



Adjunct or Junk Therapies on Pediatric Infectious Diseases: *focusing on Herbal Medicine*

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Summary

- Definitions – CAM, Herbal medicine, supplements, THPR
- Myths and benefits of Herbal medicine
- Evidence-based herbal medicine
 - common signs and symptoms associated with infections
 - treatment of selected common infections
- SCAMS



Traditional/Complementary/ Alternative Medicine

Traditional & Alternative Medicine Act (1997)

National Center for Complementary and Integrative Health, USNIH

The sum of total knowledge, skills and practices on health care, other than those embodied in biomedicine, used in the prevention, diagnosis and elimination of physical or mental disorder

Complementary- if a non-mainstream practice is used together with conventional medicine
Alternative- if a non mainstream practice is used in place of conventional medicine





Philippine FDA Definitions

Traditionally used Herbal Products-

preparations from plant materials whose claimed application is/are **based only on experience of long usage** which should be at least 5 or more decades as documented in medical, historical and ethnological literature





Traditionally used Herbal Products



Evidence for safety and efficacy- PhilFDA 2004 Guidelines

- Documentation of prolonged and permanent uneventful use of herbal product
- Absence of unsuspected potential for systematic toxicity, carcinogenicity and teratogenicity
- Evidence for claimed application shall be based on medical/ pharmaceutical literature



Label Sample for Traditionally-Used Herbal Products

INFORMATION PANEL

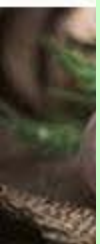
PRINCIPAL DISPLAY PANEL

INFORMATION PANEL

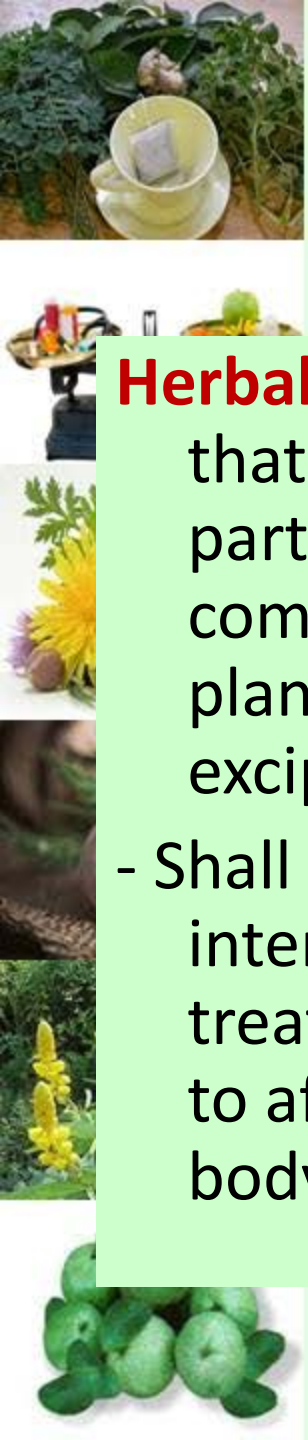
<p>Formulation: Each capsule contains: <i>Zingiber officinale</i> L.-200 mg (Ginger Rhizome)</p> <p>Folkloric Use/ Claimed Application: For relief of motion sickness</p> <p>THPR No. (Traditionally-Used Herbal Product Registration Number) Batch/Lot No.: Date Mfd.: Expiry:</p> <p>Store at temperature not exceeding 30 °C</p> <div style="border: 1px solid black; padding: 5px; margin-top: 10px;"> <p>The traditional application/use of this product has not been evaluated by the Bureau of Food and Drugs.</p> </div>	<p>Net Content 100 capsules</p> <div style="border: 1px solid black; padding: 10px; margin: 10px auto; width: 80%;"> <p><i>Zingiber officinale</i> L. Ginger Rhizome</p> </div> <p>Brand name, if any</p> <p>200 mg Capsule</p> <p>For relief of motion sickness</p> <p>Manufactured by</p> <p>For:</p>	<p>Dosage:</p> <p>Precautions:</p> <p>Side Effects:</p> <p>Contraindications:</p> <p style="margin-top: 20px;">“Not allowed for use in pregnant, lactating mothers, and children below 18 years.”</p> <p style="margin-top: 20px;">“If symptoms persist, consult your doctor.”</p>
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Herbal Supplements

- Over the counter supplements
- Evidence for quality is necessary
- No evidence for efficacy is required
- “FDA-registered” – most abused term
- FR no




Philippines FDA Definitions


- 
- Herbal medicines** -finished labeled medicinal products that contain active ingredient/s aerial or underground part(s) of plants or any other plant material or combination thereof, whether in the crude state or as plant preparations. Herbal medicines may contain excipients in addition to the active ingredient
- Shall have specific therapeutic claim(s) and shall be intended for use in the diagnosis, alleviation, cure or treatment of disease, promotion of health or intended to affect or modify the structure or any function of the body of humans or animals



Herbal medicines




Evidence of safety and efficacy- PhilFDA AO 172
2004



1. Pre clinical- Acute LD50


Pharmacological effects both in vivo and in vitro

Bioassay



Non-mutagenicity- Ames test and micronucleus
test

sub-chronic and chronic toxicity



2. Clinical- for galenicals- Phase 1 trials

For dosage forms- Phase 1,2 and 3 trials



Label Sample for Herbal Medicines

INFORMATION PANEL

Formulation:

Each tablet contains:
Vitex negundo L. - 300 mg
(Lagundi Leaf)

Indications:

For the treatment of broncho-spasm in acute bronchial asthma, chronic bronchitis and other broncho-pulmonary disorders. Also for other forms of cough due to common colds, flu and pharyngitis.

HMR No. (Herbal Medicine
Registration number)

Batch/Lot No.:

Date Mfd.:

Expiry:

Store at room temperature
not exceeding 30 °C

PRINCIPAL DISPLAY PANEL

Net Content 100 tablets

Vitex negundo L.
Lagundi Leaf

Brand name, if any

300 mg Tablet

Anti-asthma
Anti-cough

Manufactured by:

For:

INFORMATION PANEL

Dosage:

Adult: 2 x 300 mg tablet
every 4 - 6 hours
Children: 1 x 300 mg tablet
every 4 - 6 hours

Precautions:

Safety in pregnant and lactating women has not been established.

Side Effects:

Only mild side effects on few patients such as itchiness, nausea and vomiting, tachycardia, diarrhea, drowsiness and body malaise were reported without predominating complaint with similar incidence on placebo control

Contraindications:

There are no known contraindications



Myths about Herbal medicine



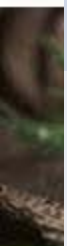
- Herbal medicine have no side effects
- Herbal products are safe
- Herbal medicines have no drug interactions
- Long term use equates to efficacy





Examples of Plant derived Anti-infective agents

Medicine	Common name of plant	Scientific name of plant source	Indication	Mechanism of action
Oseltamivir	Star anise	<i>Illicium verum</i>	Treatment and prevention of Influenza A and B	Inhibits neuraminidase
Artemisinin	Qinghousu	<i>Artemisia annua</i>	Treatment of chloroquine resistant <i>P. falciparum</i>	Inhibition of parasite Ca ⁺ dependent ATPase
Quinine	Cinchona bark	<i>Cinchona officinalis</i>	For severe malaria in combination with other anti-malarials	Inhibits hemozoin crystallization in heme detoxification, which facilitates aggregation of cytotoxic form



Other plant derived modern medicines

- Metformin from French lilac (*Galega officinalis*)
- Vincristine from periwinkle (*Vinca rosea*)
- Aspirin from bark of the white willow (*Salix alba*)
- Atropine from belladonna (*Atropa belladonna*)





Benefits of Herbal Medicine vs. synthetic medicine



Synergism



Artemesia annua herb -fresh extracts 6-18x times more efficacious against plasmodium parasite than the same amount of pure synthesized artemisinin



- five flavonoids produced by *A. annua* (*artemetin, casticin, chrysoplenetin, cirsilineol* and *chrysoplenol D*) potentiate the activity of artemisinin, although these compounds had no antiprotozoal activity of their own



IHM Algorithm of Herbal Medicine Drug Development

Survey of Traditional Healers on herbal medicines and folkloric used/ Literature review

Choose herbal medicines for a specific indication and screen for pharmacologic action

Agricultural Researches

- Cultivation
- Propagation
- Harvesting
- Post-harvest handling

Pharmaceutical Preparation Researches

- Plant material processing
- Crude drug preparation (Galenicals) and Quality control
- Drug formulation and manufacturing research
- Quality control of Pharmaceutical product

Preclinical researches

Ex. -Acute toxicity
-sub chronic/chronic toxicity
Safety pharmacology
Mutagenicity, clastogenicity
Heavy metal content
In vitro and in vivo bioassays
Isolation of active compound

Human Trials

Phase 1
Phase 2
Phase 3

Intellectual Property Rights/Herbal medicine registration with Phil FDA

The slide features several decorative images on the left side. At the top, there are green leafy herbs. Below that is a black scale with two pans, one containing colorful pills and the other containing fresh produce. Further down are images of yellow flowers, a close-up of a plant stem, and a yellow flower stalk. At the bottom left, there are green, rounded leaves.

Institute of Herbal Medicine, National Institutes of Health, UP Manila

...3. Develop safe, efficacious, and low-cost quality medicinal plant products derived from herbs for priority health problems....give jobs to Filipino farmers and promote self-reliance of Philippine Pharmaceutical Industry



Not all herbal preparations/ formulations are created equal

Potency or pharmacologic activity would differ depending on:

- Different plant parts
- Different varieties
- Type of extract
- How the plant was cultivated- type of soil, amount of water, sunlight, type of fertilizer



Evidence-based herbal medicine



Common name (scientific name)



Plant part

Evidence- RCT, animal studies



a. Common signs and symptoms associated with infectious diseases

- treat underlying cause, and provide other supportive management



b. Treatment of infectious diseases



Abdominal pain, Diarrhea

Plant	Evidence	Recommendation																		
<p>Tsaang gubat leaves (Carmona retusa)</p>	<p>-contains α-amyrin, β-amyrin and baurenol which has analgesic, anti-diarrheal and anti-spasmodic activity.</p> <p>RCT showed- safe and effective in patients with mild, moderate or severe gastrointestinal colic, as well as mild moderate and severe biliary colic and was equivalent to dicycloverine; pain relief within 30 min to 1.5 hours,</p>	<p>NIRPROMP Tsaang gubat formulation 250 mg tablet single dose</p> <table border="1" data-bbox="1134 592 1893 878"> <thead> <tr> <th rowspan="2"></th> <th colspan="2">Amount of chopped leaves needed</th> <th rowspan="2">Divide the decoction into 4 parts. Drink 1 part every 2 or 3 hours.</th> </tr> <tr> <th>If dried</th> <th>If fresh</th> </tr> </thead> <tbody> <tr> <td>Adult</td> <td>10 tbsp.</td> <td>12 tbsp.</td> <td></td> </tr> <tr> <td>7-12 years</td> <td>5 tbsp.</td> <td>6 tbsp.</td> <td></td> </tr> <tr> <td>2-6 years</td> <td>2-1/2 tbsp.</td> <td>3 tbsp.</td> <td></td> </tr> </tbody> </table> <p>Boil the needed amount of leaves in 2 glasses of water for 15 minutes or until one glass of the liquid is left. Cool and strain</p>		Amount of chopped leaves needed		Divide the decoction into 4 parts. Drink 1 part every 2 or 3 hours.	If dried	If fresh	Adult	10 tbsp.	12 tbsp.		7-12 years	5 tbsp.	6 tbsp.		2-6 years	2-1/2 tbsp.	3 tbsp.	
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Abdominal pain, Diarrhea

Plant	Evidence	Recommendation																			
<p>Guava leaves (<i>Psidium guajava</i>)</p>	<p>2 RCTs, Mexico and Cuba, animal studies for diarrhea; quercetin showed morphine-line inhibition of acetylcholine in ileum</p>	<table border="1"> <thead> <tr> <th></th> <th colspan="2">Amount of chopped leaves needed</th> <th rowspan="2">Same as Tsaang gubat</th> </tr> <tr> <th></th> <th>If dried</th> <th>If fresh</th> </tr> </thead> <tbody> <tr> <td>Adult</td> <td>6 tbsp.</td> <td>8 tbsp.</td> <td></td> </tr> <tr> <td>7-12 years</td> <td>3 tbsp.</td> <td>4 tbsp.</td> <td></td> </tr> <tr> <td>2-6 years</td> <td>1-1/2 tbsp.</td> <td>2 tbsp.</td> <td></td> </tr> </tbody> </table>		Amount of chopped leaves needed		Same as Tsaang gubat		If dried	If fresh	Adult	6 tbsp.	8 tbsp.		7-12 years	3 tbsp.	4 tbsp.		2-6 years	1-1/2 tbsp.	2 tbsp.	
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<p>Kaymito leaves (<i>Chrysophyllum cainito</i>)</p>	<p>Ex vivo and in vitro anti-diarrheal activity</p>	<table border="1"> <thead> <tr> <th></th> <th colspan="2">Amount of chopped leaves needed</th> <th rowspan="2">Same as Tsaang gubat</th> </tr> <tr> <th></th> <th>If dried</th> <th>If fresh</th> </tr> </thead> <tbody> <tr> <td>Adult</td> <td>8 tbsp.</td> <td>8 tbsp.</td> <td></td> </tr> <tr> <td>7-12 years</td> <td>4 tbsp.</td> <td>4 tbsp.</td> <td></td> </tr> <tr> <td>2-6 years</td> <td>1-1/2 tbsp.</td> <td>2 tbsp.</td> <td></td> </tr> </tbody> </table> <p>Preparation: same as Tsaang gubat</p>		Amount of chopped leaves needed		Same as Tsaang gubat		If dried	If fresh	Adult	8 tbsp.	8 tbsp.		7-12 years	4 tbsp.	4 tbsp.		2-6 years	1-1/2 tbsp.	2 tbsp.	
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DEPARTMENT OF HEALTH
100 Tablets
Carmona retusa (Vahl) Masamune
Tsaang Gubat leaf
250mg Tablet

Manufactured by:
Philippine Institute of Traditional
and Alternative Health Care (PITAHAC)
of the Department of Health
Davao Herbal Research and Processing Plant
2, P. Laurel Avenue, Begonia, Davao City

Anti-colic / Anti-spasmodic

Guava (*Psidium guajava*)



Caimito (*Chrysophyllum cainito*)



Cough

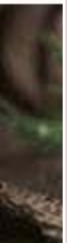


Plant	Evidence	Recommendation															
<p>Lagundi (<i>Vitex negundo</i>)</p>	<p>-active components: Chrysoplenol D is both a bronchodilator and an antihistamine; luteolin is an antihistamine; isoorientin is both an antihistamine and a leukotriene inhibitor; several iridoids have anti-inflammatory activity.</p> <p>Phase 1-3 RCT, adult and children cough of non-bacterial origin- ↓frequency of cough by 3rd day using lagundi vs placebo - ↓deceased by the 6th day; airflow/bronchodilation, improved ease of expectoration and disappearance of phlegm</p>	<p>NIRPROMP formulation of Lagundi tablet and syrup; Adult 300-600 mg tid-qid. Childn 7-12 yr 300 mg tid-qid. Ascof syr Adult 300-600 mg (5-10 mL) 1-2 tsp tid-qid. Childn 15 mg/kg/dose</p> <p style="text-align: right;">Divide the decoction in 3 parts. Take 1 part 3 times a day</p> <table border="1" data-bbox="1159 706 1593 963"> <thead> <tr> <th></th> <th colspan="2">Amount of chopped leaves needed</th> </tr> <tr> <th></th> <th>If dried</th> <th>If fresh</th> </tr> </thead> <tbody> <tr> <td>Adult</td> <td>4 tbsp</td> <td>6 tbsp</td> </tr> <tr> <td>7-12 yrs</td> <td>2 tbsp</td> <td>3 tbsp</td> </tr> <tr> <td>2-6 yrs</td> <td>1 tbsp</td> <td>1 ½ tbsp</td> </tr> </tbody> </table> <p>Boil the needed amount of leaves in 2 glasses of water for 15 minutes or until 1 glass of liquid is left. Cool and strain.</p>		Amount of chopped leaves needed			If dried	If fresh	Adult	4 tbsp	6 tbsp	7-12 yrs	2 tbsp	3 tbsp	2-6 yrs	1 tbsp	1 ½ tbsp
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Bacterial skin infections, abscesses (boils), impetigo,



Plant	Evidence	Recommendation
Guava leaves (<i>Psidium guajava</i>)	<p>-contains flavonoids- including quercetin and guaijavarin, with antibacterial activity.</p> <p>In vitro and in vivo studies show good activity against skin pathogens</p> <p>In vivo –non allergenic and non-irritating</p> <p>RCTs on guava creams and ointment for bacterial skin infections, in addition to cloxacillin vs cloxacillin alone, or vs mupirocin with good response</p> <p>To start- RCT on NIRPROMP formulation</p>	<p>Pound enough fresh material. Apply as poultice over the boil</p> <p>Or</p> <p>Boil 2-4 handfuls of leaves in a big pot of water for 5 minutes. Add enough water to make it lukewarm.</p> <p>Use to wash the affected area, vaginal wash or as bath</p>



Bacterial skin infections, abscesses (boils), impetigo,


Plant	Evidence	Recommendation
 <p>Gumamela flower bud (Hibiscus rosasinensis)</p>	<p>-in vitro antibacterial activity</p>	<p>Pound enough fresh material. Apply as poultice over the boil</p>



Fungal skin infections, tinea versicolor,

Plant	Evidence	Recommendation
Akapulco leaves lotion (Cassia/Senna alata)	<p>-active components: chrysophanol/chrysophanic acid, anthraquinones, rhein and aloe-emodine showed antifungal activity; causing leaks in cell wall</p> <p>Phase 1-3 RCT, vs Na thiosulfate for tinea versicolor, comparable for mycologic cure, disappearance of scaling and erythema</p> <p>Also vs Ketoconazole; >91% mycologic cure, comparable</p>	<p>NIRPROMP formulation Akapulco lotion; apply on affected area 2x/day for 2-4 weeks</p> <p>Pound enough fresh leaves and express the juice. Apply the juice on the affected skin 2 x/day for 2-4 weeks.</p>

Fungal skin infections, tinea versicolor,

Plant	Evidence	Recommendation
 Bawang cloves (<i>Allium sativa</i>)	<ul style="list-style-type: none">- ajoene, main antifungal , inhibitor of phospholipid biosynthesis- Good activity <i>C. albicans</i>, <i>Aspergillus</i>- Few RCTs on garlic cream on cutaneous fungal infections, comparable to terbinafine	Pound enough fresh cloves and express the juice. Apply the juice on affected skin 2 times/ day for 2-4 weeks.



Helminth infections

Plant	Evidence	Recommendation								
Ipil ipil seeds (<i>Leucena leucocephala</i>)	-contains cysteine proteases which damage the cuticle ; protease inhibitors which inhibit necessary proteins for formation of the cuticle RCTs, on seeds vs pyrantel pamoate or mebendazole; comparable for ascariasis and enterobius	Powder mature ipil-ipil seeds. Eat the seeds 2 hrs after supper. May mix with condensed milk <table border="1"><thead><tr><th></th><th>Amount of powdered seeds needed</th></tr></thead><tbody><tr><td>Adult</td><td>1 tbsp.</td></tr><tr><td>10-12 years</td><td>1/2 tbsp.</td></tr><tr><td>7-9 years</td><td>1/4 tbsp.</td></tr></tbody></table>		Amount of powdered seeds needed	Adult	1 tbsp.	10-12 years	1/2 tbsp.	7-9 years	1/4 tbsp.
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Helminth infections

Plant	Evidence	Recommendation										
<p>Niyog-nyogan kernels (Quisqualis indica)</p>	<p>-- Few RCTs on kernels for ascariasis vs pyrantel pamoate wit comparable efficacy</p>	<p>Eat the kernels 2 hrs after supper. Eat only the specified number. Do not eat the immature fruit</p> <p><u>Get mature and freshly opened fruits</u></p> <table border="1"> <thead> <tr> <th></th> <th>Number of kernels needed</th> </tr> </thead> <tbody> <tr> <td>Adult</td> <td>8-10</td> </tr> <tr> <td>1912 years</td> <td>6-7</td> </tr> <tr> <td>6-8 years</td> <td>5-6</td> </tr> <tr> <td>3-5 years</td> <td>4-5</td> </tr> </tbody> </table>		Number of kernels needed	Adult	8-10	1912 years	6-7	6-8 years	5-6	3-5 years	4-5
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Scabies




Plant	Evidence	Recommendation
Kakawati leaves (<i>Gliricidia sepium</i>)	-RCT ointment, vs sulfur ointment For scabies	NIRPROMP formulation Akapulco lotion; apply on affected area 2x/day for 2-4 weeks Pound enough fresh leaves and express the juice. Apply the juice on the affected skin 2 x/day for 2-4 weeks.



Scabies



Plant	Evidence	Recommendation
<p data-bbox="48 368 363 525">Kakawati leaves (<i>Gliricidia sepium</i>)</p> 	<p data-bbox="411 368 1089 464">-RCT ointment, vs sulfur ointment For scabies</p>	<p data-bbox="1147 368 1875 749">NIRPROMP formulation Akapulco lotion; apply on affected area 2x/day for 2-4 weeks Pound enough fresh leaves and express the juice. Apply the juice on the affected skin 2 x/day for 2-4 weeks.</p>
<p data-bbox="48 843 280 1058">Makabuhay leaves (<i>Tinospora rumphii</i>)</p>	<p data-bbox="411 843 1097 1229">-RCT of makabuhay vs permethrin pruritus, erythema, presence of primary lesions like papules, vesicles and pustules as well as the secondary lesions like excoriations, erosions and ulcerations were comparable</p>	<p data-bbox="1147 843 1837 1115">Express the juice by pounding enough fresh leaves. After bathing, apply juice on the affected skin 2 times a day for 3 consecutive days for 2 weeks</p>




Health Fraud Scams

Risks of scams

- Waste your money
- Can cause serious injury
- Can cause death
- Can delay potentially life saving diagnosis and medication that actually works
- Contain hidden drug ingredients that can be harmful; heavy metals; other drugs









Health Fraud Scams



Common types are claims related to:

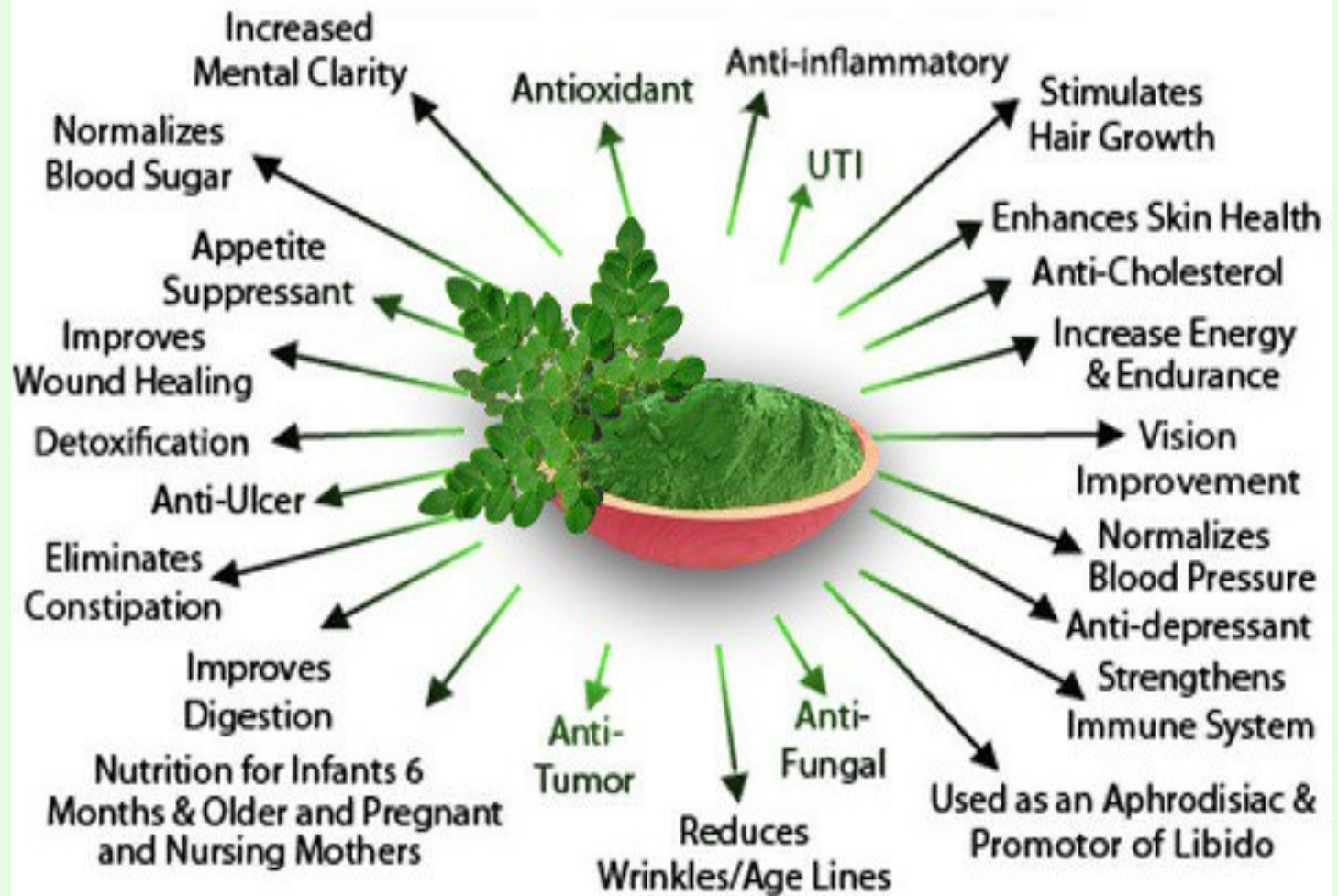
- 
- Cancer, diabetes and HIV/AIDS- these diseases require individualized treatment by physicians
 - Arthritis remedies fraud
 - Weight loss
 - Anti-aging
 - Memory loss
 - Sexual performance
- 
- 
- 



6 Tip offs to Rip offs

US FDA website

1. One product does it all, claims to cure a wide range of diseases



2. Personal Testimonials – it cured my diabetes; my tumors are gone - easy to invent

“Alzheimer’s Disease!!

My husband has Alzheimer. He began eating 1 tsp of Pure Emu Oil each day... Now in 22 days, he mowed the grass, cleaned out the garage, weeded the flower beds and took his morning walk.





Personal testimonials

- Can be completely made up or untrue
- Weakest form of scientific validity
- Benefits may be due to remission in disease
- Benefits may be due to earlier or concurrent use of approved medical treatment
- Rather than use of the fraudulent product
- Best evidence – randomized control trials

3. Quick fixes

- Lose 30 pounds in 30 days!
- Cures diabetes in minutes!



----- IT CAN KILL CANCER -----
"10000 times stronger killer of CANCER than Chemo-Therapy"



6 Tip-offs to Rip-offs

4. All "NATURAL"

- natural is not equivalent to safe
poisonous plants, mushrooms

USFDA has found numerous products which are "all natural" but are contaminated or have high doses of prescription drugs



ALOE YOUR MIRACLE DOCTOR

What Doctors Are Saying About Aloe...

An All Natural Miracle!

Click the Link Below for More Info ↓



6 Tip-offs to Rip-offs

5. “Miracle cure”

“New discovery”

“scientific breakthrough”

“secret ingredient”

- if it were a true breakthrough it would be widely reported on media and prescribed by health professionals

- not on print ads, pop-up ads on the internet or infomercials





Red Flags- favorite phrases used



- Miraculous cure!
- Quick fix
- Ancient remedy
- New discovery
- Scientific Breakthrough
- Secret ingredient
- Natural Cure
- Shrinks tumors
- Quick and painless cure
- No-risk money back guarantee
- No side effects

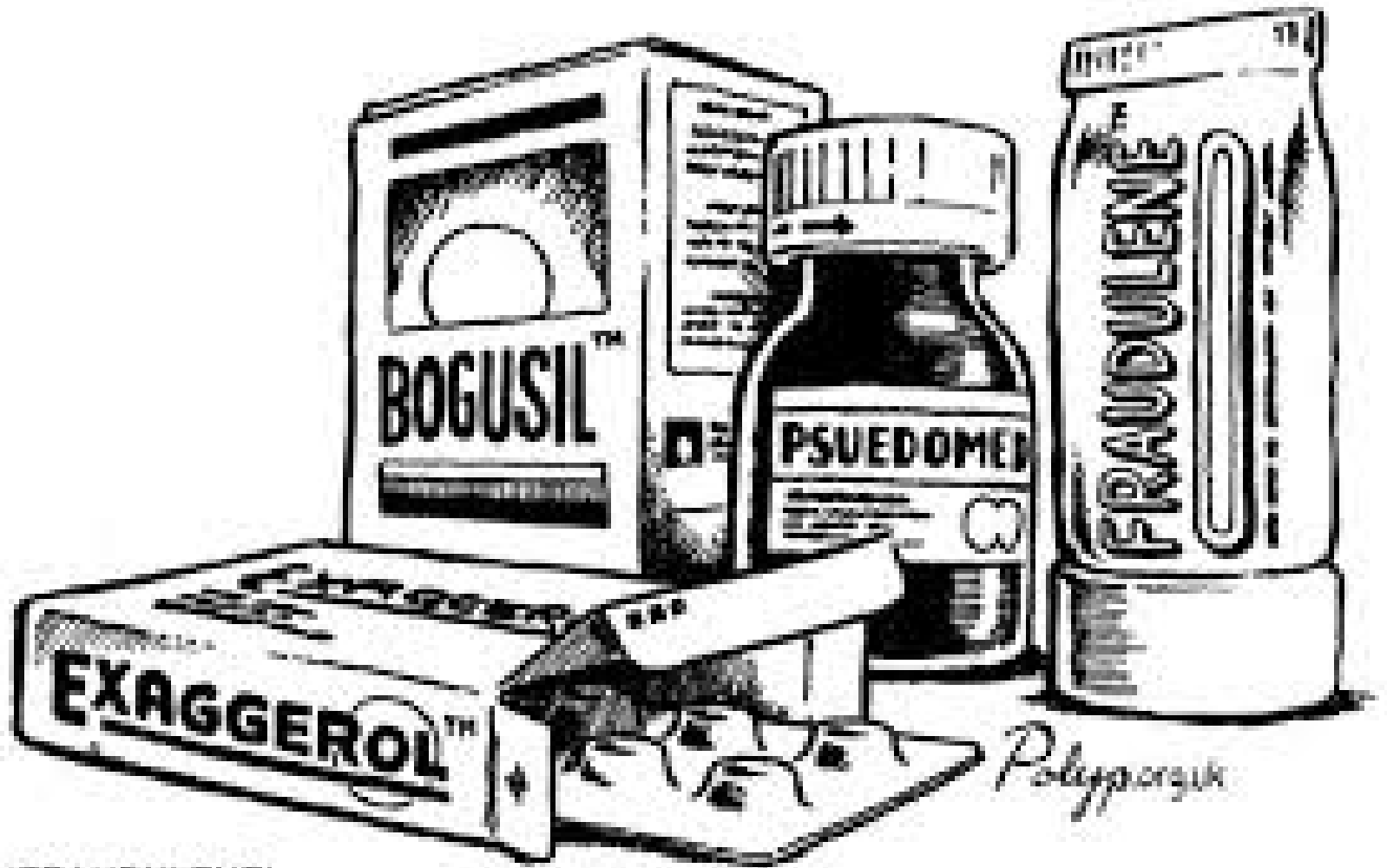
6 Tip-offs to Rip-offs

6. Conspiracy theories

“The pharmaceutical industry and the government are working together to hide information about a miracle cure.”

-always untrue and unfounded; distract consumers from common-sense questions about the so-called miracle cure.





'FRAUDULENE'





Take home messages

- Herbal medicines have been proven to be safe and effective
- Check the evidence; in vitro and in vivo data is not enough; RCT still best evidence
- Scams abound; watch out for the tip offs