

Chapter 1

The Basic Requirement for Modernisation of Chinese Herbal Medicine

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Abstract

Authentication and consistent quality are the basic requirements for TCHM and its commercial products, regardless of the kind of research conducted to modernise the TCM. The complexities of TCHM challenge the current official quality control mode, for which only a few markers were selected for identification and quantitative assay. Referring to too many unknown factors existed in TCHM, it is impossible and unnecessary to pinpoint qualitatively and quantitatively every single component contained in the herbal drug. Chromatographic fingerprinting is a rational option to meet the need for more effective and powerful quality assessment to TCHM. The optimised chromatographic fingerprint is not only an alternative analytical tool for identification, but also an approach to express the various pattern of chemical ingredients distribution in the herbal drugs and preserve such “database” for further multi-faceted sustainable studies. Some examples demonstrated the role of fingerprinting in quality control and assessment.

Keywords: Chromatographic Fingerprint; Sustainable Quality Assessment Mode.

The paradigms of traditional Chinese herbal medicine (TCHM) are featured as holistic system; the common clinical use of Chinese medicines requires the complex recipes and formulae derived from historical and anecdotal evidence of Chinese medicinal practitioners. Based on ancient Chinese philosophy, a typical therapeutic formula is symbolised as an active “cabinet” consisted of “Monarch” drug, “ministers” drug, “assistants”

drug and “messengers” or “servants” drug, which work together harmoniously and serve various functions respectively to adjust, balance, and restore the body’s function guided by Chinese ancient philosophy and culture. Consequently, no single active constituent is responsible for the overall efficacy of the whole formula, even single herbal drugs, which usually contain numerous chemical compounds with holistic efficacy rather than a single active compound. It is definitely different from the Western single chemical drug, and is also distinguished from Western herbal/botanical medicine because TCHM is the carriers loading the information of the philosophy and culture of traditional Chinese medicine. Hence, we should keep in mind it will be nothing different from Western herbal drugs once the TCM information is unloaded from TCHM matrices. On the new wave of modernisation of TCM under the economic globalisation environment, there is a trend towards the seeking of TCHM as a source for discovery of new chemical drugs without considering the synergic effect of all of the ingredients in the herbal drugs. That means such an approach is mostly concerned with only the interested single target and ignores the total quality of the herbal drug itself. The consequence would lead to a loss of ancestors’ wisdom (the culture and philosophy of TCM and exclusive clinical experiences) accumulated through generations. Referring to the complexity and difficulty in merging ancient Chinese culture and modern Western science, the first step in the process of TCM modernisation, we should preserve the total information loaded in the TCHM as much as possible in order to avoid any rash affirmation on the pros and cons of TCM without discreet study. From the viewpoint of chemistry and biology, the total chemical ingredients pattern in every entity of TCHM should be preferably expressed in the appropriate chromatograms — chromatographic fingerprint consisted of detectable ingredients. The optimised fingerprints can serve as “chemical signatures” of the TCHM for consecutive multi-faceted research. The following examples illustrate the role of chromatographic fingerprints in TCHM.

1.1 Authentication of the Species Prone to Confusion

Ginseng (root of *Panax ginseng*) and American ginseng (root of *Panax quinquefolium*) are two close species containing very similar chemical

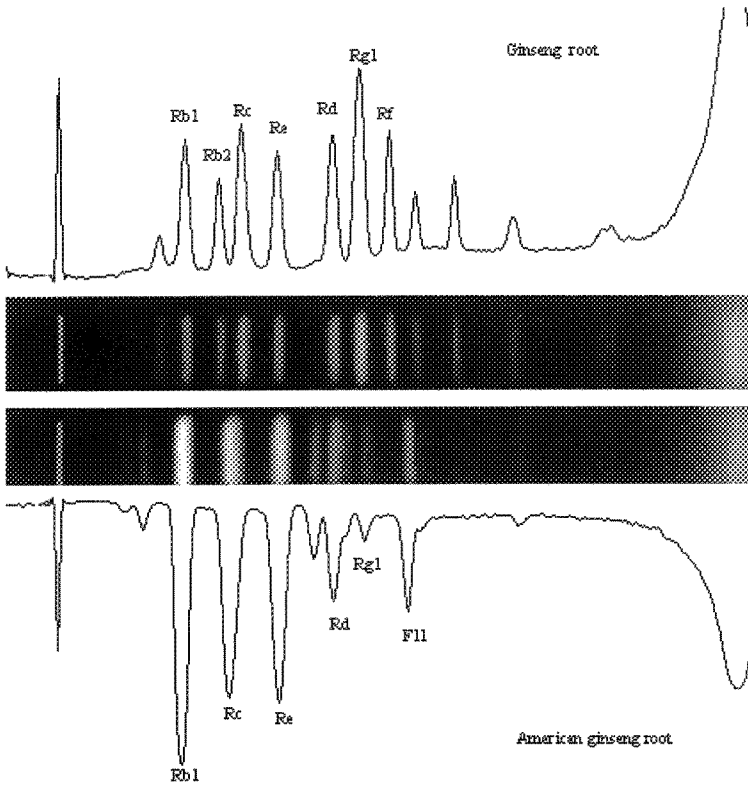


Fig. 1.1. HPTLC fingerprints of Ginseng and American ginseng.

ingredients. The functions of the two species are different according to TCM in clinical use. It is difficult to distinguish them by only selecting single ginsenosides, but the HPTLC images with digital scanning profiles as a whole can easily differentiate between them (Xie, 2005a) (Fig. 1.1).

1.2 Quality Evaluation of the Crude Drugs

There are two species of *Ge Gen* (Kudzu root) in Chinese Pharmacopoeia — *Ye Ge* (*Radix Pueraria lobatae*) and *Gan Ge* (*Radix P. thomsonii*), which were used as the same herbal drug for a long time (Xiao, 2002). But the content determination of main isoflavonoid, Puerarin and HPTLC

fingerprint analysis showed the great disparity of the content of puerarin, and the total chemical pattern expressed by the fingerprint revealed that the puerarin content and the chemical components concentration distribution in the *Gan Ge* fingerprint was eight to 15 times lower than that of *Ye Ge* (Figs. 1.2 and 1.3), thus, it is impossible that both species are bio-equivalent. Hence, *Ye Ge* should be the appropriate candidate for *Ge Gen* (Kudzu root) in the prescription by TCM practitioners.

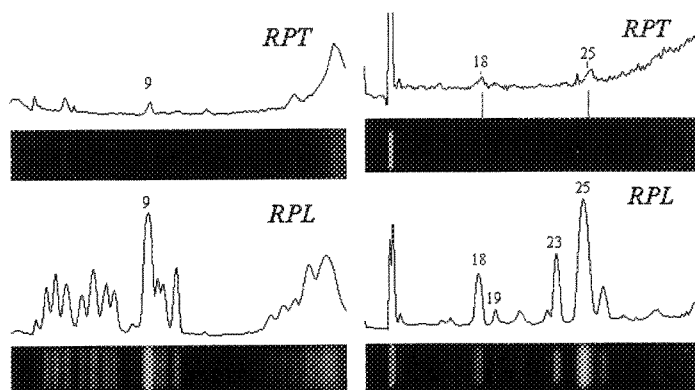


Fig. 1.2. HPTLC fingerprints of *Ye Ge* (root of *Puerariae lobatae*) and *Gan Ge* (root of *Puerariae thomsonii*). Left: Isoflavonoides, Right: Aglycones, PRL: Root of *Pueraria lobata*, PRT: Root of *Pueraria thomsonii*.

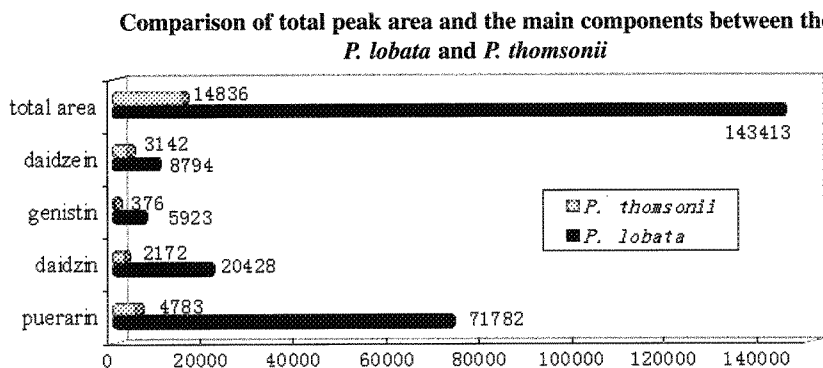


Fig. 1.3. Comparison of the discrepancy of total peak area and the main components between *Ye Ge* (black bar) and *Gan Ge* (grey bar).

1.3 Distinguishing the Adulterant from the Authentic Sample

The general practice of quality assessment of extracts of *Ginkgo biloba* leaves (EGb) is the determination of 24% of the total flavonoides and 6% of total terpene lactones without the provision of other detailed quality information. The HPLC fingerprint of total flavonoides disclosed the

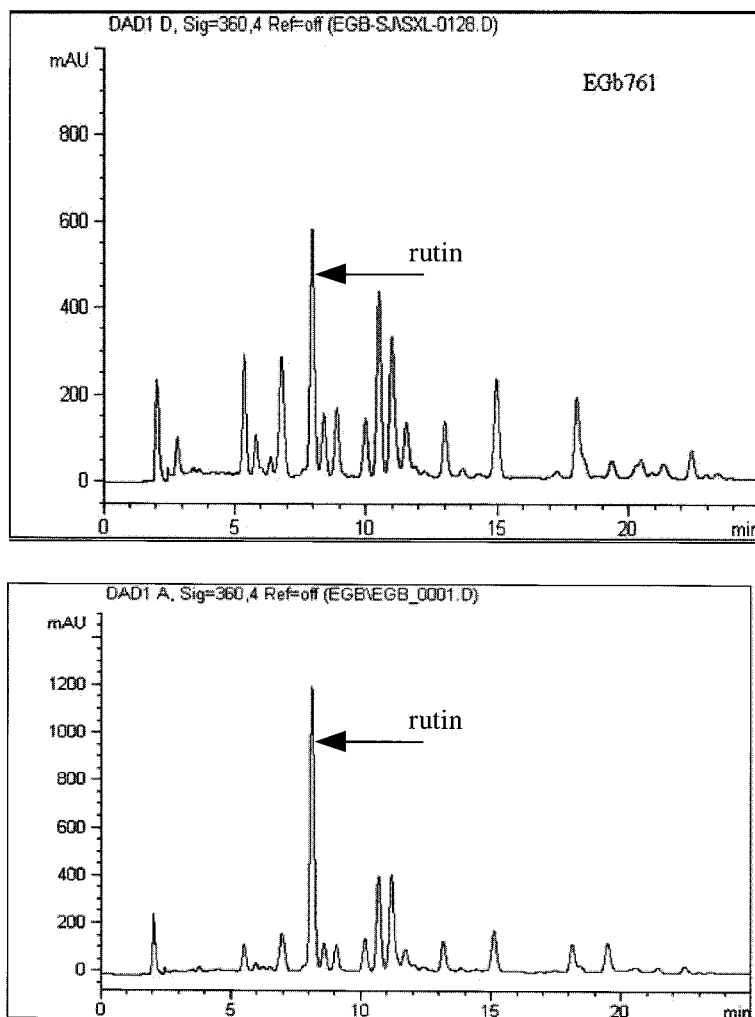


Fig. 1.4. HPLC fingerprint of the extracts of Ginkgo leaves (EGb). Upper: Standardised EGb fingerprint, Lower: A commercial EGb product fingerprint.

distribution pattern with the detectable peaks intensities and peak-to-peak ratio, which expresses the inherent quality. Any significant change in the pattern appearance will hint at the quality fluctuation of the products. For example, in a quality survey of commercial products in the market by means of comparative study of the HPLC fingerprinting, three batches of commercial extracts of *Ginkgo biloba* leaves (EGb) revealed that the rutin peak, which unexpectedly predominated in the fingerprints of those commercial products in comparison to that of standardised EGb (Fig. 1.4), is likely to be adulterated with the inexpensive flavonoid rutin to artificially increase the total flavonoids content (Qian and Xie, 2005). It would however not be evident if the adulterated ginkgo extracts had only been analysed by quantitation of total flavonoides by conventional HPLC assay.

1.4 Monitoring Rationality of Dosage Forms During R&D Period

Renewal of dosage forms of TCHM industrial products from an aged one to the modernised form, from conventional pill to tablets for example, is a trend in current modernisation of TCM industries. But it does not assure that the renewed dosage forms with modified extraction process will be successful without any analytical evidence. A typical example of fingerprint disclosed the outcome of a compound formula TCHM product BJW. It was clearly demonstrated that the chemical components of the said formula in the fingerprint were diminished more and more from pill to concentrated pill, to tablets, and finally to oral liquid (Fig. 1.5). We can say that such “innovation” of dosage forms with claimed renewed process techniques was obviously a failure in comparison to the HPLC fingerprint of the original dosage form, the pills (Fig. 1.5, top). It is noteworthy that although only part of chemical structures were elucidated currently in the chromatogram, the quality information was also able to be provided specifically with the total chemical pattern (peaks concentration distribution and peak-to-peak ratio) for comparative study between the different dosage forms. This example also demonstrated that chromatographic fingerprint is a sustainable quality assessment approach; it can be started from “black box” of fingerprint as a wholeness without reference substance being available at the beginning gradually to “grey box” and finally to a “clear box”, where step-by-step detailed phytochemical studies are exploited.

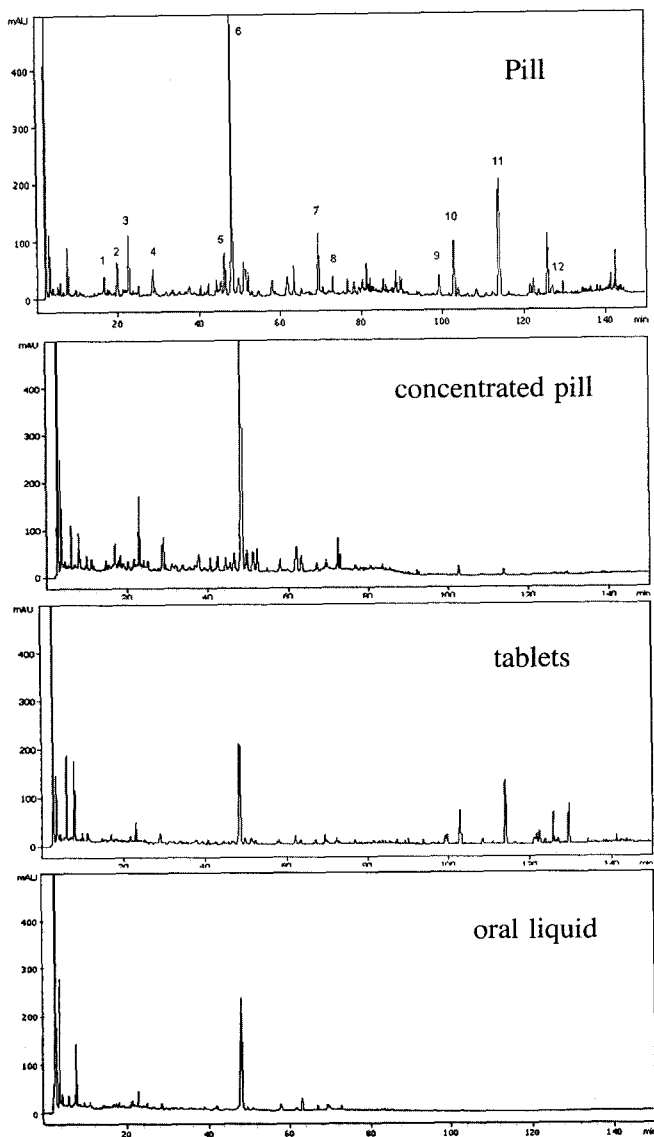


Fig. 1.5. HPLC fingerprints of various dosage forms of the same TCHM product (BJW) produced by different process techniques. Peak 1: Chlorogenic acid, peak 2: Caffeic acid, peak 3: Puerarin, peak 4: Daidazin, peak 5: 3,5-Oxy-dicafeoyl-quinic acid, peak 6: Naringin, peak 7: Luteolin, peak 8: Acacetin-7-O- β -glucoside, peak 9: Imperatorin, peak 10: Honokiol, peak 11: Magnolol, peak 12: Atractylodine.

1.5 Monitoring the Dynamic Change Due to Interaction of Mixed Herbal Drugs During Extraction

The classical empirical formula of *Sheng Mai Yin* (SMY) consisted of ginseng root (*Renshen*), Ophiopogon root (*Maidong*) and Schizandra fruits (*Wuweizi*). A quality survey of commercial SMY products in the market by means of fingerprinting revealed that the ginsenosides, the main active constituent in ginseng, had been destroyed; in some, none of the primary ginsenosides were even detected. The reason was obviously that ginsenosides in ginseng root were hydrolysed uncontrollably by the organic acids in *Wuweizi* when the mixture was subjected to extending heating in water

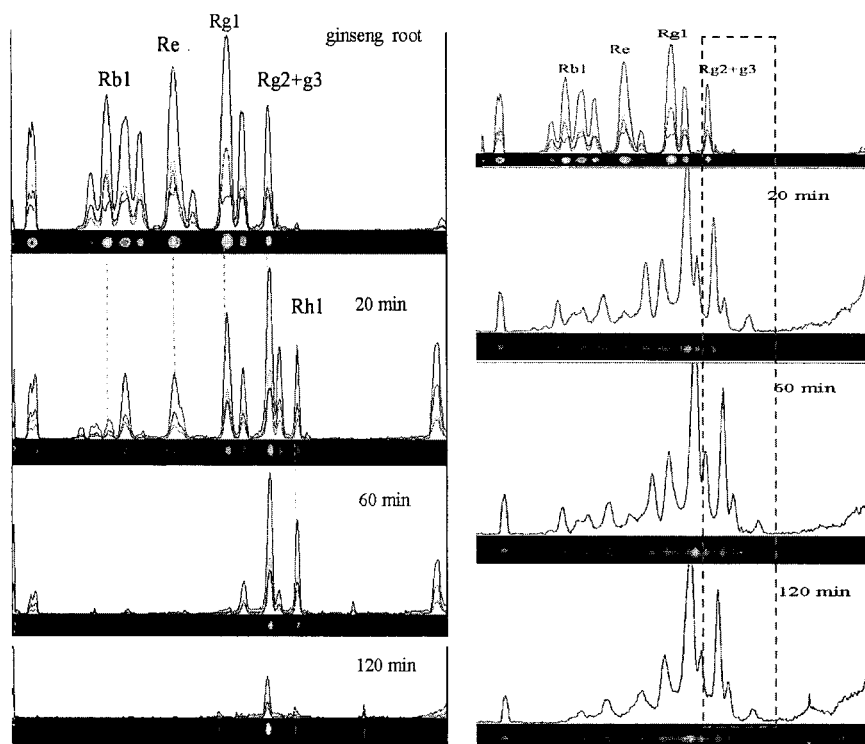


Fig. 1.6. HPTLC fingerprint of SMY decoction under rigorous heating (left) and gentle heating (right). Ginsenosides in SMY has been destroyed seriously under rigorous heating (mimic products in industry) while rather stable in a certain extent under gentle heating (home-made decoction) condition.

during manufacture. Analysis showed that the primary ginsenosides were hydrolysed rapidly when the mixed ginseng and *Wuweizi* was boiled with water under rigorous heating for only 20 minutes and destroyed gradually afterwards (Fig. 1.6, left). However, such hydrolysis behavior would stabilise under gentle heating for 120 minutes, similar to that undergone by home-made decoctions. The ginsenoside-Rb1, -Re and -Rg1 were hydrolysed into ginsenoside-Rg3 and -Rh with a rather consistent state of the hydrolysed ginsenosides pattern (Xie, 2005b) (Fig. 1.6, right). It is well known that ginsenoside-Rg3 and -Rh are active components for the cardiovascular system. The conventional home-made SMY decoction probably generated a “hidden” added positive value for preventing and curing diseases.

1.6 Conclusion

Authentication and consistent quality are the basic requirements for TCHM and its commercial products, regardless of the kind of research conducted to modernise the TCM. The complexities of TCHM challenge the current official quality control mode for which only a few markers were selected for identification and quantitative assay. Referring to too many unknown factors existed in TCHM, it is impossible and unnecessary to pinpoint qualitatively and quantitatively every single component contained in the herbal drug. Chromatographic fingerprinting is a rational option to meet the need for more effective and powerful quality assessment to TCHM. The optimised chromatographic fingerprint is not only an alternative analytical tool for identification, but also an approach to express the various patterns of chemical ingredients distribution in the herbal drugs and to preserve such wholeness-target “database” for further multi-faceted studies. Through active research and with rapid development in both analytical techniques and computer capacity, the fingerprint analysis will be constantly improved and fine-tuned. This quality assessment mode is complementary with findings from areas of pharmacology, biochemistry, clinical research and TCM philosophy. In forward-looking a viewpoint, a system to correlate fingerprinting data with the TCM efficacy can be expected and it would be the ultimate goal for developing the fingerprinting technique. However, it is important to be aware that the fingerprinting

analysis also has its limitations. The active principles in herbal medicine cannot be totally detected by the current chromatographic techniques. It will be also very difficult to distinguish the active components from the inactive components in all fractions of the chromatographic fingerprint. Moreover, there may be other unpredictable questions or difficulties in the usage of fingerprinting analysis in the development process that need to be conquered. Nevertheless, the wholeness-targeted quality assessment mode achieved by fingerprinting analysis will advance the quality control of TCHM forward another progressive step in its continual development and modernisation.

References

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