  |  |  |  |  |  |  |  |  |  |  |  beta-sitosterol = no
|  |  |  |  |  |  |  |  |  |  |  |  |  3-methoxy-4-hydroxybenzoic_acid = yes: Yang
|  |  |  |  |  |  |  |  |  |  |  |  |  3-methoxy-4-hydroxybenzoic_acid = no
|  |  |  |  |  |  |  |  |  |  |  |  |  |  astragalin = yes: Yang
|  |  |  |  |  |  |  |  |  |  |  |  |  |  astragalin = no
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  bergapten = yes: Yang
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  bergapten = no: Yin

Time taken to build model: 0 seconds
```

```
=== Stratified cross-validation ===
=== Summary ===

Correctly Classified Instances        18             51.4286 %
Incorrectly Classified Instances      17             48.5714 %
Kappa statistic                        0.0165
Mean absolute error                    0.4857
Root mean squared error                0.6969
Relative absolute error               96.378  %
Root relative squared error          137.0205 %
Total Number of Instances              35

=== Detailed Accuracy By Class ===

               TP Rate   FP Rate   Precision   Recall  F-Measure   ROC Area  Class
                 0.467     0.45      0.438     0.467     0.452      0.508    Yin
                 0.55      0.533     0.579     0.55      0.564      0.508    Yang
Weighted Avg.    0.514     0.498     0.518     0.514     0.516      0.508

=== Confusion Matrix ===

  a  b   <-- classified as
  7  8 |  a = Yin
  9 11 |  b = Yang

```