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The Turnover Rate of Marker Constituents in Chinese Herbal Medicine

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ABSTRACT

In this review, difficulties for the quality control of traditional Chinese medicine are described briefly in the introduction section. The decoction method, the necessity of setting standard decoction and the definition of standard decoction are presented in the second section. The distributions and variations of extract yields of 99 unified traditional Chinese medicine formulas are discussed in the third section. Finally, the variations in turnover rates of some marker constituents in different formulas and their influencing factors are also discussed.

Key words: traditional Chinese medicine, standard decoction, extract, marker constituent, turnover rate

INTRODUCTION

Chinese herbal medicines are obtained from natural sources such as plants, animals and minerals. Therefore, it is more difficult to ensure quality control for Chinese herbal medicines than synthetic drugs. The reasons which make it difficult are:(1) microbial contamination: Most Chinese herbal medicines are abundant in starchs, lipids and proteins, which are nutrients for microbial growth. Because there is no heat treatment in the manufacturing process, the dosage forms, slices, pills and powders do not have appropriate storage and therefore it is easy for microorganisms and molds to grow.(2) heavy metal contamination: Crude drugs are easily contaminated or polluted with mineral materials. Monitoring the limit of heavy metals becomes important for safety reasons.(3) adulteration and misuse: In large scale harvesting, it is hard to detect and remove the adulterants and foreign substances.(4) the presence of pesticide residues: As most of the organic chlorinated pesticides have a long half-life, the residues in perennial plants may result in significant problems as well.(5) limited information about active constituents: In current scientific research, knowledge concerning the active or effective constituents in most of the herbs still remains limited. Furthermore, traditional Chinese medicine (TCM) preparations except Dwu-shen-tang (獨參湯, ginseng only), are usually multi-herb preparations which makes them complicated and it is difficult to identify and quantify the active constituents.

The Decoction Method of TCM Preparations

TCM are usually taken in forms of decoction, pills, powder, medicated liquor, macerate and concentrated extract (so-called scientific preparation). People today often lack the time needed to prepare a decoction in the conventional way. Furthermore, bitter tasting, pungent and odorous properties have contributed to their unpopularity. The use of concentrated extracts therefore has become very popular in Japan and Taiwan over the past four decades.

The decoction methods shown in Table 1 are quoted from ancient Chinese and Japanese books regarding herbal medicine. Generally, crude drugs are decocted twice with water. According to Tang-tour-ge-jyue(湯頭歌訣)[1] and Yi-zong-jin-jian (醫宗金鑒)[2], the ratio of water, in terms of volume, added to the weight of crude drugs ranged from 5.3 to 30.5 in the first decoction. Whereas, the amount of water added in the second decoction is usually three-fourths of that in the first decoction. Upon combining the first and the second decoctions, the ratio of total water to the weight of crude drugs ranged from 9.3 to 53.3. The total volume of the decoctions were in the range of 25~50% relative to the original volume.

Prior to the decoction the herbs are immersed in water for thirty minutes and then decocted for 15-20 minutes until water begins to boil. The heat on the stove is then set low in order to prevent significant loss of volatile constituents through vaporization. Tonics or crude drugs with strong odors and flavors should be decocted with low heat for a long period of time. Fragrant herbs such as mentha, saussurea and perilla, which contain essential oils, are added only after other component herbs are brought to boiling, and were kept boiling afterwards for only four or five minutes[3]. As the component crude drugs in TCM preparations are natural substances, a standard decoction method should be defined for keeping the consistency of marker constituents in the decoction, the intermediate products and the final products. In Japan, the standard decoction method is defined as follows. The amounts of crude drugs equivalent to a daily dose of each formula are weighed and pulverized, water with the volume twentyfold to that of the mass was added and the mixture was boiled for more than 30 minutes to halve the original volume.

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Table 1. Decoction method of TCM preparations

	name of formula and/or literature	the amount of crude drugs in formula(g)	decoction method (express in bowl* or sheng#)	decoction method (express in mL)	the ratio between water volume to the weight of crude drugs		
					1st decoction	2nd decoction	total
Tang-tour-ge-jyue(湯頭歌訣)	Syh-jiun-tzyy-tang (四 君 子湯)	26.3	2.0→0.5	400→100	15.2	11.4	26.6
	Szu-wu-tang (四 物 湯)	35.6	2.0→0.7	400→140	11.2	8.4	19.6
	Ba-jen-tang (八 珍 湯)	61.9	3.0→?	600→?	9.7	7.3	17.0
	Shih-chuan-ta-pu-tang (十全大補湯)	71.3	2.5→1.0	500→200	7.0	5.3	12.3
	Yeang-shin-tang (養 心 湯)	88.1	3.0→1.0	600→200	6.8	5.1	11.9
	Buu-jong-yih-chih-tang (補中益氣湯)	48.4	3.0→?	600→?	12.4	9.3	21.7
	San-ao-tang (三 拗 湯)	13.1	2.0→0.8	400→160	30.5	22.8	53.3
	Shaur-yaw-gan-tsao-tang (芍藥甘草湯)	18.8	1.5→0.5	300→100	16.0	12.0	28.0
	Dah-cherng-chin-tang (大 承 氣湯)	67.5	4.0→1.5	800→300	11.9	8.8	20.7
Yi-zong-jin-jian(醫宗金鑑)	Guey-jy-tang (桂 枝 湯)	207.0	7.0→3.0	1386.7→594.3	6.7	5.0	11.7
	Ma-hwang-tang (麻 黃 湯)	111.5	9.0→2.5	1782.9→396.2	16.0	12.0	28.0
	Dah-ching-long-tang (大 青 龍湯)	337.0	9.0→3.0	1782.9→594.3	5.3	4.0	9.3
	Shaur-yaw-gan-tsao-tang (芍藥甘草湯)	111.4	3.0→1.5	594.3→297.2	5.3	4.0	9.3
	Dah-cherng-chin-tang (大 承 氣湯)	229.0	10.0→5.0	1981.0→990.5	8.6	6.5	15.1
	The practice of diagnosis and treatment in Kanpo medicine	a daily dose		600→200~300			
	The practical knowledge of Kanpo medicine	a daily dose		600→200			20~30
	The knack for making use of Kanpo medicine	a daily dose		600→300			

* The unit used in Tang-tour-ge-jyue , one bowl 200mL. # The unit used in Yi-zong-jin-jian, one sheng (升) 198.1mL. ? no description.

According to Japanese literature[4-6], the decoction methods used are the same as that of the standard decoction method mentioned above except that the final volume is from one-third to half of the original volume. The decoction method reported in Japanese literature are as depicted in the last three items listed in Table 1.

The Production Yield of TCM Extract

Even with the same name in TCM literature, the component crude drugs listed in the formula or the amount of each component drug may be different. For the sake of quality control according to the regulatory review panel for TCM, the Department of Health announced a list of unified TCM formulas in 1995[7] and 2000[8]. This list includes 200 TCM formulas, of which both the component crude drugs and the amount of each component are clearly indicated. As the uniformity of production yield of these government authorized TCM are concerned, research for exploring the traditional decoction method was initiated by the National Laboratories of Foods and Drugs in 1996, and included member factories of the Taiwan Pharmaceutical Manufacturers' Association. Each TCM formula was prepared by seven to eight factories. The formulation was decocted according to the aforementioned standard decoction method. The decoction was filtrated with a 200-mesh stainless steel sieve while it was hot. An aliquot of the decoction was transferred to an evaporator dish, and evaporated to dryness on a water bath. The residue was heated to 105˚C in an oven for 4 hours and the residue was weighed. The yield of the extract was calculated and expressed in percentage. One hundred formulas announced by DOH in 1995 were investigated except Ru-yih-jin-hwang-san (如意金黃散), as it is not in the concentrated extract dosage form. The method of preparing drug extracts and the experiments for determining the production yield were the same except the sources of the crude drugs. The crude drugs were provided by each manufacturer. A proficiency test was carried out prior to the study for all of the participating manufacturers.

The extract yields of 99 formulas are listed in Table 2[9]. The ratios of the maximum to the minimum yield for the extracts was below 1.5 for 55 formulas. According to

Table 2. The extract yields of TCM preparations

No.	formula		the extract yield (%)	mean (%)	the ratio of maximum yield to minimum yield
1	Bai-he-gu-jin-tang	(百合固金湯)	31.1 - 45.0	38.0	1.45
2	Yuh-niuh-jian	(玉女煎)	34.0- 41.7	37.8	1.23
3	Jyh-gan-taso-tang	(炙甘草湯)	29.0 - 45.5	37.3	1.57
4	Tzy-in-jiang-huoo-tang	(滋陰降火湯)	32.7 - 40.5	36.6	1.24
5	Tzyy-woan-tang	(紫苑湯)	31.2 - 39.1	35.1	1.25
6	Szu-wu-tang	(四物湯)	29.2 - 36.9	33.0	1.26
7	Gan-luh-yiin	(甘露飲)	24.6- 36.1	30.3	1.46
8	Ba-jen-tang	(八珍湯(丸))	24.6- 36.1	30.3	1.47
9	Fuh-tayy-lii-jong-tang	(附子理中湯(丸))	23.5 - 36.7	30.1	1.56
10	Dah-cherng-chih-tang	(大承氣湯)	24.6 - 34.7	29.6	1.41
11	Guei-pyi-tang	(歸脾湯)	24.5 - 34.5	29.5	1.41
12	Liow-wey-dih-hwang-wan	(六味地黃丸)	24.8 - 33.7	29.3	1.36
13	Jyy-sow-san	(止嗽散)	25.6 - 32.7	29.2	1.28
14	Dang-guei-liow-hwang-tang	(當歸六黃湯)	21.7 - 36.4	29.0	1.68
15	Shyh-chyuan-dah-bun-tang	(十全大補湯(丸))	23.8 - 33.7	28.8	1.42
16	Liarng-ger-san	(涼膈散)	18.9 - 36.4	28.8	1.93
17	Buu-jong-yih-chih-tang	(補中益氣湯(丸))	25.8 - 31.5	28.6	1.22
18	Taur-horng-syh-wuh-tang	(桃紅四物湯)	26.1 - 30.5	28.3	1.17
19	Shiee-fuu-jwu-iu-tang	(血府逐瘀湯)	23.1 - 33.2	28.2	1.44
20	Ching-shuu-yih-chih-tang	(清暑益氣湯)	23.3 - 32.2	27.7	1.38
21	Chii-jyu-dih-hwang-wan	(杞菊地黃丸)	23.9 - 31.1	27.5	1.30
22	Ren-shen-yeang-rong-tang	(人參養榮湯(丸))	20.0 - 34.4	27.2	1.72
23	Jy-bor-dih-hwang-wan	(知柏地黃丸)	22.8 - 31.2	27.0	1.37
24	Dao-shoei-fwu-ling-wan	(導水茯苓湯)	24.9 - 28.9	26.9	1.16
25	Dang-guei-long-hwey-wan	(當歸龍薈丸)	19.3 - 39.1	26.6	2.04
26	Ba-wey-dih-hwang-wan	(八味地黃丸)	22.5 - 30.6	26.6	1.36
27	Syh-jiun-tzyy-tang	(四君子湯)	21.8 - 30.4	26.1	1.39
28	Liow-jiun-tzyy-tang	(六君子湯(丸))	24.8 - 27.3	26.1	1.10
29	Wan-day-tang	(完帶湯)	15.1 - 36.7	25.9	2.43
30	Wuu-ji-san	(五積散)	20.8 - 30.2	25.5	1.45
31	Ching-fey-tang	(清肺湯)	21.2 - 29.4	25.3	1.39
32	Dwu-hwo-jih-sheng-tnag	(獨活寄生湯)	20.5 - 28.7	24.6	1.40
33	Ching-shin-lian-tayy-yiin	(清心蓮子飲)	20.6 - 28.2	24.4	1.37
34	Ching-wey-san	(清胃散)	20.5 - 28.2	24.4	1.38
35	Jia-wey-shiao-yau-san	(加味逍遙散)	19.7 - 28.8	24.3	1.46
36	Jyuan-bin-tang	(蠲痹湯)	21.2 - 27.1	24.2	1.28
37	San-bin-tang	(三痹湯)	22.6 - 25.0	23.8	1.11
38	Jih-sheng-shenn-chih-wan	(濟生腎氣丸)	18.9 - 27.8	23.3	1.46
39	Buu-yang-hwan-wuu-tang	(補陽還五湯)	15.8 - 30.5	23.2	1.93
40	Dao-chyh-san	(導赤散)	17.8 - 28.1	23.0	1.57
41	San-jong-kuey-jian-tang	(散腫潰堅湯)	18.6 - 27.2	22.9	1.46
42	Ching-tzaw-jiow-fey-tang	(清燥救肺湯)	20.5 - 25.2	22.8	1.23
43	Long-daan-shieh-gan-tang	(龍膽瀉肝湯(丸))	19.0 - 26.6	22.8	1.40
44	Ren-shen-boy-dwu-san	(人參敗毒散)	18.3 - 27.1	22.7	1.48
45	Hwan-shaw-dan	(還少丹)	18.1 - 26.9	22.5	1.49
46	Yeang-shin-tang	(養心湯)	11.7 - 33.2	22.5	2.84
47	Shiang-sha-liow-jiun-tzyy-tang	(香砂六君子湯)	19.2 - 25.6	22.4	1.33
48	Jenq-guu-tzyy-jim-dan	(正骨紫金丹)	20.3 - 24.5	22.4	1.21
49	Shin-yi-ching-fey-tang	(辛夷清肺湯)	16.4 - 28.4	22.4	1.73
50	Shen-su-san	(參蘇散)	17.8 - 26.5	22.2	1.49
51	Shiao-yau-san	(逍遙散)	17.8 - 26.4	22.1	1.48
52	Jwu-yeh-shry-gau-tang	(竹葉石膏湯)	15.3 - 28.6	22.0	1.86
53	Shen-ling-bair-jwu-san	(參苓白朮散)	17.1 - 26.2	21.7	1.53
54	Wu-tu-yu-tang	(吳茱萸湯)	18.9 - 24.3	21.6	1.29
55	Shiau-feng-san	(消風散)	18.2 - 24.8	21.5	1.36
56	Chair-ger-jiee-ji-tang	(柴葛解肌湯)	17.0 - 25.5	21.3	1.50
57	Yih-chih-tsong-ming-tang	(益氣聰明湯)	18.9 - 22.8	20.8	1.21
58	Shanp-jong-shiah-tong-yong-tong-feng-wan	(上中下通用痛風丸)	16.1 - 25.1	20.6	1.56
59	Jing-jieh-lian-chiaw-tang	(荊芥連翹湯)	18.0 - 23.1	20.6	1.28
60	Yueh-jyu-wan	(越鞠丸)	15.0 - 26.0	20.5	1.73
61	Dii-dang-tang	(抵當湯)	13.3 - 27.4	20.4	2.06
62	Jeou-wey-chiang-hwo-tang	(九味羌活湯(丸))	16.1 - 24.4	20.2	1.52
63	Shu-jing-hwo-shiueh-tang	(疏經活血湯)	17.6 - 22.4	20.0	1.28
64	Hwang-lian-jiee-dwu-tang	(黃連解毒湯)	17.0 - 22.8	19.9	1.34
65	Jing-farng-boy-dwu-san	(荊防敗毒散)	15.5 - 23.8	19.7	1.54
66	Ji-ming-san	(雞鳴散)	15.2 - 23.6	19.4	1.55
67	Chyn-jiau-bie-jea-san	(秦艽鱉甲散)	14.8 - 23.2	19.0	1.57
68	Pair-nong-san	(排膿散)	9.6 - 27.9	18.8	2.91
69	Tyau-jing-wan	(調經丸)	16.4 - 21.0	18.7	1.28

Table 2. The extract yields of TCM preparations (Continued)

70	U-yaw-shuen-chih-san	(烏藥順氣散)	14.3 - 22.3	18.3	1.56
71	Chuan-chyong-char-tyau-san	(川芎茶調散)	14.0 - 22.0	18.0	1.57
72	Gou-terng-san	(屆藤散)	14.9 - 21.1	18.0	1.41
73	Huoh-shiang-jeng-chih-san	(藿香正氣散(丸))	13.9 - 21.7	17.8	1.56
74	Bair-huu-tang	(白虎湯)	12.8 - 22.6	17.7	1.77
75	Sheau-shiuh-ming-tang	(小續命湯)	13.0 - 22.2	17.6	1.71
76	Ma-shing-yih-gan-tang	(麻杏薏甘湯)	13.7 - 21.5	17.6	1.57
77	Ding-choan-tang	(定喘湯)	14.9 - 20.2	17.6	1.36
78	Hwang-chyi-wuu-wuh-tang	(黃耆五物湯)	13.6 - 21.4	17.5	1.57
79	Guey-jy-tang	(桂枝湯)	13.4 - 21.2	17.3	1.58
80	Ger-gen-tang	(葛根湯)	13.3 - 21.1	17.2	1.59
81	Su-tzyy-jiang-chih-tang	(蘇子降氣湯)	14.5 - 19.7	17.1	1.36
82	Sheau-ching-long-tang	(小青龍湯)	12.7 - 20.3	16.5	1.60
83	Sheau-shiann-shiong-tang	(小陷胸湯)	12.5 - 20.1	16.3	1.61
84	Hwai-hua-san	(槐花散)	11.9 - 20.6	16.3	1.73
85	Wuu-lin-san	(五淋散)	13.6 - 17.7	15.6	1.30
86	In-chern-wuu-ling-san	(茵陳五苓散)	11.8 - 18.6	15.2	1.58
87	Muh-farng-jii-tang	(木防己湯)	12.5 - 17.8	15.2	1.42
88	Ma-hwang-fuh-tayy-shih-shin-tang	(麻黃附子細辛湯)	10.7 - 17.9	14.3	1.67
89	Jim-fey-taso-san	(金沸草散)	11.7 - 16.6	14.2	1.42
90	Jyh-jwo-guh-been-wan	(治濁固本丸)	12.7 - 15.4	14.1	1.21
91	Hwa-gay-san	(華蓋散)	11.9 - 16.2	14.0	1.36
92	Shiang-su-san	(香蘇散)	10.4 - 17.6	14.0	1.69
93	Bih-jie-fen-ching-yiin	(萆薢分清飲)	9.3 - 18.0	13.6	1.94
94	Gan-luh-shiau-dwu-wan	(甘露消毒丸)	10.4 - 16.2	13.3	1.56
95	Ma-shing-gan-shyr-tang	(麻杏甘石湯)	8.5 - 15.3	11.9	1.80
96	Ma-hwang-tang	(麻黃湯)	7.7 - 14.3	11.0	1.85
97	Ba-jeng-san	(八正散)	4.1 - 17.0	10.6	4.15
98	Shiang-ru-yiin	(香薷飲)	5.6 - 15.4	10.5	2.75
99	Wuu-pyi-yiin	(五皮飲)	6.9 - 11.0	9.0	1.59

Narikawa's report[10], the extract yield of Hwang-lian-jiee-dwu-tang (黃連解毒湯) excluding precipitate (4.6%) was 18.4%. It was consistent with the data (No. 64 Hwang-lian-jiee-dwu-tang, 17.0~22.8%) shown in Table 2. The extract yields of 37 formulas ranged from 1.5 ~2.0. The ratios of formulas such as Dang-guei-long-hwey-wan (當歸龍薈丸, 2.04), Dii-dang-tang (抵當湯, 2.06), Wan-day-tang (完帶湯, 2.43), Shian-ru-yiin (香薷飲, 2.75) , Yean-shin-tang (養心湯, 2.84) and Pair-nong-san (排膿散, 2.91) ranged from 2.0 ~3.0. The ratio of Ba-jeng-san (八正散) reached as high as to 4.15. This suggests that such a high variation in extract yields might be due to different sources of the component crude drugs.

The Turnover Rate of Marker Constituents

As TCM, especially the concentrated extract, is widely used, suitable assay methods are needed for the purpose of quality control. Since 1985, the Ministry of Health and Welfare of Japan has required that all concentrated extract preparations submitted for registration should include a content analysis with at least two chemical constituents as markers for inspection[11]. The regulation also requires pharmaceutical factories to provide comparison data, in terms of the content of their marker constituents between their preparation. Difference between the preparation and the product from standard decoction should be within ±30%. Dr. Masatoshi Harada was the leader of a team researching quality control for Kanpo extract preparations. His team listed two articles about the quantitative analysis of TCM preparations[12, 13].

In recent years, our National Laboratories of Foods and Drugs has developed some high performance liquid chromatography (HPLC)[14-23] methods and high performance capillary electrophoresis (HPCE)[24-26] methods for the determination of marker constituents in TCM preparations. Meanwhile, the invited professor Shuenn-Jyi Sheu[27-31] (National Normal University of Taiwan), professor Wu-Lung Wu[27-31] (National Defense Medical College) and professor Pei-Dawn Lee Chao[27-31] (China Medical College) have compiled two volumes of books regarding HPLC and HPCE methods for the assay of marker constituents in Chinese herbal medicine[32, 33]. Those will be useful for pharmaceutical factories to set up their in house quality control system.

In the manufacturing process of concentrated extract dosage form, raw materials of crude drugs should be decocted, filtrated, concentrated and then made into dosage form. As the loss of active constituents in each formula during manufacturing process is not certain, it is necessary to evaluate the turnover rate of manufacturing process for each formula.

The turnover rates given in Table 3 for TCM preparations[10, 18, 20,34-38], are defined, with some exception, as the ratio of the content of marker constituent in standard decoction to that in individual test crude drug. In case of San'o-shashin-to (三黃瀉心湯), Hwang-lian-jiee-dwu-tang (黃連解毒湯) and Ger-gen-tang (葛根湯), the decoctions obtained after reflux 1 hr with water tenfold to the crude drug mass were used as the standard decoctions. In addition, an alternative method for preparing the decoction of Ger-gen-tang (葛根湯, reference No. 35), in which a pottery pot was used instead of reflux, resulted in a turnover rate as low as 9% for

Table 3. The turnover rate of marker constituents in TCM preparations

formula \ markers a) / turnover rate (%)	Sen-A	Ber	Pal	Bai	Baie	Wog	Gly	Liq	Gen	Cin	Cin-A	Pue	Dai	Daie	Pae	Fer	Gent	Man	Mag	Hon	Hes
San'o-shashin-to (三黃瀉心湯)[34]	50	40	44	55																	
Hwang-lian-jiee-dwu-tang (黃連解毒湯)[10,38]		42[10] 38[38]		60[10] 45[38]					88[10]												
Ger-gen-tang (葛根湯)[35,36]									18[b,35], 9[c,35]			67[36]	75[36]	44[36]							
Tang-guei-shao-yao-san (當歸芍藥散)[37]															73	85					
Ling-kuei-chu-kan-tang (苓桂朮甘湯)[37]							55			94											
Shih-chuan-ta-pu-tang (十全大補湯)[37]							51								57						
Chai-hu-kuei-chih-tang (柴胡桂枝湯)[37]							59								76						
Szu-wu-tang [37] (四物湯)															47	82					
Chiung-guei-chiao-ai-tang (芎歸膠艾湯)[37]							65								52						
Hsiao-chien-chung-tang (小建中湯)[37]							86								54						
Kuei-chih-chia-shao-yao-tang (桂枝加芍藥湯)[37]							86								46						
Kuei-chih-fu-ling-wan (桂枝茯苓丸)[37]							97								64						
Hsiao-chai-hu-tang (小柴胡湯)[38]				29			49														
Chai-hu-kuei-chih-tang (柴胡桂枝湯)[38]				49			59								76						
Pan-hsia-hsieh-hsin-tang (半夏瀉心湯)[38]		28					57														
Lung-tan-hsieh-kan-tang (龍膽瀉肝湯)[38]				37			46														
Ching-hsin-lien-tzu-yin (清心蓮子飲)[38]				47			46														
Dang-guei-san (當歸散)[18]				33			24	37							28	50					
Wuu-ji-san (五積散)[20]										62	36								9	14	15

a) Sen-A: Sennoside A, Ber: Berberine, Pal: Palmatine, Bai: Baicalin, Baie: Baicalein, Wog: Wogonin, Gly: Glycyrrhizin, Liq: Liquiritin, Gen: Genposide, Cin: Cinnamaldehyde, Cin-A: Cinnamic acid, Pue: Puerarin, Dai: Daizin, Daie: Daizein, Pae: Paeoniflorin, Fer: Ferulic acid, Gent: Gentiopicroside, Man: Mangiferin, Mag: Magnolol, Hon: Honokiol, Hes: Hesperidin

b) decocted by reflux

c) decocted by pottery pot

cinnamaldehyde as compared to 13% obtained by reflux. Furthermore, the turnover rate of the same marker constituent showed a significant variation in different formulas. For example, the turnover rates of berberine, baicalin, glycyrrhizin, paeoniflorin and ferulic acid were in the range of 23~42, 19~60, 24~97, 28~76 and 50~85%, respectively. According to the quality evaluation of San'o-shashin-to (三黃瀉心湯) by Narikawa[34] , the precipitate formed rapidly when mixing decoctions of Coptidis Rhizoma and Scutellariae Radix together. Whereas for mixing decoctions of Rhei Rhizoma and Coptidis Rhizoma, the turbidity appeared. These might account for the variation in turnover rate.

Some factors affecting the turnover rate of Ma'o-to were reported by Mamoru Moguchi[39] as follows: (1) the amount of water for extraction: the more water added, the better turnover rate resulted. (2) the duration of heating: A better turnover rate resulted from a longer period of heating. However, reverse outcome might occur for some markers after certain period of time. (3) the number of extraction: Better results were obtained from 2~3 of extractions than one extraction. (4) the extraction temperature: Some constituents were difficult to dissolve at low extraction temperatures. (5) filtration: A higher turnover rate was obtained by centrifugation rather than by filtration. Moreover, a noticeable drop in temperature during filtration led to the lowering of the

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turnover rate. This might be due to the retention of certain constituents in the expanded mixture of crude drugs. (6) the pore sizes: The pore sizes (60 or 200 mesh) of the sieve and the gravity (867 or 456 G) of centrifuging also slightly affected the turnover rate of the constituents. (7) formation of the precipitate: If the filtrate was not concentrated immediately, the precipitate would form on standing when the temperature dropped.

CONCLUSION

Difficulties for quality controls on TCM are mainly due to the source of crude drugs. The origins, the place and the climate of plant growing, the processing method and the storage may have an influence on the contents of constituents in crude drugs. Therefore, the extract yields of TCM preparations from different manufacturers exhibited significant variation. In addition, the manufacturing process and conditions of individual factories are not the same. These factors lead to the marked difference in the turnover rates of TCM constituents among various individual commercial products. At this stage, the marker constituents were required for ensuring the consistency between batches. For the sake of ensuring the quality, efficacy and safety of TCM preparations, requests for whole chromatographic fingerprint analysis together with bioassay results will be the future trend for quality control.

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中藥製劑指標成分移行率

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摘　要

本論文首先簡述中藥製劑品質管制之困難點，接著介紹中藥方劑之煎煮方法與設訂標準湯劑之必要性及其定義。並列舉99種基準方之乾浸膏率分佈情形。最後介紹指標成分於不同之中藥方劑其移行率之差異情形以及製程中影響移行率之因素。

關鍵詞：中藥，標準湯劑，乾浸膏，指標成分，移行率