Remedies for Fatigue and Enhancement of Physical Performance

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Selected Botanicals for Use to Enhance Energy, Stamina and Physical Performance and Reduce Fatigue

• Cultures the world over have long used plants to improve the stamina and energy required to survive and/or travel/work in adverse harsh environments-Andes Mountains, the Siberian regions, the deserts to harsh hot dry conditions.

• Cultures the world over have long used plants to improve performance and health.

• What can we learn from these plants? What happens when we take these plants out of context and out of their traditional ways in which they are prepared and used in modern commercial products today?
Selected Botanicals for Use to Enhance Energy and Stamina

From Asia:
• Ginseng (*Panax spp.*)
• Arctic Root or Rhodiola (*Rhodiola rosea*)
• Siberian Ginseng (*Eleutherococcus senticosus*)
• Green Tea and Black Tea (*Camellia sinensis*)
• Weiweizi (*Schisandra Chinensis*)

From South America:
• Yerba Mate (*Ilex paraguariensis*)
• Maca (*Lsidium meyenii*)
• Guarana (*Paullinia cupana*)
• Coca leaf (unprocessed)

From Africa:
• Hoodia (*Hoodia gordonii*)
• Yohimbe (*Pausinystalia yohimbe*)
• Khat (*Cathus edulis*)*

From Our Traditional Fruits and from new fruits and foods

Quality Control Issues

*Illegal in the USA
Asian Plants Used for Energy:
Green, White, Black Teas and Semi-Fermented

- Beverage used in China for the last 3000 years for energy and protects against cancer, cardiovascular disease, formation of kidney stones, infections, and obesity.
- Green tea leaves contain high contents of polyphenolic compounds (catechins) with epigallocatechin gallate, epigallocatechin, and gallocatechin being the major types.

Structures of the Target Compounds:

(+)-Catechin ($\text{C}_{15}\text{H}_{14}\text{O}_6$, MW: 290)
(-)-Gallocatechin gallate ($\text{C}_{22}\text{H}_{18}\text{O}_{11}$, MW: 442)
(-)-Epigallocatechin ($\text{C}_{15}\text{H}_{14}\text{O}_7$, MW: 306)

(-)-Catechin gallate ($\text{C}_{22}\text{H}_{18}\text{O}_{10}$, MW: 442)
(-)-Epicatechin gallate ($\text{C}_{22}\text{H}_{18}\text{O}_{11}$, MW: 458)
(-)-Epigallocatechin gallate ($\text{C}_{22}\text{H}_{18}\text{O}_{11}$, MW: 458)
Ginseng

- One of the most important herbs in eastern herbal medicine.
- Used for thousands of years to combat psychophysiological tiredness and as a tonic.
- Pharmacological activity: free radical scavenging activity, immunological effects, action on the central nerve system & metabolic activity, much more.
- The saponins (ginsenosides) are the main components and marker compounds inside.
Arctic root

Latin name: *Rhodiola Rosea*

Origin: Eastern Europe & Asia

The roots are used as a plant adaptogen like ginseng, decreasing depression, enhancing work performance, eliminating fatigue, and preventing high altitude sickness. The major natural products include: salidroside, rosavins and flavonoids.
Structures of Marker compounds in *Rhodiola rosea*

- **Salidroside**
- **Rosavin**
- **Rosin**
- **Rosavin**
HPLC profile of *Rhodiola Rosea*

- ? No rosavins
- ? No rosavins
- ? No rosavins
- ? No rosavins
Weiweizi

1. Latin name: *Schisandra Chinensis*
2. Origin: Northern China
3. Part as herbal medicine: fruits
5. A drug to treat nonicteric hepatitis
6. Active components: containing over 30 lignoid-type compounds. The major one is Schisandrol A.
Structure of major lignans in Schisandra

Schisandrin A

Schisandrol A

Schidandrin B

Schidandrol B
HPLC profile of Schisandra

Schisandrol A
Schisandrol B
Schisandrin A
Schisandrin B
HPLC Profile of Schisandra Berry and Extracts

- Total 1 berry sample and 10 powder extracts (9:1 extract or 9% lignans) were tested.
- Only the berry and two extracts match the profile of schisandra.
- This rapid assessment suggests a 28% approval rating.
Ilex paraguariensis (Yerba Mate)

- Brazil, Uruguay, Argentina, Paraguay
- As with tea, leaves are used to produce the mate, but unlike the tea, all leaves of this evergreen tree can be used- all leaves, twigs of small branches
- Leaves are dried on a frame over a fire, crushed into coarse pieces, sieved, shipped
Preparation of mate

• Crushed mate leaves are placed into the gourd (with or without sugar) and filled with hot water (80 C).

• After the mix steeps, and settles, a metal straw is inserted (bombilla) with a flattened end inserted into the ground.

• The flat end has holes to allow movement of the hot tea but to small to allow for leaves and plant material to enter, and one drinks it.

*http://www.fotosearch.com/photos-images/bombilla.html
Yerba mate: Medicinal properties

- Used as a stimulating beverage, since it contains caffeine (alkaloid)
- Diuretic and digestive (drink after meals)
- Rich in potassium and manganese
- Vitamins (thiamine and vitamin C)

*Chemical formula from Sigma Chemical Co. (www.sigma-aldrich.com)
Composite yerba mate

- Yerba mate is usually blended with aromatic plants to add flavor to mate.
- In this case, yerba mate is flavoured with dried lemong peels.

*Picture by the H.R. Juliani
Yerba mate as a herbal tea

• In this case, the yerba was blended with other aromatic plants and was packed in tea bags.

<table>
<thead>
<tr>
<th>Common name</th>
<th>Botanical name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yerba mate</td>
<td><em>Ilex paraguariensis</em></td>
</tr>
<tr>
<td>&quot;Carqueja&quot;</td>
<td><em>Baccharis sp</em></td>
</tr>
<tr>
<td>Lemon verbena &quot;Cedron&quot;</td>
<td><em>Aloysis citriodora</em></td>
</tr>
<tr>
<td>sweet fennel (&quot;Hinojo&quot;)*</td>
<td><em>Foeniculum vulgare</em></td>
</tr>
<tr>
<td>&quot;Incayuyo&quot;</td>
<td><em>Lippia integrifolia</em></td>
</tr>
<tr>
<td>Coriander*</td>
<td></td>
</tr>
<tr>
<td>Chamomile &quot;Manzanilla&quot;*</td>
<td><em>Matricaria chamomilla</em></td>
</tr>
<tr>
<td>Mint*</td>
<td><em>Mentha sp</em></td>
</tr>
<tr>
<td>&quot;Poleo&quot;</td>
<td><em>Lippia turbinata</em></td>
</tr>
</tbody>
</table>

*Introduced/cultivated species

*Picture by the H.R. Juliani
Yerba Mate is now becoming a hot product in the U.S.

- The company Guayaki is sourcing yerba mate from sustainable source in Paraguay
- Since a few years, is offering yerba mate products in the U.S. market place

http://www.guayaki.com/
Paullinia cupana (Sapindaceae) “Guarana”

- Native to Brazil
- After the fleshy fruit interiors are removed, drying the seeds, seeds roasted for 2-3 hrs and shaken to remove the seed coats.
- The seeds are used to generate different products (beverages, pills) as stimulant. Antifatigue Activity, weight loss.
- Seeds are rich in caffeine (3-8%) and tanins, this latter components provide the astringency of the seed.

*Picture from www.rain-tree.com/Plant-Images/guarana-pic.htm*
Guarana (*Paullinia cupana*): From the Amazon

- Mostly used orally as stimulant
- Contains:
  - Caffeine, theophylline, theobromine, tannins
- Uses:
  - Cellulites used in creams as extract
- Activities on skin:
  - Tonifying
  - Astringent
  - Lipolytic
  - Vasodilator
### Caffeine Content Comparison

#### Common Beverage Products

<table>
<thead>
<tr>
<th>Plant Beverage</th>
<th>Caffeine Content</th>
<th>Avg. caffeine in a 6 oz beverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guarana seed (<em>Paullinia cupana</em>)</td>
<td>4–8%</td>
<td>200–400 mg</td>
</tr>
<tr>
<td>Coffee beans (<em>Coffea sp</em>)</td>
<td>1–2.5%</td>
<td>100–250 mg</td>
</tr>
<tr>
<td>Yerba mate leaves</td>
<td>0.7–2%</td>
<td>50–100 mg</td>
</tr>
<tr>
<td>Black tea (<em>Camellia sinensis</em>)</td>
<td>2.5–4.5%</td>
<td>10–60 mg</td>
</tr>
<tr>
<td>Chocolate (Cacao seed)</td>
<td>0.25%</td>
<td>13 mg</td>
</tr>
</tbody>
</table>

- Table from http://www.rain-tree.com/guarana.htm
Some biological activities of caffeine*

• General metabolism increases, breathing and urination.
• Increases the gastric acid in the stomach, thus supporting the use of these plants as digestive.
• May increase blood pressure.
• Stimulates the brain and behavior, elevating neural activity in many parts of the brain by using 75-150 mg of caffeine.

*From http://www.xs4all.nl/~4david/index.html
Common bioactivities of the caffeine-containing plants from South America

Yerba mate, Guayusa and Guarana shared some popular uses/applications because of their high caffeine content:

• Appetite suppressants

• Aphrodisiac, probable due to the stimulant effect of caffeine.
Guarana is marketed as a natural stimulant and contains about 4% more caffeine than coffee as well as other natural stimulants.

Major source of revenue for many South American countries, especially Brazil.

Much of the profits generated from this natural product are from the exports to the United States.

In the United States Guarana is being used in products such as:

- Energy drinks & bars
- Dietary supplements
- Other herbal products
Does it work as claimed?
ESPINOLA ET AL, 1997

• Tested the affects of Guarana, Caffeine and Ginseng on laboratory mice after 10, 30, 100 & 200 days
• Anti-fatigue effects
  – Conducted a forced swimming test and determined the total elapsed swimming
  – Demonstrated that on the 100th and 200th day total elapsed time was not only greater than the control but the others as well
  – This proved that the stimulant affect from Guarana was not simply due to the high caffeine levels
  – The other compounds that may have contributed to the stimulant effects were theophylline and theobromine
• Memory acquisition test
  – Determines whether or not Guarana has the potential to reverse amnesic effects
  – The lab mice were given scopolamine in order to block memory retention
  – Were then placed in an apparatus that was divided into a light and dark section
  – If the mouse went into the dark compartment it would receive an electric shock
  – It was then removed and 24 hours later was submitted to the same test and the amount of time that it took for it to enter the dark compartment
  – Both acute and chronic treatment of caffeine and Guarana proved to enhance memory in the that time
HASKELL ET AL, 2007

• First study that tested the effects of Guarana on humans
  – 26 people were assessed for their cognitive effects and acute mood changes at four different doses
  – Found that Guarana
    • improves secondary memory performance
    • Increases alertness
    • Increase mood rating in humans
    • Lower doses actually yielded more positive effects than higher doses.
MAJHNENIC ET AL, 2007

- Tested Guarana’s preservative properties using different extraction methods
  - Prepared 10 g of Guarana seed and extracted using either: distilled water; methanol, 35% acetone or 60% ethanol as solvents
- Antifungal
  - Tested on *Aspegillus niger, Trichoderma viride and Penicillium cyclopium* because these molds are known for their food poisoning and spoiling properties
  - Were incubated until the control was completely covered
  - The diameters were than measured
  - The *Aspegillus niger* was inhibited with the best success using methanol at room temp.
• Antibacterial activity
  – 3 flasks were prepared with each extraction nutrient and a bacterial suspension
  – The bacterium used were *Escherichia coli*, *Bacillus cereus* and *Pseudomonas fluorescens*
  – The growth was measured optically at 3, 5, 8, 24 and 27 hours
  – Results prove that water is was not effective as a solvent; here organic solvents worked best
  – Proved to effectively work against both gram negative and gram positive bacteria.
• Antioxidant activity
  – This was first measured using both $\beta$-carotene and linoleic acid to determine the heat induced oxidation
  – The antioxidant activity was then measured by comparing the changes in absorbance
  – The next method used was determining the antioxidant activity by observing the ability to donate a hydrogen radical
  – The acceptor of this hydrogen radical is DPPH, which is a stable free radical and is turned into a free radical
  – This can again be measured by the change in absorbance
  – The results from all of these experiments demonstrated that an organic extract of Guarana showed high antioxidant activity.
MATTEI, R ET AL, 1998

• Tested the toxic effects of Guarana on laboratory animals
  – No adverse effects were seen in:
    • Urinary frequency, defecation, piloerection (goose bumps)
    • Alteration of motor skills, tremors, convolutions, muscle tone
    • Posture, ataxia, eyelid ptosis, reflexes, lacrimation and salivation
    • Sleeping time
    • Body weight
    • Mortality
    • Spontaneous motor activity
    • Pathological activity
REFERENCES


Hoodia (*Hoodia gordonii*, *H. currorri* and other *H.* spp.)

- Also called ghapp;
- Used by the traditional Xhomani bushman in the Kalahari Desert to suppress appetite and thirst.

Photos from: Van Wyk and Gericke, 2000. People’s Plants
Hoodia

“We are thankful that the traditional knowledge of our forefathers is acknowledged by national and international laws and policies.”


• A compound named P57 was discovered from this succulent.
• Appears to be more on the Market than exists in the wild.
• The exports from this region are high and it is unclear as to which *Hoodia* spp. is exported.
• Not all *Hoodia* spp are the same—chemically.
It is the juice/sap of the bitterghaap (*Hoodia gordonii*) that has been long used as an appetite and thirst suppressant. 

Questions to Consider

- Many cultures have used plants to improve the stamina and energy required to survive and/or travel/work in adverse harsh environments—Andes Mountains, the Siberian regions, the deserts to harsh hot dry conditions. What can we learn from these plants? What happens when we take these plants out of context and out of their traditional ways in which they are prepared and used?
A Selected List Herbs used to enhance sexual performance and fertility

- Yohimbe (*Pausinystalia yohimbe*)
- Ginkgo
- Ginseng (*Panax* spp.)
- *Cordyceps sinensis* - a fungus that parasitizes adult catepillars in Chuna. (fungus). Male sexual dysfunction
- Maca (*Lpidium meyenii*)
- Damiana (*Turnera diffusa*)
- Quebrachho

*This powerpoint in part comes from Tyler’s Herbs of Choice, Haworth Press and from Talbott and Hughes, The Health Professionals Guide to Dietary Supplements, 2007.*
Maca (*Lpidium meyenii*)

- Maca is a South American tuber that has only recently been highlighted as a product of interest in increasing the libido in both men and women (Balik and Lee, 2002).
- One of the few that is reported to increase the libido for both men and women and that is is reported to increase the libido and fertility independent of sexual hormone functioning and parameters of mood (Cicero et al. 2001, 2002; Gonzales et al. 2001b; Zheng et al. 2000).

*From: Talbott and Hughes, 2007*
Yohimbe (*Pausinystalia yohimbe*),
Fam. Rubiaceae

- Contains ca. 6% alkaloids, including yohimbine. Has CNS activity and blocks alpha-2-adrenergic receptors acting as an antagonist, theoretically increasing energy levels, and a vasodilator increasing blood flow to the genitals of both men and women (Riley, 1004).
- Should be ca. 7,000-10,000ppm yohimbe.
- Used as an aphrodisiac
- More specifically used to enhance male sexual performance.
- Safety and adulteration are major concerns

*From: Talbott and Hughes, 2007*
Ginkgo

• Reports of ginkgo benefitting persons suffering from erectile dysfunction are preliminary.
**Ginkgo** *(Ginkgo biloba L.)*

- **Latin name:** *Ginkgo Biloba L.*
- **Origin:** Northern China
- **Part used in herbal medicine:** leaves
- **Pharmacological activity:** Antiaging, Alzheimer's disease, asthma, depression, attention deficit disorder, blood clots, circulatory insufficiency, memory loss, respiratory disease, senility, stress, stroke, tinnitus and vascular disease.
- **Active components:** flavonoid glycosides and terpene lactones.
HPLC profiles of flavonoid glycosides in Ginkgo

Spiked with quercetin
**Damiana (Turnera diffusa)**

- Damiana is a traditional herbal aphrodisiac from Mexico, used to produce a mild euphoria, alleviating depression, induce relaxation, and decrease anxiety.
- An ingredient in the commercial product Argin-Max, which claims to improve sexual function in women.
- No clinical evidence to support claims.

*From: Talbott and Hughes, 2007*
Tribulus

• Tribulus terrestris is a weed that grows around the world and is commonly known as “Puncture Vine” or Caltrop fruit.
• Used to treat a wide variety of health problems including loss of libido (sex drive), impotence, infertility, edema, liver, kidney and heart problems.
• The major chemicals in tribulus include saponins with protodioscin as the dominated component.
HPLC profiles of *Tribulus* from different regions
Asparagus as a Medicinal

• A vegetable and a medicinal (Asian and European)

• In China, asparagus has been used in Traditional Chinese Medicine as a tonic, hair-growth stimulator and diuretic agent

• Asparagus root is also formally listed by the German Commission E as an approved medicinal product in the treatment of inflammatory diseases of the urinary tract, for prevention of kidney stones, and with a noted diuretic effect

• Extracts show activity as antifungal, diuretic, cytotoxic, antiviral, and molluscicide.
BioActive and Health Compounds in Asparagus

• Early work at Rutgers showed that asparagus could be a rich source of unique saponins which appeared promising against colon cancer in vitro studies (Food Science, Plant Biology, Cancer Institute);

• Our thrust is to examine a wide range of asparagus varieties to identify lines rich in rutin and saponins. Collaborative work by Garrison and Chin-breeding; Rosen, Ghai and ChiTang Food Science and our New Use Program, where we conduct the chemical analyses using HPLC and LC-MS.
Contents of protodioscin (LC/MS with SIM) and rutin (HPLC) in three asparagus breeding lines, A34, IIIJ, IID (T=top, M=mid., B=bottom)
Protodioscin \((C_{51}H_{84}O_{22})\), the major saponin in asparagus has attracted intense attention

- Protodioscin associated with cytotoxicity against several human cancer cell lines, especially selectively against one leukemia line (MOLT-4), one NSCLC line (A549/ATCC), two colon cancer lines (HCT-116 and SW-620) in a brand-new pattern when compared in the NCI’s anticancer drug screen database (13), anti-herpes simplex virus type 1 (HSV-1) activity (14), cytotoxic activity against Human Leukemia HL-60 cells (1, 5), cytotoxicity on cultured C6 glioma cells (15), xanthine oxidase inhibitors (16), antineoplastic activity (17, 18).
Protodioscin-con’t

• This compounds has also been associated with improving sexual desire and enhance erection*
• Protodioscin is the major component in a popular libido increasing dietary supplement-*Tribulus terrestris **

Questions to Consider

• Each culture and over time appear to have such aphrodisiacs. Does that mean they work?
• Are there natural products that are effective and safe that address issues of sexual performance, fertility?
• What plants are most commonly sold and marketed for these attributes in the USA as dietary supplements?
• Is there any scientific validity? If so, what is the mode of action?
• What are some of the adverse side effects of those plants and plant extracts and plant-mixtures that have been seen?
• Consider your role as a registered pharmacist- what can you discuss and recommend to your clients?
Dietary Supplements Used Against Fatigue and Physical Performance: Your Task is to Look each up; define each and then assess reality

• Many sports supplements commercially available
• Amino acids and protein supplements
• Androstenedione
• Branched-chain amino acids (BCAAs)
• Carnosine
• Cordyceps Mushroom (*Cordyceps sinensis*)
• Creatine
• DHEA (dehydroepiandrosterone)
Energy Supplements: Your Task is to Look each up; define each and then assess reality

- Bee Products
- Brewers Yeast (*Saccharomyces cerevisiae*)
- Ginseng
- Inosine
- NADH (Nicotinamide adenine dinucleotide)
- Rhodiola
- Sea Buckthorn (*Hippophae rhamnoides*)
- Vitamin B1 (Thiamin)
- Vitamin B2 (Riboflavin)
Sport Supplements, cont

- Glycerol
- HMB (b-Hydroxy-b-Methylbutyrate)
- Medium-Chain Triglycerides (MCTs)
- Protein (Casein, Whey, Soy, Collagen, Colostrum)
- Proteolytic Enzymes
- Ribose
- Tribulus (Tribulus terrestris)
### How To Answer This HW?

<table>
<thead>
<tr>
<th>The Dietary Supplement</th>
<th>Define it (Source-animal, Plant, fungi, synthetic, other)</th>
<th>Does it work?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>***=YES</td>
</tr>
<tr>
<td></td>
<td></td>
<td>**=some indication</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*=research support is weak</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0=Would not recommend as a pharmacist</td>
</tr>
</tbody>
</table>

- List each one
- Give definition
- Provide your assessment