

The HATC Project and Standard Kampo Formula Nomenclature

HFF 3rd Standard Committee Meeting
Tokyo, 30 June 2005

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UMC Second Herbal Reviewers Meeting, RSM, London, 29 April 2005

The Herbal ATC project for Kampo Formulae in Japan

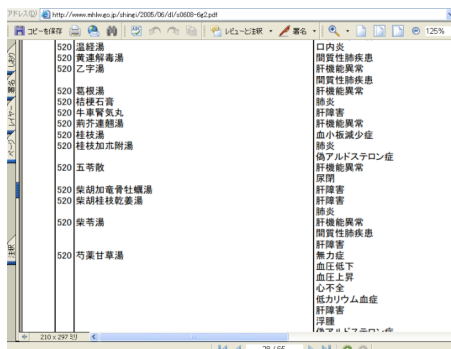
First HFF International Forum
Shanghai, China, 22 September 2004

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AE Line list on MHLW web (8 June 2005)



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AE Line list by Drug Safety Control Meeting

FY 2003	covering period
2 nd meeting (23 Jan. 2004)	30 July - 26 Oct. 2003
FY2004	
1 st meeting (2 June 2004)	27 Oct 03 - 31 Mar.04
2 nd meeting (20 Oct.2005)	1 Apr. - 31 July 2004
3 rd meeting (22 Feb. 2005)	1 Aug. - 30 Nov 2004
FY2005	
1 st meeting (8 June 2005)	1 Dec.04 - 31 Mar.05

For 20 months	herb-AE combination
Single herb	3
Kampo formula	298
OTC herb/Kampo	33
total	334 ca. 200 / year

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Where are line list ?

<http://www.mhlw.go.jp/shing/yakuji.html#yougu>
⇒ Find 医薬品安全対策部会 (Drug Safety Control Meeting)
⇒ ... 資料 (documents) ⇒ 資料No.2-2 ⇒ code 510 and 520
⇒ 資料No.2-3 (OTC)

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Safety of herbal drugs became political issue between Western doctor and Korean Oriental Medicine (KOM) Doctor in ROK since 2004

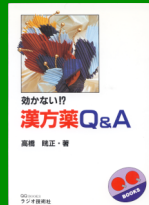
Feb 2004 Western doctor sued a KOM doctor for the use of CT scan.

Feb 2005 Criticized KOM pediatrician's poster
"KOM drugs has no side effect, effective, painless"

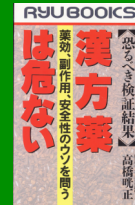
Used Dr. Takahashi's book on Kampo drug to criticize KOM

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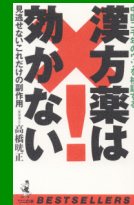
Three books on Kampo drugs written by Late Takahashi K
高橋暁正 1990年代漢方三部作



"Q&A of Kampo drug"
Dec. 1990



"Kampo drug is dangerous", Dec 1992



"Kampo drug is not effective", June 1993

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Future action

- Share the experiences between Japan and Korea, etc
日韓、他、の経験交換
- Common problems in the age of EBM 共通の問題
 - safety issue 安全性
 - re-evaluation of Kampo drug 漢方薬再評価
 - health insurance coverage 保険収載
 - WHO/WPRO clinical practice guidelines (CPG)
- Health system - Policy and politics 政策と政治
 - dialogue 対話
 - No "Uyamuya" うやむやにしない
(Not be dropped in vague)

<Tsutani K. at 4th J-K Symposium on Oriental Medicine, Toyama, 21 May 2005>

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The HATC Project in Japan since 2002

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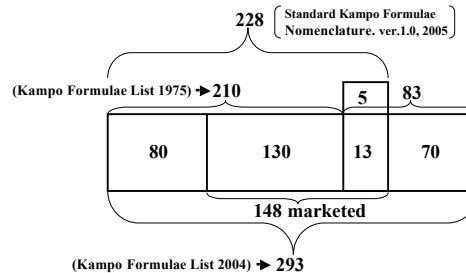
一般用漢方処方の手引き

厚生省薬務局 監修

薬業時報社

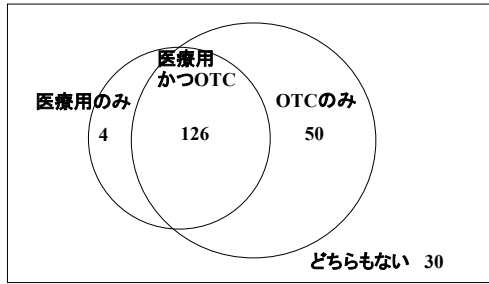
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Relation between the number of Kampo Formulae listed in the authorized document and those marketed (in ethical form)



(c) Tsutani K, 2005

「210処方」内の医療用とOTCの数



210処方以外医療用: 18

医療用として販売されている漢方処方の数=148 (4+126+18)

Key documents in PV of HM and HATC



2004

2005

2005

HA ALIMENTARY TRACT AND METABOLISM

HA01 STOMATOLOGICAL PREPARATIONS

HA01A STOMATOLOGICAL PREPARATIONS

HLA01AD Other agents for local oral treatment

- 5001 Palaquium gutta (Hook.) Baillon, gum
- 5002 Pistacia lentiscus L., resin

HA01W HERBAL STOMATOLOGICAL REMEDIES

HLA01WA Herbal stomatological remedies containing tannins

- 5001 Agrimonia eupatoria L., herb
- 5002 Ocimum basilicum L., herb
- 5003 Pimpinella major (L.) Hudson, root
- 5004 Pimpinella saxifraga L., root
- 5005 Quercus petraea (Matt.) Liebl., bark
- 5006 Quercus robur L., bark

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Herbal ATC Classification – Main Groups

The main groups (level I) of the Herbal ATC classification system are listed below. A survey of each main group is given in the beginning of each of the following chapters:

- HA Alimentary tract and metabolism 消化管・代謝系
- HB Blood and blood forming organs 血液・造血系
- HC Cardiovascular system 心血管系
- HD Dermatologicals 皮膚系
- HG Genito urinary system and sex hormones 泌尿生殖系・性ホルモン
- HH Systemic hormonal preparations excl. sex hormones 性ホルモンを除く全身性ホルモン製剤
- HJ Antiinfectives for systemic use 全身性抗感染薬
- HL Antineoplastic and immunomodulating agents 抗腫瘍剤・免疫調整剤
- HM Musculo-skeletal system 筋・骨格系
- HN Nervous system 神経系
- HP Antiparasitic products, insecticides and repellents 抗寄生虫薬・殺虫剤・駆除薬
- HR Respiratory system 呼吸器系
- HS Sensory organs 感覚器官
- HV Various その他

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- 5056 Syzygium aromaticum (L.) Merr. & Perry, flower bud
- 5057 Thymus serpyllum L., essential oil
- 5058 Thymus serpyllum L., herb
- 5059 Thymus vulgaris L., essential oil
- 5060 Thymus vulgaris L., herb
- 5061 Valeriana officinalis L., root
- 5062 Veronicastrum virginicum (L.) Farw., root
- 5063 Zanthoxylum americanum Mill., bark
- 5064 Zanthoxylum americanum Mill., fruit
- 5065 Zanthoxylum clava-herculis L., bark
- 5066 Zanthoxylum clava-herculis L., fruit
- 5067 Zingiber officinale Roscoe, rhizome
- 9001 Mentha x piperita L., essential oil with Carum carvi L., essential oil

HA03W HERBAL ANTISPASMODIC REMEDIES

HLA03WA Herbal antispasmodic agents containing furanochromones and/or coumarin derivatives

- 5001 Ammi visnaga (L.) Lam., fruit

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Ex. anchan 安中散

- Herb H
- Anatomy Alimentary tract and metabolism HA
- Therapeutic/pharmacological
 - Antiacids, Drugs for Treatment of peptic ulcer and flatulence HA02
 - Herbal Remedies for Treatment of Peptic Ulcer HA02W
 - Other herbal remedies for treatment of peptic ulcer HA02WX
- Chemical HA02WX 9xxx

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The number of HATC codes of Kampo Formulae in Japan

1 code 2 codes 3 codes

48	74	106
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acetylsalicylic acid

A01AD05 local oral treatment
B01AC06 platelet aggregation inhibitor
N02BA01 analgesic and antipyretics

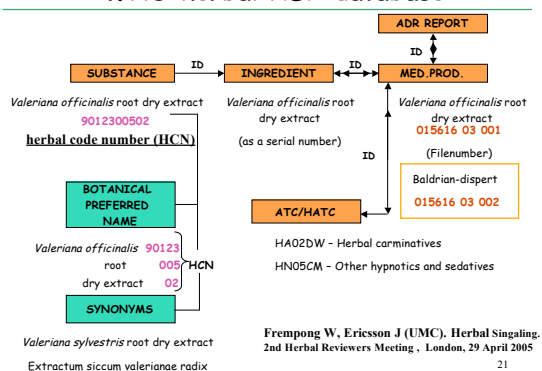
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Next actions of HATC project in Japan

- Change/add name in Roman alphabet to current classification
- Discuss with UMC on 5th level
 - 9500 China or 8000 ?
 - 9600 Japan
 - 9700 Korea
 - 9800 Vietnam
 -
- Discuss with UMC, IST, FHH on multi-code
- Expand scope
- Develop table of SKFN-herb

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WHO herbal ADR database



Frempong W, Ericsson J (UMC). Herbal Singaling. 2nd Herbal Reviewers Meeting, London, 29 April 2005

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Lexicon table * for "Part" of herbal drug

1. AERIAL ROOT
2. BARK
3. BUD
4. BULB
5. CAPSULE
6. CONE
7. CORM
8. DEBARKED ROOT
9. DESEDED FRUIT
10. DRY FRUIT
- ...
81. YOUNG LEAF

* Currently under revision

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Lexicon table * for "Extract" of herbal drug

1. ACETONE EXTRACT
2. BALSAM
3. BUTTER
4. DRY ETHANOL EXTRACT
5. DRY EXTRACT
6. DRY METHANOL EXTRACT
7. ESSENTIAL OIL
8. ETHANOL EXTRACT
9. EXTRACT
10. FLUID EXTRACT
- ...
26. WAX

* Currently under revision

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9 members for HATC project in Japan (Since 2002)

1. 東京大学大学院薬学系研究科医薬経済学講座 津谷喜一郎
2. 国立医薬品食品衛生研究所生薬部 合田幸広
3. 日本生薬学会 相見則郎
4. 日本東洋医学会 山田享弘, 鳥居塚和生
5. 日本漢方生薬製剤協会(日漢協) 篠原 宣
6. 北里研究所東洋医学総合研究所 山田陽城, 伊藤剛
(WHO伝統医学協カセンター)
7. 富山医科薬科大学医学部和漢診療部門 引網宏彰
(WHO伝統医学協カセンター)

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7 members for Standard Kampo Formula Nomenclature (SKFN), Since 2003

1. 東京大学大学院薬学系研究科医薬経済学講座 津谷喜一郎
2. 国立医薬品食品衛生研究所生薬部 合田幸弘
3. 日本生薬学会 佐竹元吉
4. 日本東洋医学会 鳥居塚和生, 山田和男
5. 和漢医薬学会 引網宏彰

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HA02WX (not final)

HA02WX9xxx	安中散	anchusan
HA02WX9xxx	茯苓沢瀉湯	bukuryotakushato
HA02WX9xxx	附子理中湯 (附子人參湯)	bushirichuto or bushininjinto
HA02WX9xxx	半夏瀉心湯	hangeshashinto
HA02WX9xxx	平胃散	heisan
HA02WX9xxx	堅中湯	kenchuto
HA02WX9xxx	香砂六君子湯	kosharikkunshito
HA02WX9xxx	柴胡桂枝湯	saikokeishito
HA02WX9xxx	柴芍六君子湯	saishakurikkunshito
HA02WX9xxx	四逆散	shigyakusan

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Principles for HATC classification in Japan

1. Registered indication (label / package insert)

2. Frequency of use (rather than classical text)

3. Three methods:

- (1) Use "major" herb (主薬)

黄芩 SCUTELLARIA RADIX	桂枝 CINNAMOMI CORTEX
柴胡 BULPLEULI RADIX	大黃 RHEI RHIZOMA
地黄 REHMANNIAE RADIX	附子 PROCESSI ACONITI RADIX
麻黄 EPHEDRA HERBA	
- (2) Use basic formula
ex. 桂枝湯 guizhi tang ?
- (3) Use concept of Kampo diagnosis
ex. 瘀血 (blood stagnation ?)

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Use of SKFN

1. For report to UMC
2. For JP 2006
3. In all journals
 - Japan Society of Pharmacognosy
日本生薬学会
 - Japan Society of Oriental Medicine
日本東洋医学会
 - Medical and Pharmaceutical Society for WAKAN-YAKU
和漢医薬学会
 - others

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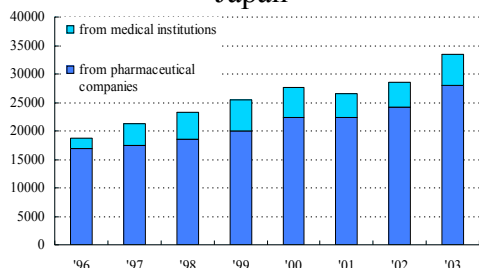
Herbal reporting from Vigibase

(1968 - 25 June 2004)

1. Germany	3,008
2. USA	2,325
3. United Kingdom	1,269
4. France	1,195
5. Australia	898
6. Spain	466
7. Canada	461
8. Sweden	442
9. Japan	286
10. Switzerland	205
.....	
total	11,489

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The number of ADR reporting in Japan



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Selection of Kampo formulae to be included in WHO/WPRO terminology

- to be based on evidence of actual use of it, not in terms of monetary value (i.e., Yen, US\$), nor of volume (i.e., ton, package unit), but in terms of number of users.-

Kampo Formula	WPRO code (2004)	1,000 user/year*	sales rank(億円)*	volume rank*
1 葛根湯	9.1.6	931	11(22)	5
2 芍薬甘草湯	9.6.72	509	12(22)	2
3 猪苓湯	JPN	459	18(55)	18
4 小青龙湯	9.15.16	367	8(33)	13
5 麦門冬湯	9.6.55	275	7(33)	11
6 大黄甘草湯	JPN	221	37(5)	17
7 加味逍遙散	9.10.3	179	5(36)	7
8 補中益氣湯	9.6.2	169	1(68)	4
9 大建中湯	9.5.8	160	3(50)	1
10 牛車腎氣丸	JPN	150	8(28)	3

*Above figures not be quoted. Validation of calculation is undergoing for ca 150 formula. About 30 formulae from Japan to be included in WHO/WPRO terminology.

The seven deadly sins

1. Complacency 驕傲 ひとりよがり
2. Fear 恐怖 恐れ (訴訟, 経済)
3. Guilt 罪悪感 罪の意識
4. Ambition 野心 功名心
5. Ignorance 無知 無知 (報告すべきことの)
6. Diffidence 無信心 気おくれ
7. Lethargy 無力 無気力

Inman WHW. Monitoring for Drug Safety. Lancaster: MTP Press, 1980: 36-37.
[吉利和(監訳). 医薬品の安全性確保. 薬業時報社, 1981:48-51.]

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Cultural bias in East Asia

- Recognition of AE/ADR reporting, including herbal products, among health professional and the public has to be elevated.
- Necessary action should be taken by relevant parties.
- Certain official relation should be developed between UMC and FHH, i.e, exchange of staffs, sending PhD students and others.

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Arigato
ありがとう

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