



Traditional and Herbal Remedies

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Developed in cooperation with
AACCC's
Therapeutic Drug Management
and Toxicology Division



Worldwide perspective

- Complementary
- Alternative
- Traditional
- Used for
 - Primary medical care
 - Treatment of minor ailments
 - Health maintenance



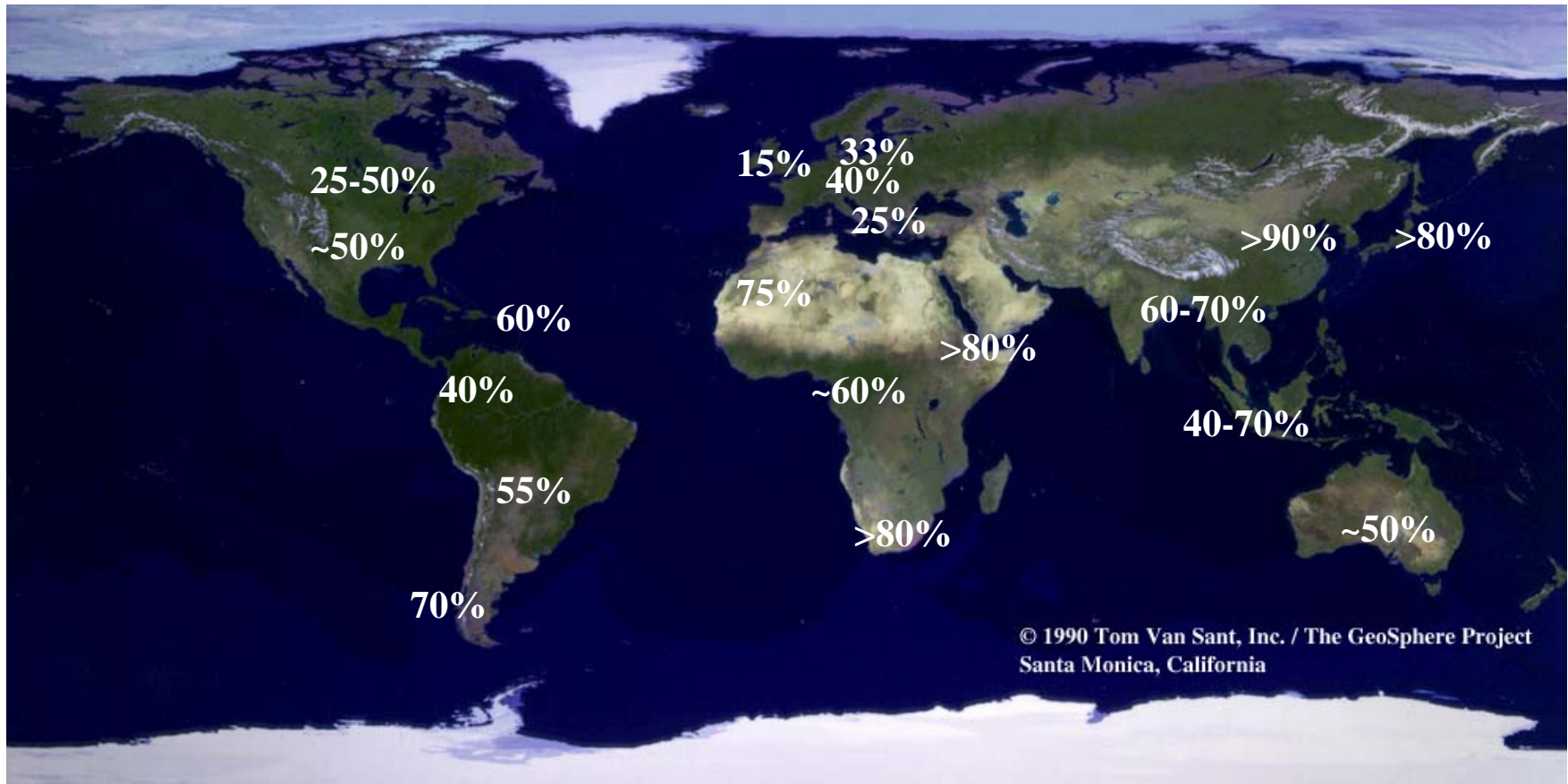
What is used or practiced?

Numerous alternative and traditional practices are found around the world. NCCAM has divided these into mind-body interventions, biological based therapies, alternative medical systems, manipulative And body based methods, and energy therapies.



Acupuncture/Acupressure Alexander Technique Aromatherapy Aryuvedic Medicine
Autogenic training Autologous blood therapy Bach Flower Remedies Balneotherapy
Biofeedback Bioresonance Bonesetting Chelation Chinese Herbal Medicine
Chiropractic Therapy Colonic Irrigation Counter-irritation Craniosacral therapy crystal
therapy Cupping Diets Electromagnetic therapy Enzyme therapy Herbal Medicine
Homeopathy Hydrotherapy Hypnotherapy Iridology Kampo Kinesiology Kirlian
photography Laser therapy Massage midwifery Naturopathy Phytomedicine Prayer
Pulse diagnosis Qi gong Reiki Reflexology Relaxation therapy Spa therapy
Spiritual Healing Tai Chi Thallasotherapy Tongue diagnosis Transcranial magnetic
stimulation Vega testing Water injection Yoga

Reported or Surveyed Prevalence of Use




Regulations and Education

- Varied from stringent to none
- Canada
 - Federal and provincial regulations
 - 2004 National Health Products Regulations
- European Union
 - Directive to register and license products
- Mexico
 - Traditional birth attendants, homeopathic practitioners, chiropractors licensed
 - Registry of traditional practitioners
- China and India
 - Integrated with allopathic medicine, regulated
 - Formal training

Folk or Traditional Medicine

- Range of remedies
 - prayer, touch, charms, rituals, teas, tinctures, poultice, etc
- Formal training vs apprenticeships vs observation, imitation, practice
 - In some cultures, skill is inherited
- Found in all cultures



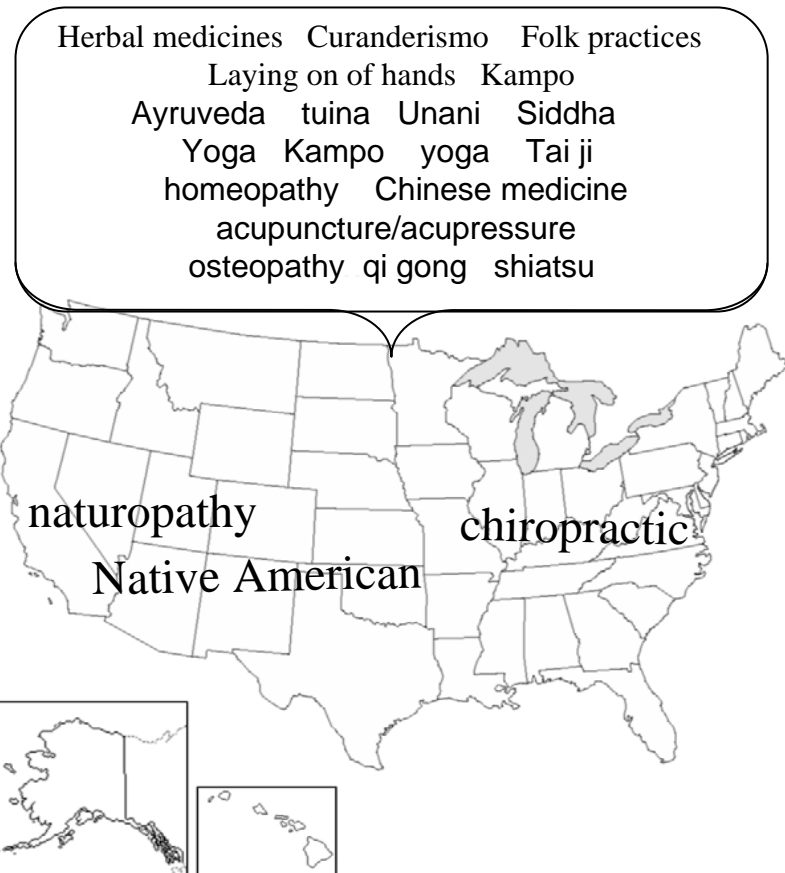
Traditional and Alternative Medicines in the USA

The Melting Pot: CAM/TM Practices in USA

2002 NHIS survey (www.cdc.gov)

Statistics and demographics for individuals

- 31,044 completed interviews
 - >18y, any use: 75%
 - Within past year: 62%
 - Female > male
 - Higher education level
 - Ethnicity determines type of CAM use
 - Hospitalized within past year



CDC NHIS data

- Prayer (10-43%), natural products (19.9%), deep breathing exercises (11.6%), meditation (7.6%), chiropractic (7.5%), yoga (5.1%), massage (5%), diet-based therapies (3.5%)

- Medical conditions treated:
 - Pain (back – 17%, joint – 5%, neck – 7%), colds (10%), anxiety or depression (5%)
 - ~1% each for sinusitis, hypercholesterolemia, asthma, hypertension, menopausal symptoms*

- Natural products used:
 - Echinacea (40%), ginseng (24%), ginkgo biloba (21%), garlic supplements (20%), glucosamine (15%), St John's wort (12%), peppermint (12%), fish oils/omega fatty acids (12%), ginger supplements (11%), soy supplements (9%), ragweed/chamomile (9%), bee pollen/royal jelly (7%), kava (7%), valerian (6%), saw palmetto (6%)

Prevalence and Demographics

- Swan survey (Menopause, 2005; 12:31-9)
 - 2002, 2,565 women
 - Multiethnic population, 7 clinical sites
 - 42-52 y, pre- to peri-menopausal
 - CAM use 51% at baseline, 58% FU2
 - Nutritional remedies 34%, 37%
 - Herbal remedies 19%, 26%
 - Folk medicine 6%, 5%
- Rutgers undergrad survey (J Am Acad Nurse Pract 2004; 16:166-73)
 - 2002, 1,754 students
 - >50% using herbals
 - Relief of symptoms, prevention, general health

Use of CAMs and TM

- Earlier NHIS data demonstrated that diabetes was an independent predictor of CAM and TM use
 - Diabetes >17.0 million people (6.2%)
 - diagnosed 11.1 million
 - undiagnosed 5.9 million
 - 6th leading cause of death
- Massage therapy, herbal remedies, spiritual healing, nutritional advice and lifestyle diets, meditation, folk remedies
- Herbal remedies
 - Gymnema, psyllium fenugreek, bilberry, garlic, Chinese ginseng, dandelion, burdock, prickly pear cactus, bitter melon
 - Goat's rue (*Galega officinalis*) guanidine ⇒ hypoglycemia
 - 3rd generation biguanidines ⇒ metformin^{Mar}

Use of CAMs and TM

Type 2 Diabetes: increased prevalence among Hispanic and Native American/American Indian populations

- Northern Plains Am Indian Tribes
 - Talking circles
 - Diabetes education

- South Texas:
 - 44% Mexican Americans consulted an alternative practitioner
 - 66% did not report to primary care provider
 - 53-64% used herbal/home remedies or rituals
 - Shared information regarding drug-herbal interactions

Qual Health Res 2003;13:1094-115
Clin Nurs Res 2003; 12:304-323



Regulations and Impact on Health Care

Herbals and Supplements

- 1994: Dietary Supplement Health and Education Act (DSHEA)
- classified as food products regardless of historical use
- allows claims of:
 - affects toward structure or function of the body
 - benefits related to correcting nutrient deficiency
 - description of general well-being from consumption
 - characterization of the mechanism of action

allowed: *“maintains cardiovascular function and a healthy circulatory system”*

not allowed: *“reduces the risk of heart disease”*

Regulations: EU and herbals

- Claim
 - Treatment or prevention of illnesses
 - Restore, correct or modify physiological function
- Classified as medicinal product
- Safety and quality standards
 - Bibliographic review of safety data
 - Expert report
- Efficacy
 - Document 30 y of traditional use with 15 y use in EU
- Labeling include information and instructions for use
 - Warning to consult qualified health care provider

Regulations for other practices

- Governed by federal and state laws
 - Varies from full licensure to certification to business license to no recognition

- Example: Massage therapy
 - 33 states require certification, registration, licensure
 - Board certification
 - Accreditation commission for training programs
 - Reimbursement

Impact of CAMs

■ US Healthcare

- Americans using an alternative therapy
 - 34% in 1990 to 42% in 1997
 - 20-40% self-report use to health care provider
 - 18% use herbal with prescription medication
 - 2003 ~ 50% of all perimenopausal women (SWAN)
- Most popular
 - herbal medicine, massage, megavitamins, folk remedies, energy healing, homeopathy

■ US Consumers

- 1990 to 1997
 - \$10.3 billion to \$27-34 billion
- 2004
 - CAMs > \$30 billion
 - herbal supplements: > \$5 billion

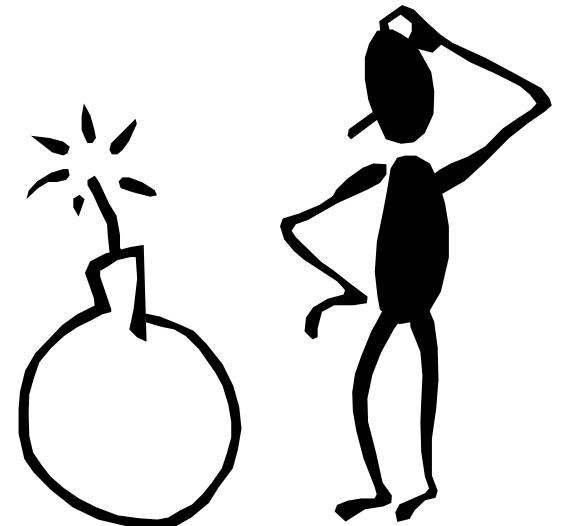
JAMA 1998; 280:1569-75
www.nih.gov; www.cdc.gov
www.fda.gov

Laboratory Issues

Analytical interference

Pharmacological effects

Adverse and toxic reactions

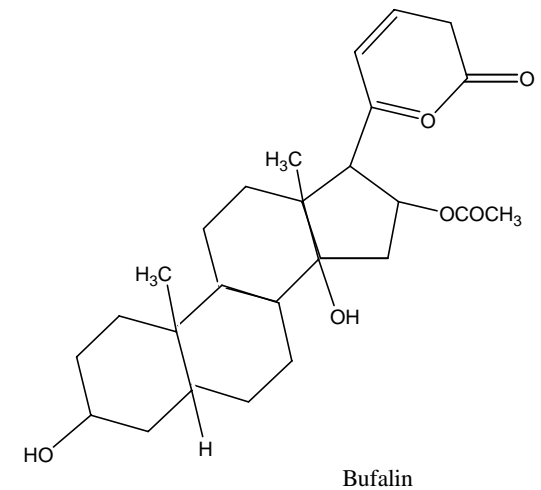
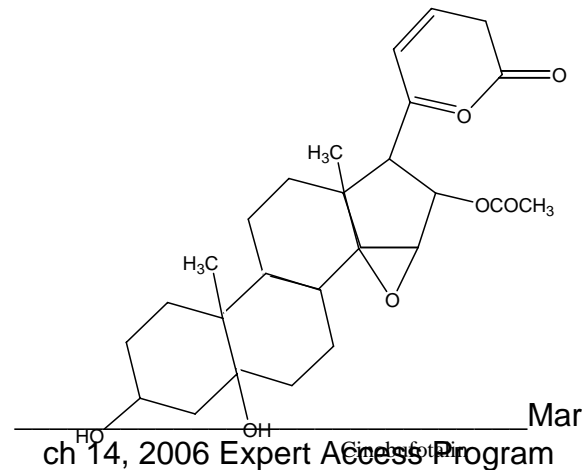
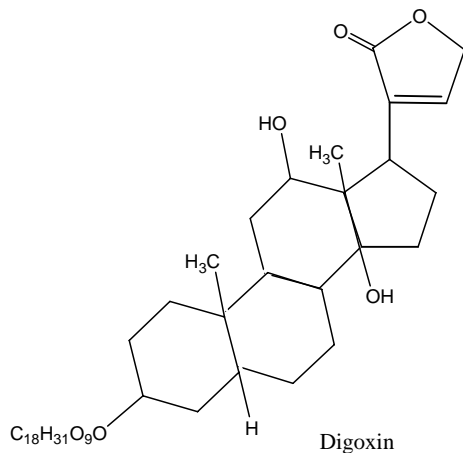


Analytical Interference

- Urine drug screens (immunoassay)
 - Amphetamine
 - ephedra: cross-reactivity; Golden seal root: increase FPIA-methods
 - Barbiturates
 - Golden seal root: decrease FPIA-methods
- Catecholamines (HPLC, electrochemical detection)
 - diet and weight loss products
- Creatinine (enzymatic methods)
 - creatine: increased background
- Digoxin - immunoassay
 - Siberian ginseng, Kyushin, Dan Shen, uzara root, Chan su, Lu-Shen-Wan: Ab cross-reactivity, interference with detection methods
- Urinalysis
 - Senna – red, orange or rust color

Digoxin Interference

- Siberian ginseng, Asian ginseng, Kyushin, Dan Shen, uzara root, Chan su, Lu-Shen-Wan
 - contain cardinolides
 - ↑ antibody cross-reactivity
 - ↑ interference with detection methods



Digoxin Interference

Herbal	Analytical method Interference	No interference	~ protein binding	Elimination using free digoxin?
Chan Su	FPIA ↑, MEIA ↓, TIIA ↑, TIA ↑, EMIT ↑	CIA	>90%	yes
Dan Shen	FPIA ↑, MEIA ↓	EMIT, TIA, TIIA, CIA	>90%	yes
Lu Shen Wan	FPIA ↑, MEIA ↓, TIIA ↑, TIA ↑, EMIT ↑		?	yes
Uzara root	FPIA ↑, MEIA ↓, TIIA ↑, TIA ↑, EMIT ↑		?	?
Siberian ginseng*	FPIA ↑, MEIA ↓	EMIT, TIA, TIIA, CIA	<50%	no
Asian ginseng*	FPIA ↑, MEIA ↓	EMIT, TIA, TIIA, CIA	<50%	no

* variable, lot and
vendor

Common Adulterants and Contaminants

- ***steroids:*** prednisolone, hydrocortisone, triamcinolone, methyltestosterone
- ***benzodiazepines:*** diazepam, estazolam, chlordiazepoxide
- ***heavy metals:*** mercury, lead, arsenic, antimony, cadmium
- ***analgesics and NSIADs:*** acetaminophen, aspirin, indomethacin, mefenamic acid
- ***other drugs and chemicals:*** hydrochlorothiazide, digitalis, caffeine, scopolamine, atropine, strychnine, carbamazepine, phenytoin, valproic acid, dipyrrone, diacetyldiphenolisatin

CAMs and Drug Interactions

TDM

digoxin

ETOH

lithium

phenytoin

protease
inhibitors
(saquinavir)

steroids

warfarin

CAM

Siberian ginseng, Chan Su, uzara root

aloe, ginseng, Dan Shen, kava

plantain

Shankhapushpi, piperine

SJW, garlic

licorice (glycyrrhizin)

ginseng, ginkgo, feverfew, Dong quai, danshen,
Lycium barbarum L (Chinese tea), boldo-fenugreek,
SJW, Dan Shen, ? *garlic, ginger*

Pharmacological and Toxicological Effects

■ Glucose

- ↑: licorice, ma huang
- ↓: fenugreek, garlic, ginger, ginseng, nettle, sage
- ↓ ↓: chromium

■ ↓ Potassium: licorice (glycyrrhiza) pseudoaldosteronism

■ Hematology and coagulation

- ↓ Platelet aggregation: garlic, ginger, ginkgo, Dan Shen, feverfew
- agranulocytosis - yohimbin
- thrombocytopenia/leukocytosis - Dysosma pleianthum

Pharmacological and Toxicological Effects

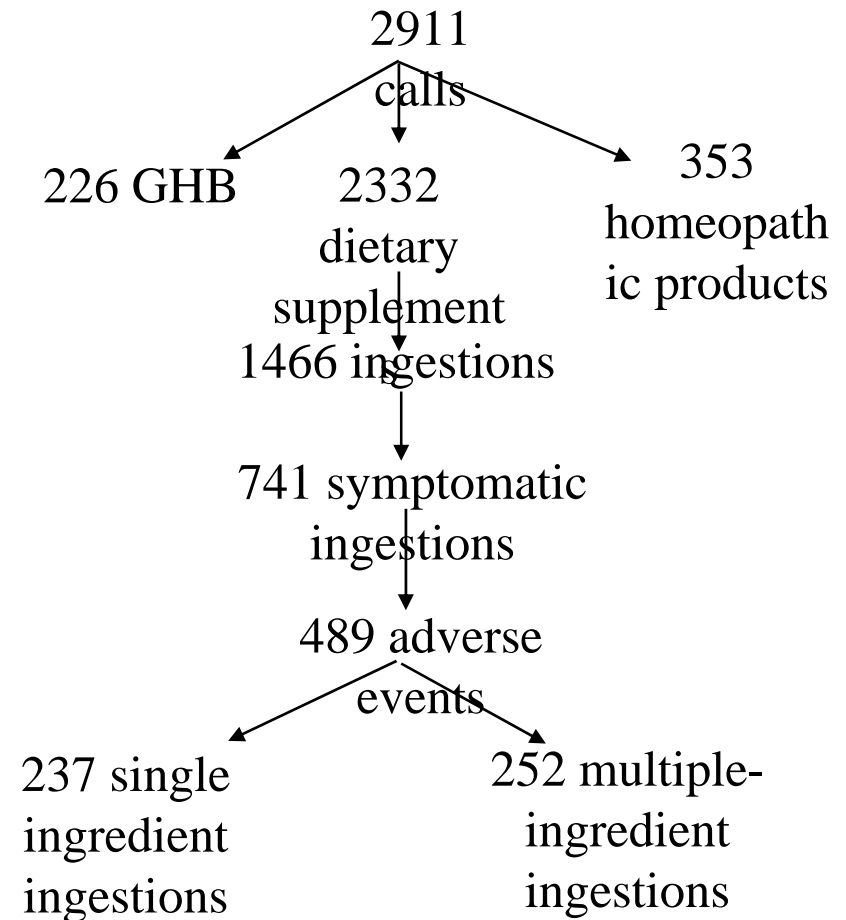
- ↓ TSH, ↑ T4: kelp
- Urinalysis:
 - ↑ low MW proteins: Aristolochia fangchi, Tripterygium wilfordii hook, comfrey
 - ↑ casts/cells: licorice, germanium supplements, Mylabris phalerata/sidae
- Protein binding: Dan Shen, St Johns Wort, Coptis chinensis/japonicum, Artemisia scoparia, goldenseal (berberine)

Tess Reports

	2000	2001	2002	2003	2004
Essential oils	4960	6456	7242	7310	6125
Dietary supplements/ herbals/ homeopathics	16929	19468	22928	24412	24842
Treated	7650	7850	9619	9419	8348
Deaths	15	12	5	13	11

Adverse Events

- 14 poison control centers
- 1998
- age range <1 to >70 y
 - 493 1-5y
 - 638 18-69y
- botanical/nonbotanical
 - foraged plants under herbalist instruction, chromium, zinc, melatonin, GHB



Adverse Events

- 489 symptomatic ingestions
 - Ma huang, guarana, ginseng, St John's Wort, chromium, melatonin, zinc
- 340 mild; 117 moderate; 28 severe; 4 deaths
 - hepatic/hematological (39), chest pain (20+), coma (18), arrhythmias (14), seizures (13), bradycardia (9), electrolyte abnormalities (4), MI (2)

The Dirty Dozen

- Consumer Reports, April 2004
- Aristolochic acid, Comfrey, Androstenedione, Chaparral, Germander, Kava, Bitter orange, Organ extracts, Lobelia, Pennyroyal oil, Scullcap, Yohimbe

Comfrey

- *Symphytum officinale*

- blackwort, bruisewort, knitbone,

- active compounds

- allantoin, pyrrolizidine alkaloids and N-oxides, tannins, fructanes, triterpenoid saponins

- form/preparation

- topical only*
- above ground parts of plant
 - tea for gargle
 - paste under bandage

- Uses

- antiinflammatory
 - bruises, sprains
- antibacterial
- antioxidant
- *few internal uses
“reported” for gastritis, gastroduodenal ulcers, rheumatoid arthritis, bronchitis, allergies, diarrhea

Comfrey Toxicity

■ Mechanism

- pyrrolizidines and N-oxides
 - hepatotoxic, carcinogenic

■ dose

- depends on pyrrolizidine content
- 100 µg/d max - absorbed via skin
 - 0.1-0.4% detected in urine

■ Signs/symptoms

- Budd-Chiari like syndrome
- veno-occlusive disease
- acute
 - RUQ pain, hepatosplenomegaly, ascites
 - rapid progression to cirrhosis, portal hypertension, death from hepatic necrosis (20%)

Comfrey Toxicity

■ Symptoms cont.

□ chronic

- asthenia, fatigue, diarrhea, portal hypertension
- cirrhosis (hepatic vein thrombosis), cholestasis, jaundice, bleeding, portosystemic encephalopathy
- right heart hypertrophy
- primary pulmonary hypertension

■ Treatment

□ supportive

- pressors, aldosterone antagonists, fluid-Na restriction, controlling ascites, shunts,
- anticoagulants not effective in preventing occlusive processes
- liver transplantation

□ avoidance

■ Laboratory

- LFT's, renal function, CBC/diff, platelet count, identification
- biopsy

Yohimbine

- *Pausinystalia yohimbe*
 - yohimbe, johimbe, aphrodien
- active compounds
- indole alkaloids
 - yohimbine
- form/preparation
 - bark
 - 16-18 mg daily, divided doses
- Uses
 - aphrodisiac
 - impotence
 - skin diseases
 - weight control

Yohimbine Toxicity

■ Toxic dose

- 20-30 mg/d
 - tachycardia
 - hypertension

■ Mechanism

- α_2 adrenergic blocking activity

■ Signs/symptoms

- CNS stimulation/psychosis
- hypertensive crisis, hypotension
- tachycardia and reflex bradycardia
- nausea/vomiting
- cardiac and cerebral infarcts

Yohimbine Toxicity

■ Treatment

emergent

- think of as opposite of clonidine
- nitroprusside
- esmolol

nonemergent

- clonidine

■ Laboratory monitoring

electrolytes

LFT's

renal function

troponin

Pennyroyal Oil

- *Hedoma pulegiodes* or *Mentha pulegium*
 - member of mint family
 - squaw mint
- Form/preparation
 - ingested as tea made from leaves or alcohol extract
- Active compound
 - pulegone

■ Uses

- relieve gas, abdominal colic
 - has been confused with *Yerba buena*
- diaphoretic to purge toxins
- relieve nausea
- relieve cough
 - folk remedy for cold and flu
- toothache
- flea repellent
- emmenagogue or abortifacient

Pennyroyal Oil Toxicity

■ Toxic dose

- <10 mL gastritis, mild CNS toxicity
- 30 mL centilobular hepatitis
- 5-15 mL lethal

■ Mechanism

- pulegone → methylfuran
 - depletes glutathione stores, blocks G-6-PDH
- *looks like*

acetaminophen toxicity

■ Sign/symptoms

- GI: burning throat, nausea, vomiting, right upper quadrant pain
- CNS: mental status changes, dizziness, seizures, coma
- metabolic: hypoglycemia,
- liver failure, coagulopathy, centilobular hepatitis (higher doses)
- renal failure

Pennyroyal Oil Toxicity

■ Treatment

- decontamination by lavage
- activated charcoal
 - efficacy is unproven
- N-acetylcysteine
 - successful in several cases
- support

■ Laboratory

- creatinine, urea nitrogen
- AST, ALT
- electrolytes
- coags

- GC detection of methylfuran in blood, urine, tissues

Investigations:

CAMs, the Lab, and Tox

- Documenting and reporting adverse reactions
 - Dosage, formula, duration of exposure, etc
 - Preparation and use
 - Oral vs topical
 - Teas, infusions, decoctions, extractions
 - Product purity
- <http://www.fda.gov/medwatch/>

- Polypharmacy



Mar

Expect the unexpected...

- family practice clinic:
 - “Can anise tea cause positive urine cocaine?”
- patients denied insurance due to (+) drug test

tea: Delisse

source: Peru

ingredients:

60% *Erythroxylon coca*

40% *Pimpinella anisum*



Foraging and harvesting Issues, problems, etc....

- Misidentification
- Potencies vary from batch to batch.... season to season....
- Chemical composition varies between cultivars, geography, environmental conditions
- Changing nomenclature
 - Botanical and medical

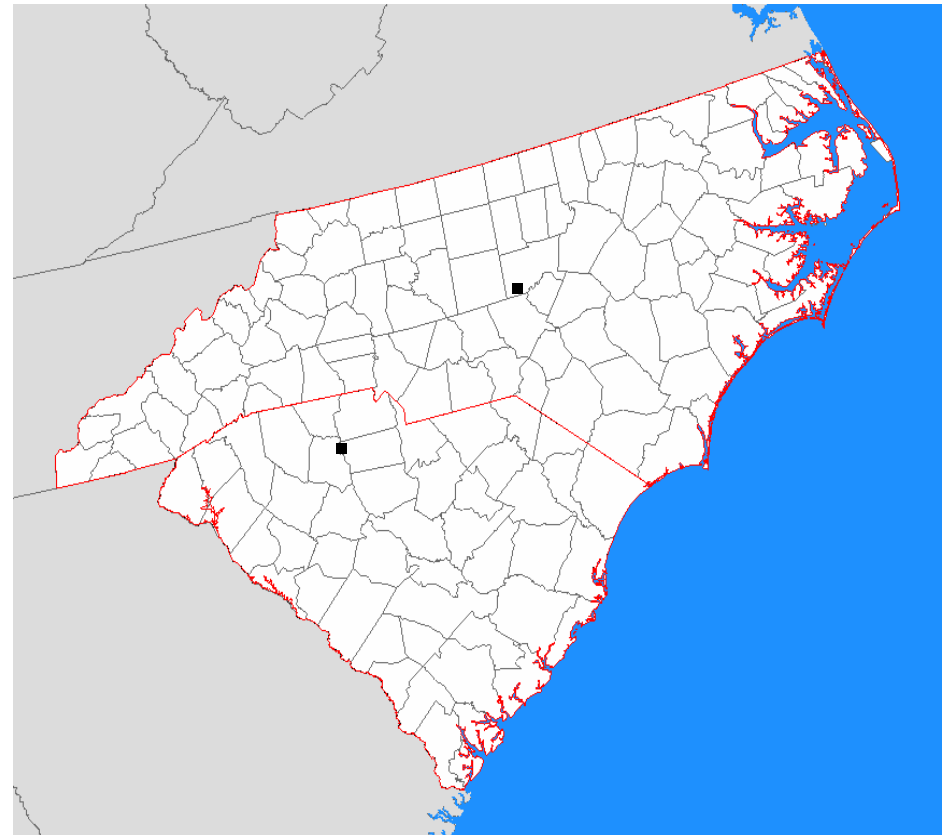
Herbs and Plants with Traditional Uses in Southern Appalachia

■ History

- Native Americans used ~12% of available plants for medicinal purposes.
- Settlers and slaves brought medicinal plants to new country or “found” similarly appearing species.
- Sharing of information

■ Current practitioners

- undocumented



Sassafras

(*Sassafras albidum*)

- Laurel family, eastern US (saxifrax, saloop, ague tree, cinnamon wood)
- Medicinal parts: root bark, leaves gathered after August
- Solvents: boiling water, alcohol
- Uses: stimulant, diaphoretic, diuretic, tonic, rheumatism, varicose ulcers, menstrual cramps, childbirth pain, tooth ache, flavor enhancer, eye irritations, poultices for ulcers, bruises, swellings
“Antagonistic to narcotic effect of alcohol”
- Dose: *infusion of 1 oz crushed bark to 1 pt boiling water. Of the tincture, 15-30 minims.*
- Cautions: oil can cause liver and kidney damage
“should not be used by thin-blooded persons”
- Active compounds: oil (safrole, anethole, apiole, asarone, camphor, caryophyllene, eugenol, 1-menthone, myristicin, pinene, thujone, connamolaurine, tannin)



Sweet gum

(Liquidambar styraciflua)



- Witch hazel family, eastern US, red gum, star-leaved gum, styrax, storax
- Medicinal parts: bark, juice
- Solvents: boiling water, warm alcohol
- Uses: stimulant, expectorant, diuretic, antiseptic, disinfectant, amenorrhea, asthma, phthisis (wasting disease, consumption – TB); ointment for ulcers, frostbite, scabies, ringworm, hemorrhoids

“excellent for bloody flux, dysentery, and all bowel complaints of children”

- Dose: 1 t of the cut or granulated bark to 1 c boiling water; drink 1-2 c at a time; adjust for condition and age
- Also mixed with other materials.

- Active compounds: cinnamic acid, tannin

Witch hazel

(Hamamelis virginiana)

- Alder family, eastern and central US, five species
- Medicinal parts: bark, leaves
- Solvents: boiling water
- Uses: astringent, tonic, sedative, dysentery, ointments
“given internally to stop all kinds of hemorrhages”
- Dose: *simmer 10 m 1 oz of the leaves or bark to 1 pt water. Take in wineglassful doses 3-4 times daily.*
- Cautions: skin irritation if applied directly to skin
- Active compounds: tannins (?), safrole



Common Mullein

(*Verbascum thapsus*)

- Velvet Plant, Flannel Leaf, Jacob's Staff, Shephard's Club
- Medicinal parts: root, leaves, flower
- Solvents: water
- Uses: diuretic, antispasmodic, congestion; decoction with equal parts horsemint is used to treat kidney diseases

"I don't think there is any ailment that mullein wouldn't offer some relief."

- Active cpds: leaves (saponin, coumarin, mucilage, rotenone, resin); seeds (saponin, mucilage, oleic acid, linoleic acid); blossom (thapsic acid); root: (coumarin, phytosterin, verbasterol)



- Pipsissewa (*Chimaphila umbellata*)
Wintergreen, spotted wintergreen
 - blood purifier, fever, rheumatism, kidney, liver, diuretic
 - tea, with mullein to stop bedwetting
 - tannins, arbutin, chimaphilin



- Spotted Pipsissewa (*Chimaphila maculata*)
rat's vein, spotted wintergreen, wintergreen, princess-pine
 - heart trouble, poor appetite
 - can kill rats
 - ? chimaphilin, arbutin

Wild ginger

(*Hexastylis heterophylla*)

- Heart leaf, little pigs

Common names applied to *Asarum virginicum*, *heterophylla*, *A. shuttleworthii*, *Aristolochia serpentaria*

- Medicinal parts: rhizome
- Solvents: water
- Uses: emetic, cathartic



- Use may have originated because of its similar appearance to European species
- Warnings of toxicity may relate to mistaken identity (Virginia snakeroot)

Bee Balm

(Monarda didyma)

- Red mint, oswego-tea, mountain mint
- Medicinal parts: leaves, flowers
- Solvents: water
- Uses: fever, nervine, menstrual cramps, trouble, gas, nausea
“good against the stinging of bees and waspes”
- Active compounds: oil (carvacol, thymol, cymene); blossom (monardin);
leaves (linalyl acetate, limonene, linalool, ocemene, camphene, caravacrol, ursolic acid, beta-carotene, naringenin, prunin)



Future prospects:

From Old to New

- Ethnobotany, ethnopharmacology
 - 300,000-500,000 plants
 - 20,000-55,000 used medicinally
 - ~15-20% evaluated for pharmaceutical potential
 - Fingerprinting and screening of plants and medicines
 - NCI: 1960-82; 35,000 samples, 114,000 extracts
 - International Cooperative Biodiversity Groups
 - Chemical profiling using combination of separation techniques
 - Recognition and protection of ownership
- Bioinformatics and bioprospecting: Document mining
 - Ancient texts
 - Books

Future prospects:

From Old to New

- Atropine; scopolamine: *Atropa belladonna*
- berberine: barberry, *Berberis vulgaris*
- Morphine and codeine: poppy, *Papaver somniferum*
- Digoxin digitoxin: foxglove, *Digitalis*
- Reserpine: Indian snakeroot, *Rauwolfia serpentina*
- Quinine: *Cinchona* spp
- Vinblastine: *Catharanthus roseus*

Conclusions and your role

- Recognize that traditional medical practices are found in US
 - Practices varied and typically include use of botanicals, minerals, or animal products.
 - Often include meditation, prayer, rituals, etc.
 - Patients must feel comfortable with practitioner to admit use.
- Investigate and report testing interferences and adverse reactions.
 - MedWatch www.fda.gov
 - Publications
- Stay tuned: Bioprospecting and ethnopharmacology – may bring the past into the future.
 - Identify active and toxic compounds
 - New drug development

References

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- John K. Crellin and Jane Philpott, *Herbal Medicine Past and Present*, 1990