SYMPOSIUM
TRADITIONAL CHINESE MEDICINES
14-15 NOVEMBER 2013

Location: EDQM Premises, 7 allée Kastner, Strasbourg, France
Duration: 1.5 days. Working language: English

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Presentations

Introduction
“Current status and future perspectives of Traditional Chinese Medicine in China”

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Current Status and Future Perspective of Traditional Chinese Medicine

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Outline

• General features of TCM;
• TCM Laws and Regulations;
• TCM Education and Research;
• TCM New Drug Development;
• Chinese Pharmacopoeia;
• TCM Industry;
• Main Challenges and Opportunities;
• TCM future perspective.
Traditional Chinese Medicine

General Features of TCM

- Treasure of culture heritage
- Long history in clinics
- Effective treatment
- Multi-components
- Wholly-regulating
General Features of TCM

Drug Registration Regulation (TCM)

- **TCM new drugs**: 9 categories (mainly 3)
- **Pure chemical entity**: Category 1;
- **Active fractions (over 50%)**: Category 5;
- **Composite formula**: Category 6
  - 6.1--traditional formula
  - 6.2--modern formula
  - 6.3--TCM+chemical drug formula

New: Natural medicine registration regulation
TCM Education

TCM universities & colleges: 47
Education structures with TCM majors: 793
Students at present: 270,000

Mode A

SATCM organizes master-pupil educational model to inherit experiences and knowledge.

Mode B

Inheriting organized: 3 times
Elderly masters: 1,607
Inheritors: 2,285
TCM Research

Research institutes, universities, hospitals and related structures

Development Plan for TCM Innovation (2006-2020)

Government funds (MOST, NSFC, 1.5 Billion $/year), private investment and other funding resources

TCM Research (medical)

diabetes
oncology diseases
HIV/AIDS
hepatitis
SAES
cerebrovascular diseases
TCM Research (herbal)

- Resources
- Phytochemistry
- Quality control
- Pharmacology
- Toxicology
- Systems biology
- ..........
GAP of Medicinal Plants in China

About 100 TCM species were cultivated in GAP base

*Salvia miltiorrhiza*

*Panax notoginseng*

*Radix Astragali*

*Astragalus mongholicus* (Huangqi)

Panax notoginseng:
- Constituent: saponins
- Action: To eliminate blood stasis, arrest bleeding etc.
**GAP of Medicinal Plants in China**

*Panax notoginseng:*
- **Constituent:** Saponins
- **Action:** To eliminate blood stasis, arrest bleeding etc.

**Phytochemical Study of TCM**

Over 600 TCM species have been phytochemically investigated in the past 50 years, from which around 18,000 natural products were isolated including over 5000 new compounds.
Active Natural Products Discovered from Herbs in China

2000.1—2011.6, 150 active natural products in TCM

Phytochemical Analysis of *Ginseng, American Ginseng and Notoginseng*
### Saponins identified from Three Ginseng Species

<table>
<thead>
<tr>
<th>Structure type</th>
<th>Ginseng</th>
<th>American Ginseng</th>
<th>Notoginseng</th>
</tr>
</thead>
<tbody>
<tr>
<td>FPD</td>
<td>48 (20)</td>
<td>40 (22)</td>
<td>60 (27)</td>
</tr>
<tr>
<td>FPT</td>
<td>70 (50)</td>
<td>50 (38)</td>
<td>69 (44)</td>
</tr>
<tr>
<td>OA</td>
<td>15 (13)</td>
<td>10 (8)</td>
<td>4 (2)</td>
</tr>
<tr>
<td>GT</td>
<td>4 (4)</td>
<td>9 (6)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Malonylated</td>
<td>25 (15)</td>
<td>6 (1)</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Acylated</td>
<td>75 (53)</td>
<td>17 (40)</td>
<td>83 (38)</td>
</tr>
<tr>
<td>Peroxidized</td>
<td>-</td>
<td>2 (1)</td>
<td>12 (10)</td>
</tr>
<tr>
<td>Variant C-17 side chains</td>
<td>93 (38)</td>
<td>92 (43)</td>
<td>97 (65)</td>
</tr>
<tr>
<td>Unknown sapogenins</td>
<td>24 (24)</td>
<td>6 (6)</td>
<td>2 (2)</td>
</tr>
<tr>
<td><strong>Sum</strong></td>
<td><strong>334 (210)</strong></td>
<td><strong>262 (182)</strong></td>
<td><strong>309 (203)</strong></td>
</tr>
</tbody>
</table>

Totally 623 saponins characterized with 437 newly reported ones.

### Comprehensive Quality Control Model of TCM

**Micro-identification**

- Conventional Quality control Method
- TCM quality control
- Fingerprint Analysis
- Multi-marker quantitation

**TLC analysis**
Fingerprinting of Chinese Salvia (Danshen)

HPLC fingerprints of Danshen extract and its preparations

Multi-component Assay of Ganoderma Triterpenoids

Sample of Ganoderma lucidum

Single Standard
Pharmacokinetics Research (Liquorice)

The most frequently used Chinese herb.

Three species: *G. uralensis*, *G. glabra*, *G. inflata*

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Metabolite identification

glycyrrhiza uralensis

gluconylation (Δ176)

Database searching M.W. 366

Enzymic hydrolysis

SRM validation

Neutral loss scan m/z 176

Neutral loss scans m/z 176

Mother ion scan m/z 366

Daughter ion scan m/z 366

Daughter ion scan m/z 366

SRM scan m/z 541>366

Mol Wt. 542 (365+H+176)

Retention time and 2nd MS spectrum same as glycyrol

(176 Da)
Multi-component pharmacokinetics

- Stage scanning
- Reduce the internal SRM baseline interference by improving separation
- Online 24-min to monitor the 64 components
- Draw PK curves of 55 components

PK curves of multiple components

Different structures with different PK model

Flavonoid gly/isoflavone
Fast absorption, fast excretion

Saponins
Slow excretion, \( T_{\text{max}} \), 5-15 h
(GLY, LSA1, LSG2, GA)

flavones/coumarin
Second peak phenomenon
(LG, ILG, GCM)
Metabolic process of Licorice decoction

Excrete by degree, order and timeframe to give the different effects

TCM Pharmacology—Mode of Action

berberine

Hepatic LDLR mRNA/protein

LDL-cholesterol

Serum cholesterol

Jiang JD et al. Nature Medicine, 2007;10:1344-1351
The important contribution of TCM pharmacology to global public health to date

Discovery and development of artemisinin (Qinghaosu) and its derivatives as anti-malarial drugs

awarded the Lasker award in 2011


Systems Biology Research of TCM

Compound → Fraction → Single TCM → Formula

SB, SA → Salvinic acids

Tanshinones A, B → Chinese Salvia

Tanshinones → Formula (with Saqı)

References:
- J Chromatogr B 2007;846:33–41

**Ganoderma Proteomics**

*Ganoderma lucidum*

Predicted binding of GAD with 14-3-3-zeta

New Drugs developed from TCM

- Over 20 TCM chemical entities marketed;
- Around 50 TCM active fractions approved;
- Over 9000 TCM composite formulas products in market.

![Hupezine A](image1)

New Drugs developed from TCM

- Significantly improve memory deficiencies;
- Its derivative, ZT-1, in Phase II clinical trials in Europe and China.
Leading TCM products in Marketplace

- **Notoginseng saponins**
  - Name: Xueshuantong
  - lyophilized powder
  - Sale: 5 billion RMB/year
  - 0.8 billion US Dollars

- **Salvia phenolic acids**
  - Name: Danshen depside
  - lyophilized powder
  - Sale: 3 billion RMB/year
  - 0.5 million US Dollars

New TCM Product Developed - Dan Qi Tablet

- **Phenolic acids**
- **Netoginsenosides**
- Sanqi saponins
- Saponins
- Water-soluble phenolic acids
- Lipophilic tanshinones
- Flavones, proteins, amino acids

Now in Phase two clinical trial
SFDA IND Approval

Chinese Pharmacopoeia


- **Three volumes,** Volume I – TCM, Volume II – Chemicals, Volume III – Biologicals;

- **2136 monographs** for TCM including crude drug, slices and finished products;

- **New methods adopted:** LC-MS, Chromatographic fingerprint, DNA fingerprint, etc.

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**TCM Industry**

- **1500+ TCM Pharmaceutical Enterprises**
- **11000+ TCM Commercial Companies**
- **RMB 180Billion Annual Gross Product**

- **9000+ TCM Products with 40+ dosage forms**
Main Challenges in TCM Modernization

• To maintain consistent quality;
• To overall-evaluate the safety;
• To provide standard clinical trial evidence for efficacy;
• To clarify the mode of action;
• To develop suitable methodologies;
• To develop modern TCM products.

Opportunities in TCM Modernization

• Investment in TCM research more than ever;
• Scientists, industry and government’s enthusiasm;
• New development in research methodology;
• Scientific innovation and revolution;
• Growing therapeutic requirement for chronic and other hard-to-cure diseases;
• Disadvantages in modern medicine: toxicity, high cost, etc.
TCM Modernization-future perspectives

Phytochemistry + HTP screening = Lead compounds

Main route

TCM Modernization
Safety + Efficacy + Quality + Mechanism

Safety
(toxicology + analysis)

Efficacy
(standardized clinical trials)

Quality
(comprehensive)

Mode of Action
(system biology)

TCM Modernization

Modern TCM

Evidence-based and Science-based!
Meeting Announcement

3rd Annual Meeting of GP-TCM Research Association & 5th Annual Meeting of TCM Analysis Society of WFCMS
July 19-20, 2014, Nanjing, China

6th Shanghai International Conference on TCM and Natural Medicines
October 16-17, 2014, Shanghai, China

Welcome to attend the conferences!

THANK YOU!