

There has been renewed interest in herbal products. Two recent randomized trials have shown **Echinacea** has no effect in adults<sup>2</sup> or kids<sup>3</sup> for the common cold. For **ginseng** in the form of **COLD-FX** a trial in 2003-4 reported a modest effect for prevention of colds but no significant effect for treatment (see below).<sup>4,5</sup> In the Glucosamine/Chondroitin Arthritis Intervention Trial (**GAIT**),<sup>6</sup> **glucosamine and chondroitin sulfate** alone or in combination was not more effective than placebo or celecoxib in reducing pain in patients with osteoarthritis of the knee after 24 weeks or after 2 years of treatment. A subgroup of patients with moderate-to-severe pain appeared to benefit at 24 weeks but this effect was lost at 2 years. In addition, glucosamine and chondroitin sulfate alone or in combination showed no benefit over placebo in slowing loss of cartilage in knee osteoarthritis after 2 years. Even despite no direct evidence, **LAKOTA'S** (which contains glucosamine plus 8 other ingredients) continued marketing efforts has generated much interest in herbal remedies.

GENERIC/TRADE	POSSIBLE USE/LIMITED EVIDENCE	CONTRAINDICATIONS CI/ADVERSE EVENTS AE/ DRUG INTERACTIONS DI	INITIAL, USUAL & MAXIMUM DOSE	Canada COST
<p><b>GINSENG</b> ROOT EXTRACT/ <b>COLD-FX</b><sup>4,5,8,9</sup> ⓧ  200mg CVT-E002™ cap 200mg chewable tab <b>COLD-FX EXTRA</b> ⓧ  300mg CVT-E002™ Extra strength capsule (~95% Panax quinquefolium)</p> <p><b>FIRST SIGNS</b> ⓧ 4:1 root extract, zinc, ginger, Vit C, Echinacea, Valerian CBC Marketplace Video: <a href="https://www.cbc.ca/marketplace/m_episodes/2012-episodes/what-fx">https://www.cbc.ca/marketplace/m_episodes/2012-episodes/what-fx</a></p> <p><b>IMMUNITY-FX</b> Discontinued</p>	<p><b>Tx</b> at onset of cold/flu sx or help <b>prevent</b> cold/flu sx.</p> <ul style="list-style-type: none"> <li>•?? Activates macrophages/?? ↑ acquired immune response, only preliminary <u>not</u> conclusive evidence</li> <li>•Less people acquired at least 1 cold in the tx group, any difference did not reach significance</li> <li>•Differences were statistically significant in favour of treatment for those suffering recurring colds</li> <li>•Cold duration was ↓, however, cold or flu confirmation testing was not done.<sup>4</sup></li> </ul>	<p><b>CI</b> pregnancy &amp; lactation, kids&lt;12, allergy to herb, MAOIs/neuroleptics</p> <p><b>AE</b> Other ginseng product reports→ nervousness, excitation, diarrhea, insomnia, inability to concentrate, headache, HTN, epistaxis, allergies &amp; skin eruptions.</p> <p><b>DI</b> alcohol→may ↑ alcohol clearance from the body corticosteroids →herb may affect [steroid] estrogens/corticosteroids →herb may have additive effects reported furosemide →report of ↓ furosemide effect; heart &amp; BP meds→herb has negative chronotropic &amp; inotropic activity, &amp; possible ↓BP; hypoglycemics→herb may add to ↓BG MAOIs/ neuroleptics→ may inhibit reuptake of neurotransmitters &amp; ↑ tremor/ mania thus <b>CI</b> mood stabilizers→ herb may induce mania oral contraceptives→may interfere in effectiveness of sex hormone tx sedatives→ herb may potentiate/ antagonize sedative AE warfarin ↑↓ INR →may ↑ bleeds by itself or ↓ INR (Case reports<sup>10</sup>)</p>	<p><b>COLD-FX</b> (200mg caps) <b>Treatment:</b> Day 1→3caps TID Day 2→2 caps TID Day 3→1 caps TID then 1 or 2 caps daily until feeling better (7d~25 caps)</p> <p><b>Prevention:</b> 2 cap daily x 4 month (Canadian study<sup>4</sup>) 1 cap BID x 8-12wk (USA study<sup>22</sup>)</p> <p><b>COLD-FX EXTRA</b> (300mg caps) 1 cap BID x10 days at 1st sign of cold/flu</p>	<p>~\$25/ 60 caps</p> <p>\$55/ 150 caps</p> <p>\$25/ 45 caps</p>
<p><b>GLUCOSAMINE</b> ⓧ  500mg tablet/capsule 500mg chewable tablet 750mg caplet 1500mg/15mL oral liquid</p>	<p>Adjunctive tx for symptomatic relief of osteoarthritis.</p> <ul style="list-style-type: none"> <li>•May be efficacious in patients with moderate to severe pain<sup>6,11,12</sup>; however not recommended. ACR</li> <li>•Consider stopping IF no relief of pain after 3 months.</li> <li>•Currently better evidence with the <b>sulfate</b> Guide 12, Cochrane 18, <b>vs HCl salt</b>. Gait, 18, 19</li> </ul>	<p><b>CI</b> allergy (shellfish), lactation (Caution adulterants: pregnancy)</p> <p><b>AE</b> may cause GI AE such as diarrhea.</p> <p><b>DI</b> Hypoglycemics/insulin→does not significantly affect BG or ↑A1C<sup>13</sup>; may cause insulin resistance doxorubicin &amp; etoposide ?↑resistance</p>	<p><b>Usual Dose:</b> 500mg po TID <b>Maximum Dose:</b> 1500mg/day</p>	<p>\$22/ 360 tab</p>
<p><b>LAKOTA JOINT CARE FORMULA</b><sup>7</sup> ⓧ  Capsule contains: (Glucosamine Sulfate 150mg &amp; Glucosamine HCL 150mg, Boswellia extract, Collagen type 2, White Willow bark powder, Devil's Claw, Sarsaparilla, Yucca root, Feverfew leaf &amp; Bromelain)</p> <p><b>LAKOTA OSTEO</b> ⓧ  contains only Collagen type 2 &amp; L-proline</p>	<p>For arthritis pain &amp; to ↓ cartilage breakdown</p> <ul style="list-style-type: none"> <li>•?possibly effective; some evidence for glucosamine, but at higher doses; contains 8 other ingredients which lack outcome evidence.</li> <li>•Consider stopping IF not some relief of pain after 3 months therapy.</li> </ul>	<p><b>CI</b> pregnancy &amp; lactation, Reye's syndrome, kids &lt;12 or if allergy (herbs, shellfish or ASA)</p> <p><b>AE</b> Some GI irritation (caution if peptic ulcer)</p> <p><b>DI</b> Antihypertensives→Devil's Claw may further ↓ BP &amp; affect HR &amp; contractility ASA/Warfarin→White Willow Bark contains salicin &amp; therefore may have additive effect to ASA Feverfew→may inhibit platelet aggregation Bromelain →may add to anticoagulant/platelet effects (↑ bleeding risk) Digoxin→ Sarsaparilla may ↑digoxin absorption Hypoglycemics/insulin→glucosamine may cause insulin resistance Iron→may precipitate because of high tannin content</p>	<p><b>Initial Dose:</b> 4-6 capsules daily with food <b>Usual Dose:</b> 2-4 capsules daily to maintain benefit <b>Maximum Dose:</b> 8 capsules daily</p>	<p>\$27 /120 caps</p>

ⓧ=not Sask. formulary ⓧ=not NIHB A1C=glycated hemoglobin ACR=American College of Rheumatology AE=adverse effects ASA=aspirin BG=blood glucose BP=blood pressure CDN=Canadian CI=contraindication DI=drug interaction HIV=human immunodeficiency virus HR=heart rate HTN=hypertension hx=history INR=international Normalized Ratio MS=non significant pts=patients sx=symptoms TB=tuberculosis tx=treatment USA=United States of America

**Summary of the COLD-FX trial for PREVENTING colds** (American Ginseng: Panax quinquefolium)<sup>4,5</sup>

**BACKGROUND:** **COLD-FX** was studied in 323 adults age 18-65 with a hx of 2 colds in the previous year; **COLD-FX** was given 400mg(2 caps)/day vs placebo for ~4mths from Sep 2003 to April 2004 in Edmonton, Alberta. (Trial funded by CV Technologies<sup>Afexa</sup>; 4 of 6 authors have connection with company)

**Jackson Score:** sum of severity ratings (1=mild, 2=moderate, 3=severe) for 8 cold sx: sneezing, runny nose, nasal obstruction, sore throat, cough, headache, chilliness, & malaise.

**EXCLUSION:** vaccinated against influenza in the previous 6 months; if MS, TB, diabetes, cancer, lupus, HIV, heart/lung/renal/liver/neurological diseases; if on immunosuppressives, corticosteroids, warfarin, phenazine, pentobarbital, haloperidol or cyclosporine; & if pregnant, lactating or heavy smokers.

**RESULTS:** 55 vs 64% NS had 1 cold Jackson defined; 10 vs 22.8 % had ≥2 colds during the 4 months; & Duration of cold: 8.7 vs 11.1days (2.4 days less)

**LIMITATIONS:** ?active ingredient & mechanism; Jackson 2 vs 6 day score used thus only more severe illness were evaluated; not intention-to-treat analysis, symptom self-reporting & many excluded In adults, **COLD-FX** ↓d 0.25 colds/person in those who had ≥2 colds in the previous year. Further verification of this result is awaited.

**BOTTOM LINE:** ✓ Handwashing,<sup>14</sup> possibly gargling,<sup>15</sup> & the influenza vaccine<sup>16</sup> are proven to prevent upper respiratory infections. (other interventions lack evidence)<sup>17,20</sup>

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- Clegg et al . National Institutes of Health (NIH) Glucosamine/Chondroitin Arthritis Intervention Trial (**GAIT**) Clegg DO, et al. Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. N Engl J Med. 2006 Feb 23;354(8):795-808. CONCLUSIONS: Glucosamine and chondroitin sulfate alone or in combination did not reduce pain effectively in the overall group of patients with osteoarthritis of the knee. Exploratory analyses suggest that the combination of glucosamine and chondroitin sulfate may be effective in the subgroup of patients with moderate-to-severe knee pain. (The 1,538-pts GAIT trial compared the effectiveness & safety of these supplements taken alone and in combination in patients with painful knee osteoarthritis (WOMAC Pain 125-400 mm) treated at 16 academic medical centers in the U.S. The response rate for all patients was 60.1% in a placebo group, 64% in a glucosamine hydrochloride arm (500 mg TID); 65.4% in a chondroitin alone arm (400 mg TID); & 66.6% in a glucosamine-plus-chondroitin arm (500 mg/400mg TID) (p=0.09), according to a study results reported at the American College of Rheumatology meeting in San Diego Nov/05). <http://nccam.nih.gov/news/19972000/121100/ga.htm> (InfoPOEMs: Glucosamine HCl and chondroitin provides modest if any symptomatic benefit for patients with mild osteoarthritis of the knee. This study was well designed and avoided many of the design flaws of earlier studies. However, it had a high dropout rate (20%) and used a different glucosamine salt than most previous studies. In addition, post-hoc analysis suggests a large benefit in patients with moderate to severe pain. There were also consistent trends toward benefit for many secondary outcomes. (LOE = 1b) )
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