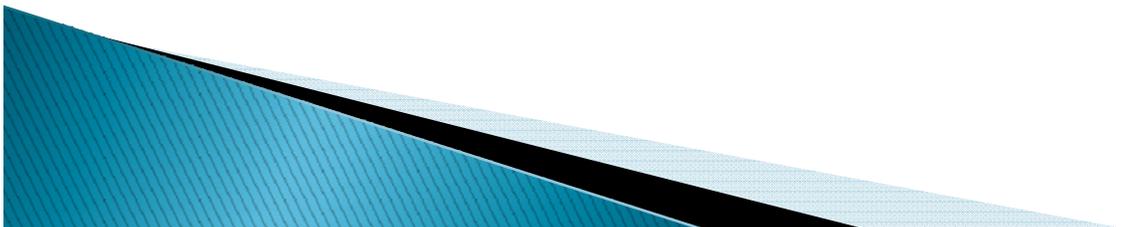


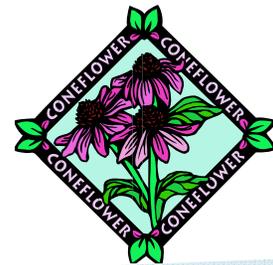
- ▶ This Telehealth presentation will be available for CNE's until September 18, 2016
www.health.utah.gov/diabetes/telehealth.archives
- ▶ Measures have been taken, by the Utah Department of Health, Bureau of Health Promotions, to ensure no conflict of interest in this activity.





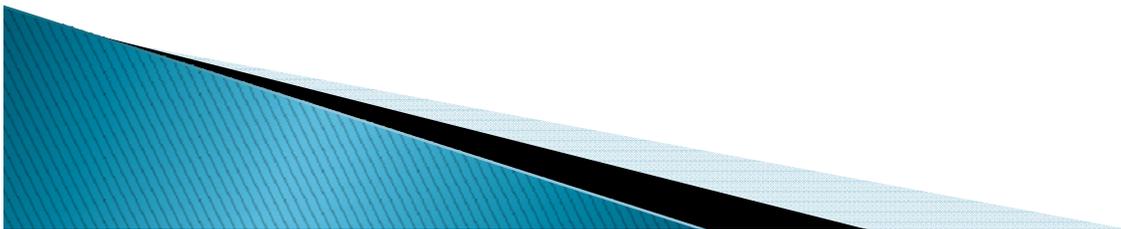
Dietary Supplements for Diabetes: Understanding the Issues

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Objectives

- ▶ List appropriate references to provide accurate information to patients.
- ▶ List popular supplements for diabetes.
- ▶ Discuss the theoretical mechanism of action, side effects, and drug interactions of popular supplements for diabetes.



Basic Definitions

- ▶ Dietary supplements
 - “... a product taken by mouth that contains a dietary ingredient intended to supplement the diet...”¹
- ▶ Dietary ingredients may include:
 - Vitamins
 - Minerals
 - Herbs or botanicals
 - Amino acids
 - Other substances



¹<http://cfsan.fda.gov/~dms/ds-oview.html>

Useful References



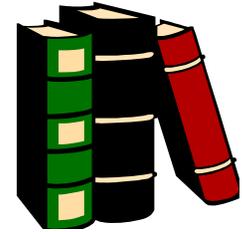
Patients

- ▶ NIH Office of Dietary Supplements
www.ods.od.nih.gov
- ▶ National Center for Complementary and Alternative Medicine: <http://nccam.nih.gov/>
- ▶ www.usp.org
- ▶ FDA 101: Dietary Supplements (www.fda.gov/consumer/updates/supplements080408.html)

Providers

- ▶ Natural standard:
www.naturalstandard.com
- ▶ Natural Medicines Comprehensive Database:
www.naturaldatabase.com
- ▶ NIH Office of Dietary Supplements
www.ods.od.nih.gov
- ▶ National Center for Complementary and Alternative Medicine:
<http://nccam.nih.gov/>

Useful References

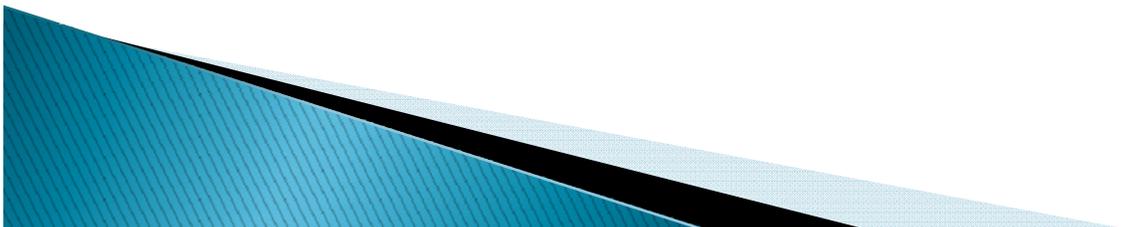


Patients

- ▶ Tips for the Savvy Supplement User
<http://www.cfsan.fda.gov/~dms/ds-savvy.html>
- ▶ Natural Medicines Comprehensive Database:
www.naturaldatabase.com
- ▶ McWhorter, LS: The ADA Guide to Herbs and Nutritional Supplements: What You Need to Know from Aloe to Zinc

Providers

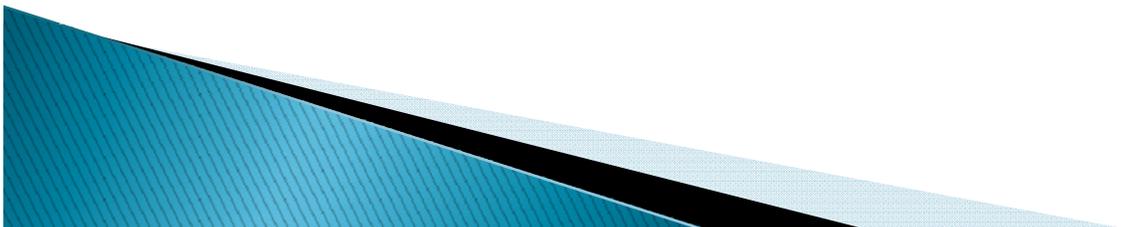
- ▶ www.usp.org
- ▶ FDA 101: Dietary Supplements (www.fda.gov/consumer/updates/supplements080408.html)
- ▶ McWhorter, LS: Complementary and Alternative Medicine (CAM) Supplement Use in People with Diabetes: A Clinician's Guide



Internet Information



- ▶ How to evaluate information on the internet
 - <http://ods.od.nih.gov/> (Click on “How to evaluate health information on the internet”)
 - Who is the site sponsor?
 - Purpose of the site – information or “link” to sell products?
 - Assessment of accuracy, quality, objectivity of information
 - Cautions in using the site
 - Example of “suspect” statements:
 - “These are not medicines so taking these herbs in larger amounts or over a long period of time is not harmful”
 - “There are no ingredients available for this product”
 - To “determine dose for a child or pet, divide the weight by 150 and that determines the fraction of the adult dose”



Reasons for Caution

- ▶ Adverse Effects^{1,2}
- ▶ Drug interactions^{3,4}
- ▶ Surgery precautions^{5,6}



1 Drug Safety 1997;17:342-56 2 N Engl J Med 2000;342:1686-92

3 JAMA 1998;280:1569-75 4 Lancet 2000;355:134-38

5 www.asahq.org/PublicEducation/herbal.html

6 AORN J 1999;69:173-5,177-8,180-3

Other Reasons for Caution

- ▶ Recalls¹
- ▶ Illegally sold treatments²
 - “Lowers your blood sugar naturally”
 - “Replaces your diabetes medicine”
- ▶ Confusing labeling (mislabeling) and information^{3,4}

¹ JAMA Internal Medicine 2013;April 15:1-3. doi: 10.1001/jamainternmed.2013.379

² FDA Consumer Health Information/ U.S. Food and Drug Administration. July 2013.
(www.fda.gov/consumer)

³ N Engl J Med 1998;339:827-30.

⁴ Consumer Reports September 2012 “10 surprising dangers of vitamins and supplements”

Other Facts

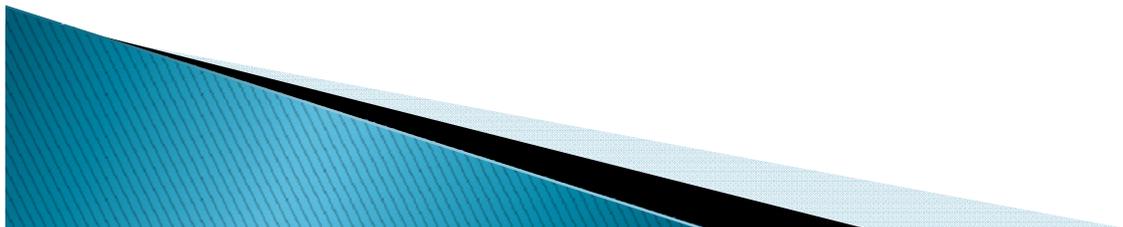
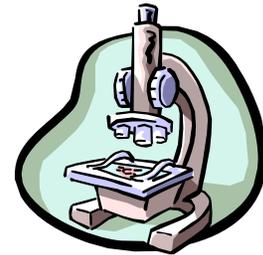
- ▶ Number of diabetes patients that take supplements varies (22% to 82%)¹⁻³
- ▶ Patients with longer diabetes duration, severity use supplements⁴

1 Clin Ther 2005;27:1847-58

2 Diabetes Care 2006;29:15-19

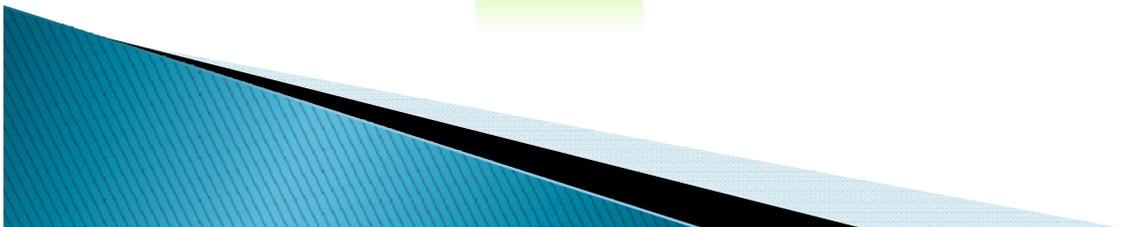
3 Complement Ther 2010;18:241-248

4 Diabetes Educ 2011;37:419-425.



Which Agents?

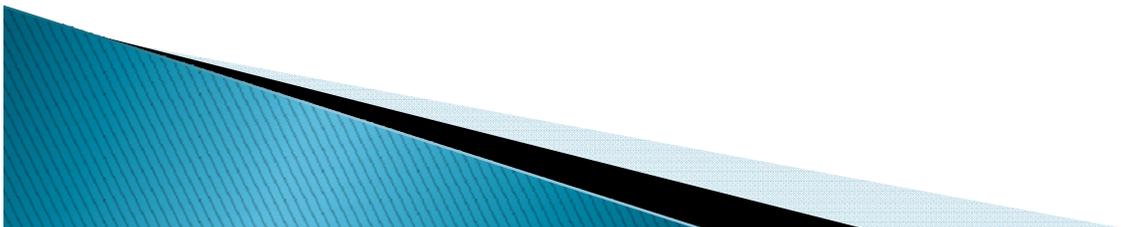
- ▶ Aloe vera
- ▶ Berberine
- ▶ Cinnamon
- ▶ Fenugreek
- ▶ Garlic
- ▶ Gymnema sylvestre
- ▶ Hibiscus
- ▶ Milk thistle
- ▶ Turmeric
- ▶ Non-botanicals





Aloe

- ▶ Background
 - Lily family
 - Dried leaf juice-laxative
 - Aloe gel-wounds, DM
- ▶ Mechanism
 - Fiber? Similar to glucomannan/guar
- ▶ Uses
 - Diabetes
- ▶ Side Effects
 - Leaf juice - hypokalemia; fluid or electrolyte problems
 - Exacerbate GI diseases (Crohn's)
- ▶ Drug Interactions
 - Leaf juice - ↓ K with steroids or diuretics
 - Sevoflurane - bleeding



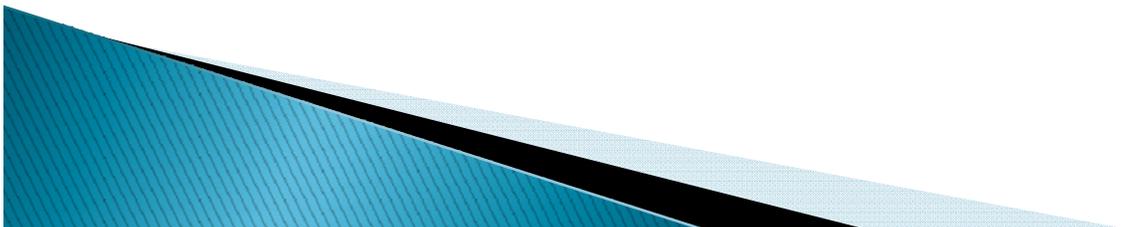
Aloe

Phytomedicine 1996;3:241-3

- SBPCT in 40 pts with new diagnosis (no meds)
- 42 days
- 1T aloe gel bid or pl
- ▶ FBG
 - AV: 250 to 142 mg/dl
 - PI: 251 to 257 mg/dl
 - P=0.01 vs PI
- ▶ Other parameters
 - TG ↓ in AV gp
 - TC: no change

Phytomedicine 1996;3:245-8

- SBCT in 40 pts on glibenclamide 5 mg bid
- 42 days
- 1T aloe gel bid + glb in half; others only on glb
- ▶ FBG
 - AV+ gl: 288 to 148 mg/dl
 - GI: 289 to 290 mg/dl
 - P=0.01 vs control
- ▶ Other parameters
 - TG ↓ in AV gp
 - TC: no change



Aloe – A 2 Month Trial

- Patients on glyburide, metformin
- N=30 on aloe 300 mg bid; N = 30 on PI

A1C	Baseline	Endpoint	p
Aloe	7.3%	6.6%	0.036
PI	7.3%	7.8%	

FBG	Baseline	Endpoint	p
Aloe	173	168	0.036
PI	185	191	

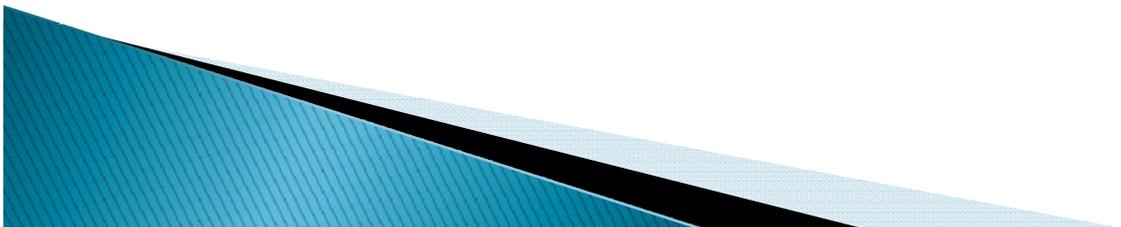
LDL	Baseline	Endpoint	p
Aloe	135	126	0.004
PI	123	101	

Planta Med 2012;78:311–316



Aloe – Summary

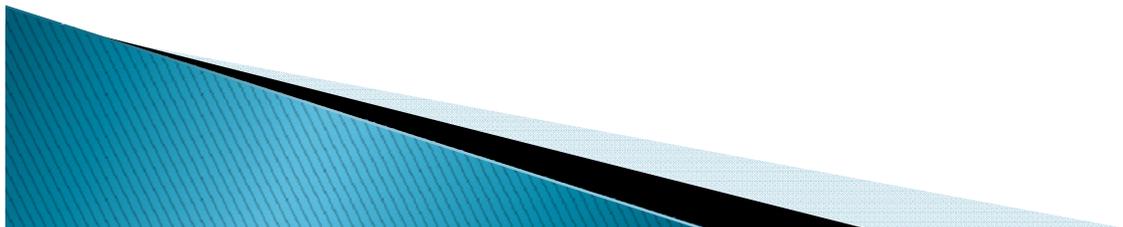
- ▶ Aloe uses: topical
- ▶ For DM: Aloe leaf gel
- ▶ Leaf juice: possible diarrhea, electrolyte depletion
- ▶ Highly used by Hispanic patients – sábila (aloe vera was second most used product in border city)
- ▶ Dose: 50–600 mg/d of aloe leaf gel
- ▶ Natural Standard: Grade “C”



Berberine

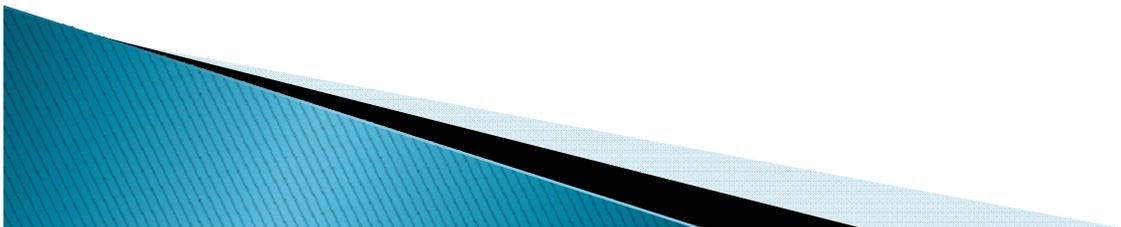


- ▶ *Coptis chinensis* (Huanglian or French)
- ▶ Isoquinoline alkaloid
 - Ingredient of goldenseal, goldthread, European barberry, tree tumeric
- ▶ Uses
 - Antibiotic, antidiarrheal
 - Discovered to have BG/lipid lowering effects
- ▶ Mechanism of action
 - ↑ glucose stimulated insulin secretion
 - Facilitates glut-4 transport systems
 - Alpha glucosidase inhibitor activity



Berberine

- ▶ Side effects
 - Constipation
 - Kernicterus; do not use in pregnancy!
- ▶ Drug interactions
 - Inhibits CYP 3A4 (↑ SDCs of CyA, certain statins)
 - P-glycoprotein modulator (caution with chemo, azoles, verapamil/diltiazem, some protease inhibitors)
 - Additive effects with diabetes drugs?



Berberine

- ▶ RDBPCT in 116 new T2DM with dyslipidemia
- ▶ Given 0.5 gm bid or placebo x 3 months

	Ber	Pl	p
FPG BL	126 mg/dL	122 mg/dL	
FPG End	101	115	<0.0001
PPG BL	216 mg/dL	220 mg/dL	
PPG End	160	198	<0.0001
A1C BL	7.5%	7.6%	
A1C End	6.6	7.3	<0.0001

Berberine

	Ber	Pl	p
Wt BL	68.7 kg	71.8 kg	
Wt End	66.4	70.5	<0.001
TC BL	204 mg/dL	207 mg/dL	
TC End	167	203	<0.0001
TG BL	221 mg/dL	174 mg/dL	
TG End	142	181	0.001
LDL BL	124	130	
LDL End	98	125	<0.0001

Berberine

- ▶ RCT in 2 groups of T2DM pts – newly diagnosed and poorly controlled (Ber or Met; Ber + other agents)
- ▶ Gp A: 0.5 gm tid or metformin 500 mg tid x 3 months (N=36)

	Ber	Met
FPG BL	191 mg/dL	179 mg/dL
FPG End	124 p<0.01	129 p<0.01
PPG BL	357 mg/dL	370 mg/dL
PPG End	199 p<0.01	232 p<0.01
A1C BL	9.5%	9.2%
A1C End	7.5 p<0.01	7.7 p<0.01

e.g., berberine = metformin

Berberine

- ▶ Gp B: 0.5 gm tid + other agents (insulin or orals) x 3 months
- ▶ N=45

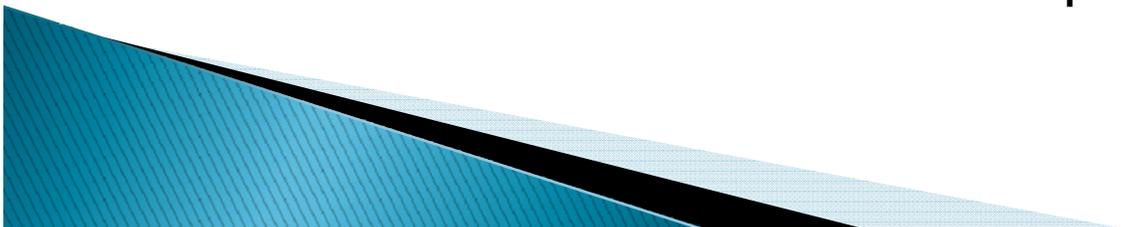
Ber + Other Agents

FPG BL	173 mg/dL
FPG End	137 p<0.001
PPG BL	266 mg/dL
PPG End	194 p<0.001
A1C BL	8.1%
A1C End	7.3 p<0.001

Berberine – Summary



- ▶ Alkaloid contained in several different plants
- ▶ Has insulin sensitizing and AGI activity
- ▶ May ↑ SDCs of drugs metabolized by CYP 3A4 (CyA, some statins, CCBs, etc.)
- ▶ Constipation is main side effect
- ▶ Should not be used in pregnancy
- ▶ Has shown benefit on A1C, FPG, PPG, lipids, weight, and even BP
- ▶ Being compared to conventional drugs and has similar effects (metformin, TZDs) on lowering A1C but also decreased lipids



Cinnamon

- ▶ Background
 - Spice
- ▶ Mechanism
 - Procyanidin type-A polymers may enhance insulin action (cinnamaldehyde)
 - In vitro increases glucose uptake, glycogen synthesis
 - Increases phosphorylation of insulin receptor
 - May aid in triggering insulin cascade system
 - May increase PPAR activity; AG inhibition
- ▶ Uses
 - Diabetes
 - GI upset
- ▶ Side Effects
 - Topical allergic reactions
 - Bleeding?
- ▶ Drug Interactions
 - Blood-thinners?
 - Additive hypoglycemic activity?



Cinnamon: Studies

Meta analysis of 5 RPCT clinical trials¹ (N=282)

- Follow-up: 5.7 to 16 weeks
- Dose – 1 to 6 g/day of cinnamon (cassia)
- ▶ No significant decrease in mean A1C but:¹
 - FBG: - 17 mg/dL
 - TC: - 9.6 mg/dL
 - LDL: - 4.7 mg/dL
 - TGs: - 28.4 mg/dL
 - HDL: + 1.6 mg/dL
- ▶ Under-powered (may need 1200-7000 persons)

¹ Diabetes Care 2008;31:41-42



Cinnamon: Studies

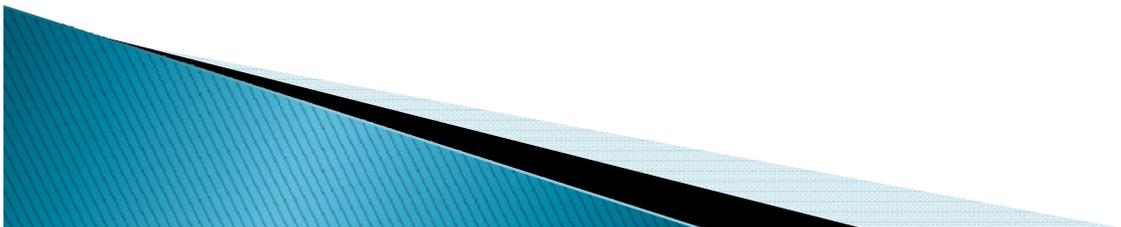
2009 study in 102 T2DM¹

- ▶ A1C ↓ 0.83% from baseline after 3 months

2010 study in 58 T2DM²

- ▶ A1C ↓ 0.36% from baseline after 3 months (2 gm/day) vs 0.12% increase in PI (p=0.002)

¹ ²JABFM 2009;22:507-512 ² Diab Med 2010;27:1159-67



Cinnamon: New Meta Analysis

10 RCTs in 543 T2DM¹

- ▶ FPG ↓ significantly: -24.6 mg/dL (95% CI -40.5 to -8.7)
- ▶ TC ↓ significantly: -15.6 mg/dL (95% CI -29.8 to -1.44)
- ▶ LDL ↓ significantly: -9.4 mg/dL (95% CI -17.2 to -1.6)
- ▶ TG ↓ significantly: -29.6 mg/dL (95% CI -48.3 to -10.9)
- ▶ A1C ↓ NS: -0.16% (95% CI -0.39 to 0.02)

Comparison with conventional treatment:

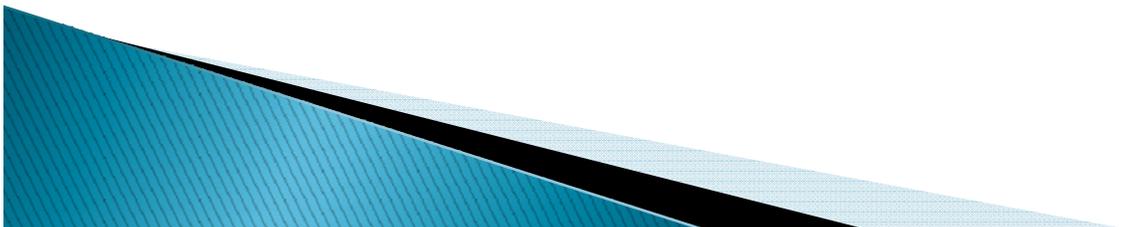
FPG

- ▶ ↓ -25 mg/dL
- ▶ ↓ with metformin: -58 mg/dL
- ▶ ↓ with gliptin: -16 to 21 mg/dL

TG

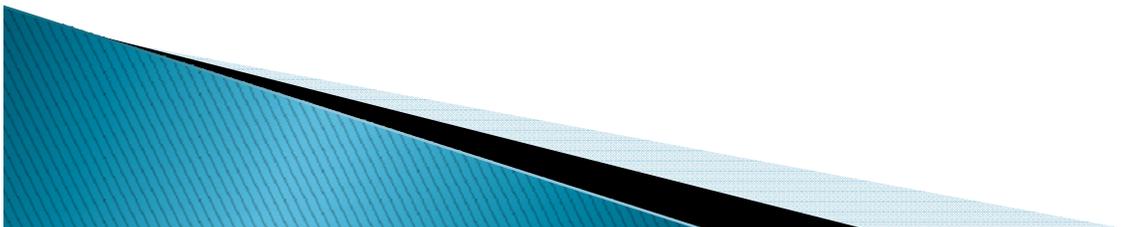
- ▶ ↓ -30 mg/dL
- ▶ ↓ with fibrate 50 mg/dL

¹ Ann Fam Med 2013;11:452-459



Cinnamon – Summary

- ▶ Cinnamon decreases fasting glucose and lipids
- ▶ Inconsistent A1C benefit
- ▶ Active ingredient: Procyanidin type-A polymers (Cinnamaldehyde)
- ▶ May enhance insulin sensitivity
- ▶ May also delay gastric emptying; decrease PPG
- ▶ Side effects are benign; no known interactions
 - Caution with concomitant anticoagulants
- ▶ The dose is 1–6 g/day
- ▶ Most appropriate form: aqueous form?
- ▶ Natural Standard: Grade “C”

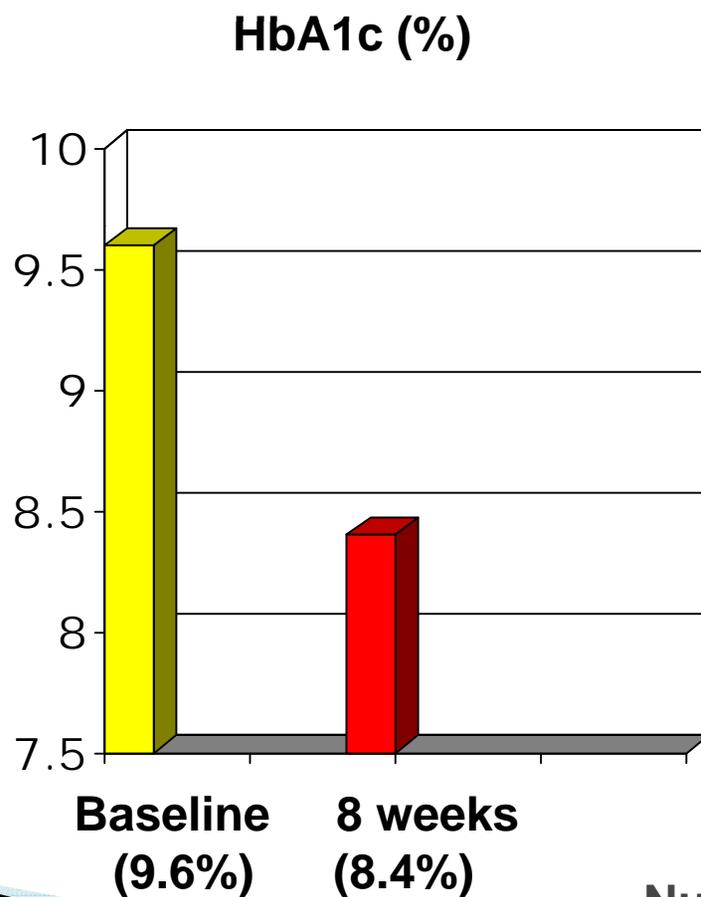


Fenugreek (*Trigonella foenumgraecum*)

- ▶ Background
 - Saponins/alkaloids
coumarins/glycosides
- ▶ Mechanism
 - Fiber (guar gum)
 - Delayed gastric emptying;
inhibits glucose transport
 - 4-hydroxy-isoleucine
stimulates insulin secretion
- ▶ Uses
 - DM/hyperlipidemia
 - Galactagogue
- ▶ Side effects
 - GI/hypersensitivity
 - Dermatitis
 - Uterotonic
 - “Sweet” urine
- ▶ Drug interactions
 - Hypoglycemics
 - Anticoagulants (boldo
+ fenugreek)



Fenugreek – Studies



- N = 60 (type 2 DM)
- 25 gm/d fenugreek seed powder (2 equal doses/with meals)
- FBG:
 - Baseline: 151 mg/dl
 - 24 week: 112 mg/dl
- OGTT improved from baseline

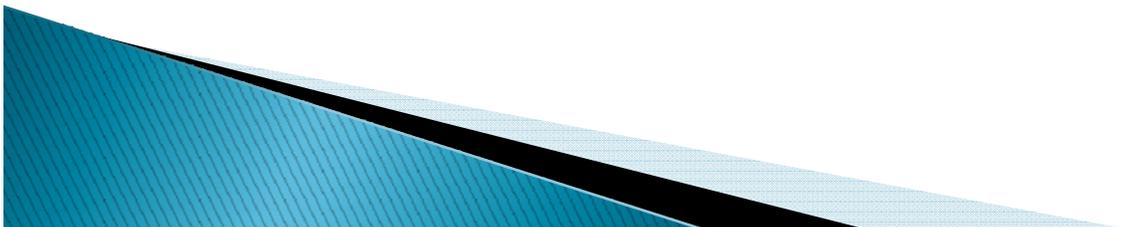
Nutr Res 1996;16:1331-9

Fenugreek – Another Study

- ▶ FG or PI added to SU in T2DM x 12 weeks
- ▶ N=46 (FG); N=23 (PI); 100.8 gm/day

FPG (mg/dL)	BL	End	P
FG	155	122	< 0.05
PI	152	151	
PPG (mg/dL)	BL	End	P
FG	240	170	< 0.01
PI	242	216	
A1C (%)	BL	End	P
FG	8.02	6.56	< 0.05
PI	8.6	8.2	

Chin J Integr Med 2008;14:56–60



Fenugreek – Summary

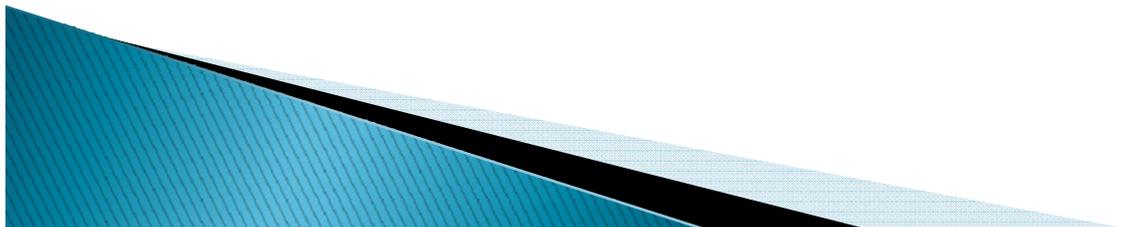
- ▶ ↓ A1C, FBG, PPG, lipids (in some studies)
- ▶ Studies are mostly short-term with small numbers
- ▶ Study design is faulty
- ▶ Allergies – caution with Leguminosae family
- ▶ Hypoglycemia, bleeding, “maple syrup” urine odor
- ▶ Do not use during pregnancy
- ▶ Caution if on other DM meds, anti-platelets, hormones, steroids, MAOIs
- ▶ Take with meals (bitter)
- ▶ Dose: 10–15 gm/day (defatted fenugreek)
- ▶ Natural Standard: Grade “C”



Garlic



- ▶ Alliin must be converted to allicin by alliinase
- ▶ Ajoene formed by acid catalyzed reaction of 2 allicin molecules – ↓ activity of factors needed for lipid synthesis
- ▶ ADRs – bleeding, GI
- ▶ Drug interactions
 - Bleeding if combined with antiplatelets
 - Induces CYP3A4 (↓ efficacy of OCPs, some HIV meds, chemo, CyA)
 - ↓ INH levels 65%
- ▶ Used for HTN, hyperlipidemia, diabetes



Effects of Garlic on Uncontrolled HTN: 2010 Analysis

- ▶ N=50¹
 - 12-wk DB parallel randomized placebo CT
 - 960 mg/day of AGE or placebo
 - On BP meds(hypertensive or normotensive)
 - Divided into SBP > 140 mm Hg or less
- ▶ Results
 - ↓ 10.4 mm Hg for SBP > 140 in garlic group vs PL (p=0.0361)
 - 151.2 to 136 mm Hg after 12 wks in AGE
 - 152.8 to 145.4 mm Hg after 12 wks in PL
 - No difference in DBP
- ▶ BUT...small number of subjects

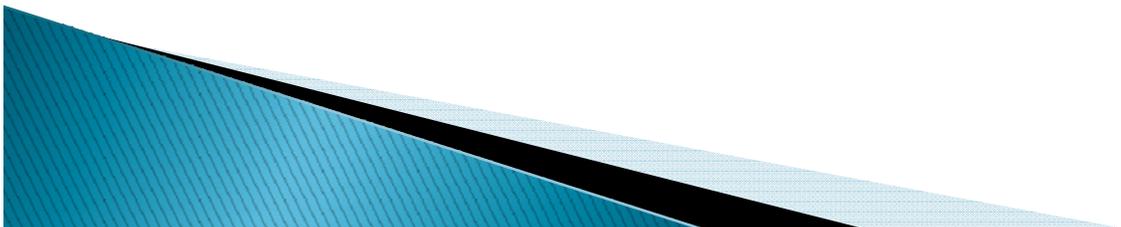
¹Maturitas 2010;67:144-150



Garlic: Meta analysis of RDBPCT for Lipids

- ▶ 24 studies included
- ▶ Results (compared to placebo)
 - TC: ↓ 10.9 mg/dL (p=0.001)
 - TG: ↓ 11.5 mg/dL (p<0.001)
- ▶ Effects greater in subjects with long-term use and higher baseline TC levels
- ▶ Aged garlic extract and garlic powder more effective in reducing TC levels; garlic oil more effective for TGs
- ▶ Other lipids not affected: LDL, HDL

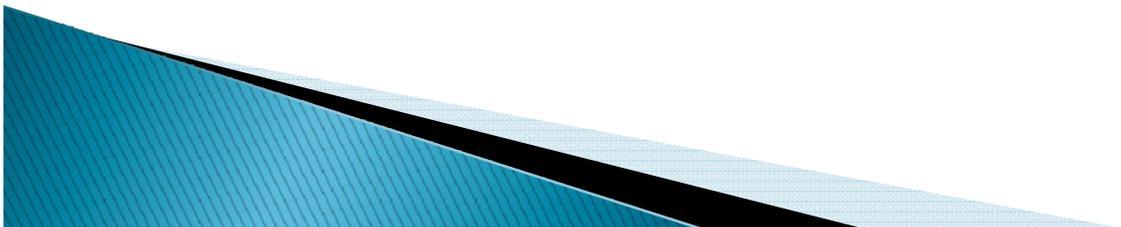
J Sci Food Agric 2012; DOI 10.1002/jsfa.5557



Garlic for Diabetes

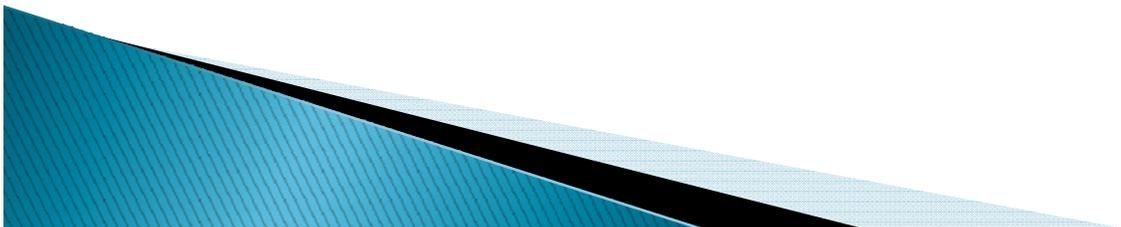
- ▶ Open label 12 week study
- ▶ N=30 on metformin + garlic; N=30 on metformin only
- ▶ Results (compared to baseline)
 - A1C: ↓ 7.48 to 7.05% (NS)
 - FBG: ↓ 157 to 121 mg/dL ($p < 0.001$)
 - PPG: ↓ 188 to 141 mg/dL ($p < 0.001$)
 - LDL: ↓ 188 to 179 mg/dL ($p < 0.05$)

Diabetes Metab Syndr Obes 2013;6:49–56



Garlic – Summary

- ▶ Historically used for BP, lipid control
- ▶ Emerging studies for diabetes
 - May increase serum insulin, improve hepatic glycogen storage
 - May inhibit formation of advanced glycation end products
- ▶ For lipids, BP: 600 to 1200 mg/day
- ▶ For diabetes, 500 to 900 mg/day
- ▶ Consider adverse effects of bleeding
- ▶ Consider drug interactions – may decrease serum concentrations of important drugs (HIV meds, OCPs)



Gymnema Sylvestre

- ▶ Background
 - “Gurmar”
 - Gymnemic acids, gymnemosides
- ▶ Mechanism
 - Blocks “sweetness” taste/cravings
 - Binds to intestinal receptors and impairs glucose absorption
 - ↑ activity of enzymes involved in glucose absorption
- ▶ Mechanism (cont’d)
 - ↑ cell permeability of insulin
 - Stimulates beta cell function
- ▶ Uses
 - Diabetes
- ▶ Side effects
 - Hypoglycemia
- ▶ Drug interactions
 - Potential additive effects with hypoglycemics



Gymnema – Studies

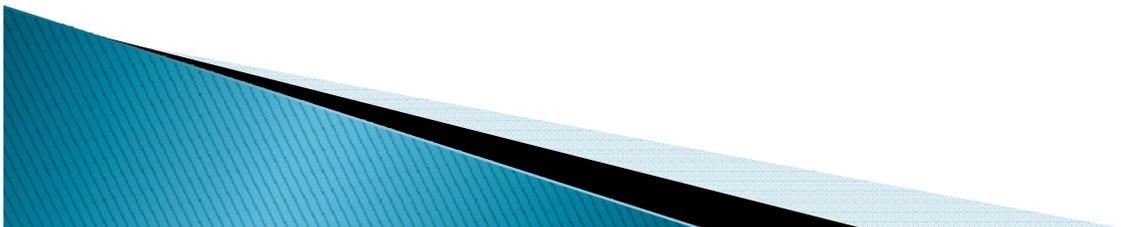
- ▶ N = 22 patients with type 2 DM
- ▶ Gymnema 400 mg/d x 18–20 mo + sulfonylurea
- ▶ N = 25 controls
- ▶ HbA1c decrease: 11.9% to 8.5%
- ▶ FBG ↓: 174 to 124 mg/dl (after 18–20 mo; $p < 0.001$)
- ▶ N = 5 D/C sulfonylurea

Gymnema – Studies

- ▶ N = 39 on Gymnema and 19 on PI (type 2 DM)
- ▶ Gymnema 250 mg bid or PI x 3 months
- ▶ A1C decrease: 9.6% to 8.6% (significant but p value stated as < 0.000)
- ▶ FBG ↓: 189 to 163 mg/dL (p < 0.005)
- ▶ PPG ↓: 275 to 216 mg/dL (p stated as < 0.000)
- ▶ SBP ↓: 139 to 132 mm Hg (p < 0.005)

Gymnema – Summary

- ▶ Animal research prolific
- ▶ New emerging human research; new research with standardized products
- ▶ Dose: 200-600 mg/d
- ▶ Better not to start with combo agents
- ▶ May cause hypoglycemia
- ▶ Do not use without medical supervision
- ▶ May have to adjust secretagogue doses
- ▶ Natural Standard: Grade “B” (T1 and T2 DM)





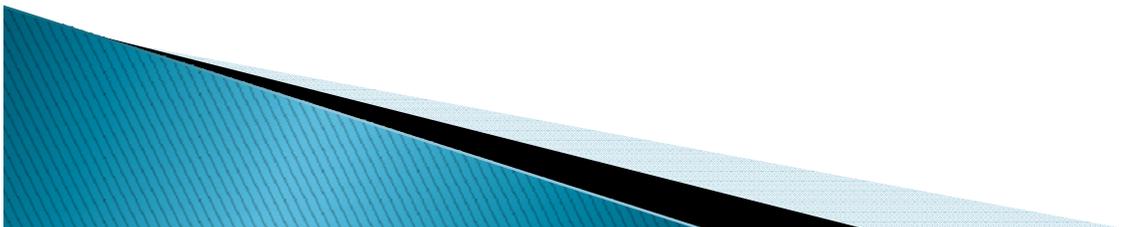
Hibiscus (*Hibiscus sabdariffa* L.)

- ▶ “Agua de Jamaica” “Karkade” “Sour tea”
- ▶ Part used: calyx
- ▶ Uses: BP, liver disease, fever
- ▶ Active ingredients: anthocyanins
 - Delphinidin-3-sambubiosides
 - Cyanidin-3-sambubiosides
- ▶ Mechanism:
 - ACE inhibition
 - Vasorelaxation (CCB-like effect?)
 - Diuretic



Hibiscus (*Hibiscus sabdariffa* L.)

- ▶ Adverse effects
 - Bitter taste
 - Hepatic, renal function assessed in short-term trials and no problems reported
- ▶ Drug interactions
 - ↓ elimination half-life of APAP
 - ↓ elimination of diclofenac
 - Additive effects in combo with ACE Is



Hibiscus: Effects on BP in T2DM

- ▶ DBRCT in 53 T2DM persons with mild HTN (<160/100 mm Hg; not on BP meds)
 - N=27 on Sour Tea N=26 on Black Tea x 1 mo
 - Given one tea sachet and added 240 mL of boiling water (allowed to steep 20–30 min)

▶ SBP Results (mm Hg)

Tea	BL	4 weeks	P (vs BL)
ST	134.4	112.7	<0.001
BT	118.6	127.3	0.002

P < 0.001 for ST vs BT

Results not significant for DBP

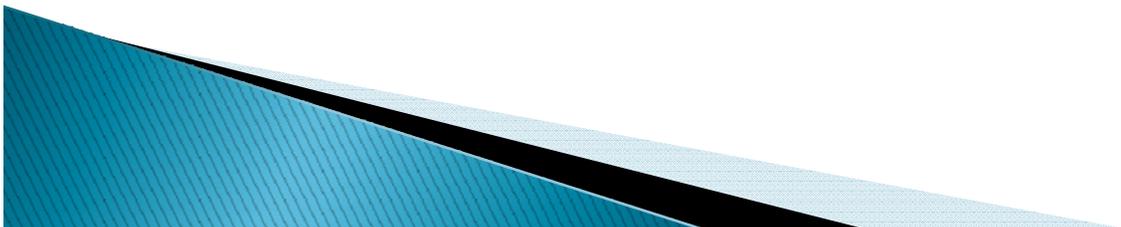
Hibiscus: Effects on Lipids in T2DM

- ▶ DBRCT in 53 T2DM persons (not on antilipidemics)
 - N=27 on Sour Tea; N=26 on Black Tea x 1 mo
 - Given one tea sachet and added 240 mL of boiling water (allowed to steep 20–30 min)
- ▶ Lipid Results (mg/dL)

	Sour Tea		Black Tea		P (ST vs BT)
	BL	4 wks	BL	4 wks	
LDL	137.5	128.5	124.9	130.1	0.003
HDL	48.2	56.1	46.2	52.01	0.6
TG	246.1	209.2	247.5	247.8	0.09

Hibiscus – Summary

- ▶ Commonly used product
- ▶ Studies evaluating use lack optimal design
- ▶ Best study is use in mild HTN; better effect on SBP than DBP
- ▶ Has been compared to ACEIs (less effective)
- ▶ Studies assessing glucose control are emerging
- ▶ Studies don't do a good job of reporting SEs
- ▶ More study is needed



Milk Thistle



▶ Background

- Aster family (daisies, thistles)
- Silymarin

▶ Mechanism

- Inhibits hepatotoxin binding
- Antioxidant
- Restores MDA levels (oxidative stress marker)
- May benefit pts with insulin resistance secondary to hepatic damage

▶ Uses

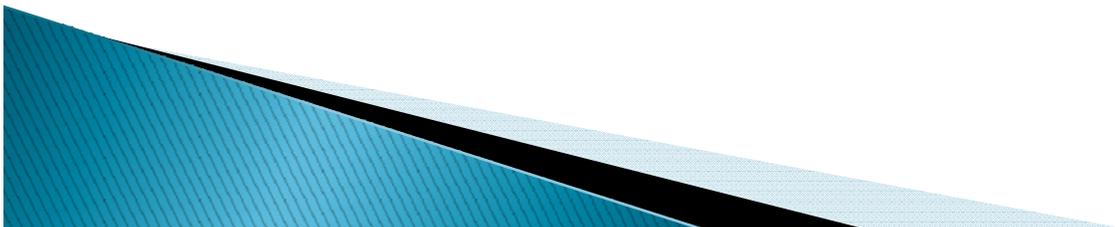
- Hepatic disorders
- Hepatoprotectant
- Decrease insulin resistance

▶ Side Effects

- GI, sweating, estrogenic effects

▶ Drug Interactions

- Beneficial interactions with hepatotoxins
- ↑ Cl of oral estrogens
- Inhibits CYP 2C9



Milk Thistle in T2DM

- ▶ Randomized double blind study in 51 pts
- ▶ PL or silymarin seed extract (300 mg bid) + metformin and glibenclamide x 4 months
- ▶ FBG
 - ↓ from 156 mg/dL BL to 133 mg/dL in silymarin group ($p < 0.01$ vs BL)
 - ↑ from 167 mg/dL BL to 188 mg/dL in PL group ($p < 0.001$)
- ▶ A1C
 - ↓ from 7.8% BL to 6.8% in silymarin group ($p < 0.001$ vs BL)
 - ↑ from 8.3% to 9.5% in placebo group ($p < 0.0001$)
- ▶ Lipids ↓ significantly in the silymarin group
 - LDL and triglycerides

Milk Thistle – Summary

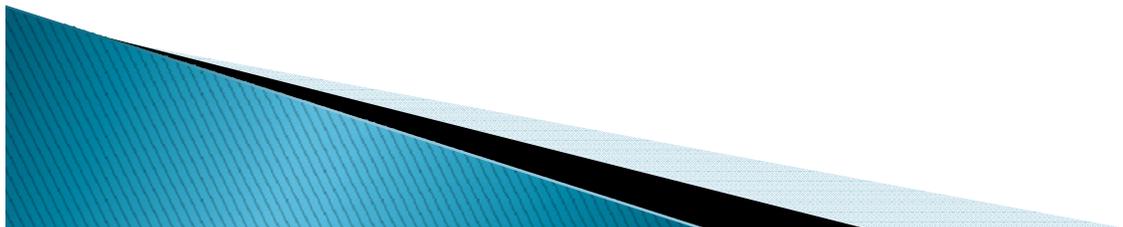
- ▶ May protect against toxicity of hepatotoxic agents (APAP, etc)
- ▶ Pts may use to protect against potentially hepatotoxic DM drugs (glitazones, statins)
- ▶ May see a role in decreasing insulin resistance and NASH; may help decrease insulin doses in persons with liver disease
- ▶ New studies: may help decrease proteinuria when added to ACEIs
- ▶ Doses vary according to silymarin extract (studies used 280-800 mg/day)
- ▶ Use in DM is emerging
- ▶ Natural Standard: Grade “C”



Turmeric



- ▶ *Curcuma longa*
- ▶ Curcumin is active ingredient
 - Diferuloylmethane (hydrophobic polyphenol)
 - Major constituent of curry powder
- ▶ Uses
 - Indigestion (Stimulates bile production)
 - Ulcerative colitis
 - Osteoarthritis
 - Atherosclerosis
 - Cancer (anti-angiogenic)
 - Uveitis
 - Diabetes?
- ▶ Mechanism – antioxidant, anti-inflammatory, anti-platelet
- ▶ ADRs – In large amounts, GI upset, diarrhea, kidney stones, ↓ BG
- ▶ Drug interactions with anticoagulants (warfarin, clopidogrel, ASA)



Turmeric



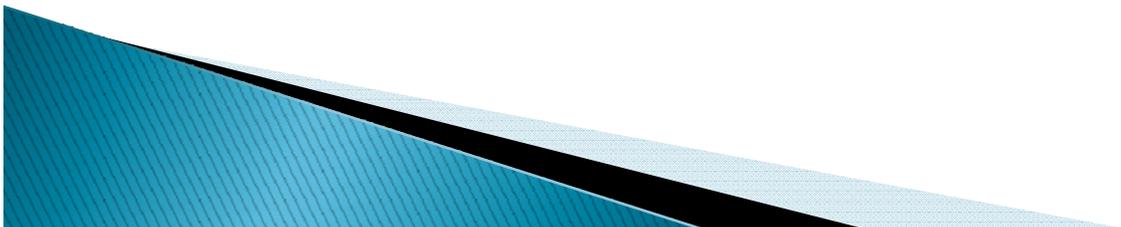
- ▶ Effect on PPG/insulin in 14 healthy subjects
- ▶ Cross-over design
- ▶ Subjects given 75 g OGTT along with 6g *C longa* or PI.
- ▶ Fingerticks/venous samples obtained q 15 min for 120 min.
- ▶ Results:
 - Insulin response higher after 30 min ($p=0.048$) and 60 min
 - Results significant ($p=0.033$), but no effect on glucose
- ▶ Conclusions:
 - No change in glucose levels, but possible effect on insulin secretion

Turmeric



▶ Other effects

- Human trial in 36 elderly individuals found no ↓ in lipid levels
- Murine research: significant improvement in glycemic control/insulin sensitivity
- Increased adiponectin (↓ levels correlates with insulin resistance)
- Anti-inflammatory effects on endothelial cells (prevention of atherosclerosis)



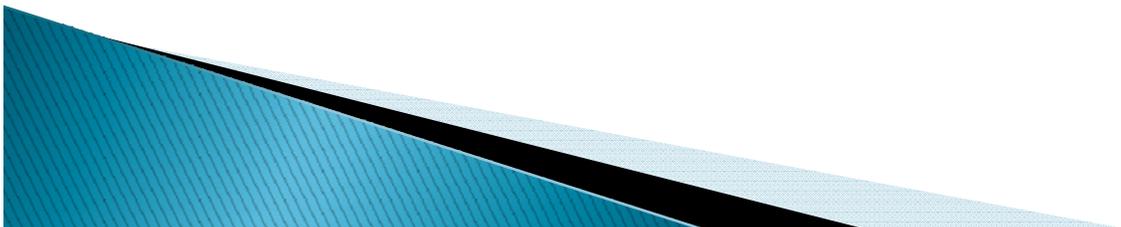
Turmeric



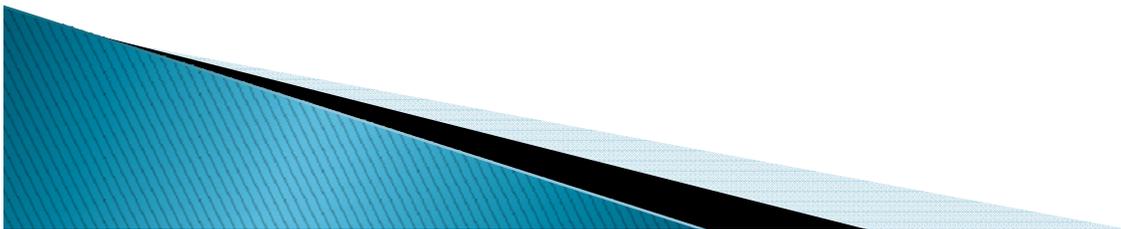
- ▶ 9 month RDBPCT in 240 individuals with prediabetes
 - 750 mg or PI BID
- ▶ Results for curcumin vs PI
 - HOMA- β 61.6 vs 48.7; $P < 0.01$
 - C-peptide 1.7 vs 2.17; $P < 0.05$
 - HOMA-IR 3.2 vs 4.04; $P < 0.001$
 - Adiponectin 22.5 vs 18.45; $P < 0.05$
- ▶ New onset T2DM
 - Curcumin 0%
 - Placebo 16.4%

Turmeric – Summary

- ▶ Curcumin is active ingredient; found in curry powder
- ▶ Has anti-inflammatory properties
- ▶ Emerging use for diabetes and its co-morbidities
 - Proteinuria
 - Retinopathy

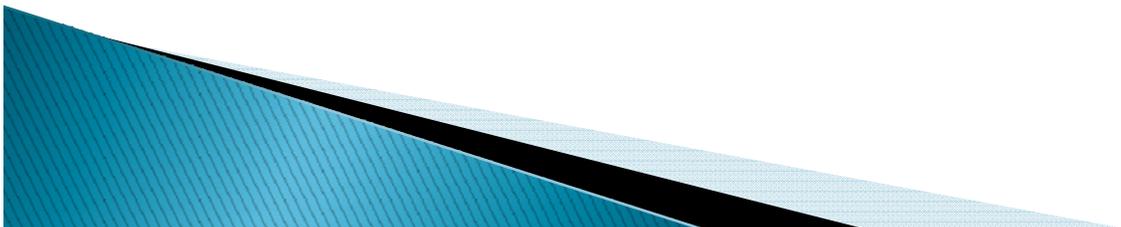


Non-Botanical Products



Alpha-Lipoic Acid

- ▶ Used for decades in Germany
- ▶ Coenzyme serves as a cofactor in enzyme complexes involved in energy production
- ▶ May help ↓ oxidative stress caused by hyperglycemia
- ▶ Side effects and drug interactions are benign
- ▶ Many randomized controlled trials
- ▶ Stabbing, burning pain improve (not paresthesias, numbness)
- ▶ Typical oral doses are 400–800 mg/day
- ▶ Natural Standard: Grade “A”



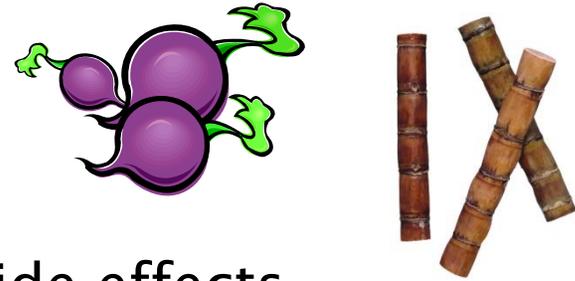
Chromium Picolinate

- ▶ Trace element that may be deficient in DM
- ▶ Studied in both type 1 and type 2 diabetes
- ▶ Over all, chromium is safe
- ▶ No accurate assay for body chromium stores
- ▶ Picolinate salt: form that may have benefit
- ▶ Typical dose: 200 mcg/day; higher doses safe (600 mcg GRAS)
- ▶ Recent evidence: 600 mcg/day, possibly + biotin
- ▶ FDA: authorized a qualified health claim that chromium may decrease the risk of insulin resistance¹
- ▶ Natural Standard: Grade “C”

¹ USFDA: <http://www.cfsan.fda.gov/~dms/qhccr.html>



CoQ10

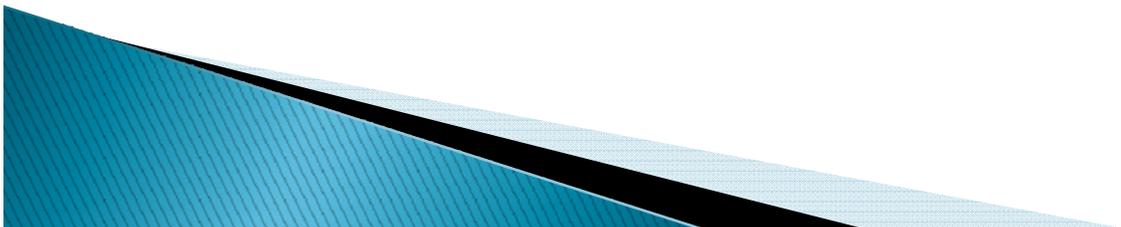


- ▶ Vitamin-like substance; ↑ ATP production; Scavenges OFRs; Membrane stabilizer
- ▶ Small studies have resulted in slight ↓ in FBG and A1C (NS)
- ▶ Symptomatic HF improvement; may ↓ BP, improve angina, Parkinson's, ↓ statin-induced myopathy, offset statin-induced BG ↑; improves endothelial dysfunction
- ▶ Long-term safety – 6 years
- ▶ Use soybean oil formulation
 - Better absorption
- ▶ Side effects
 - GI, rash, increased LFTs
- ▶ Drug interactions
 - Warfarin, statins, BP meds
 - Adriamycin® (less cardiac toxicity but less efficacy?)
- ▶ Some evidence for use in several diseases
- ▶ DM dose – 100–200 mg/d
- ▶ Natural Standard: Grade “D”

Asking the Right Questions: Clinicians

▶ Clinicians:

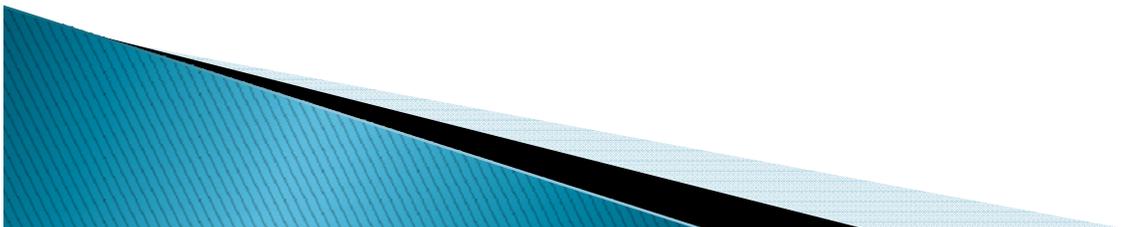
- Be respectful and do your homework on finding “EBM”
- Ask patient what supplements they are using
- Ask patient where they obtained the product – internet, manufacturer?
- Ask patients what they hope to achieve (discuss targets)
- Ask patients if they are taking their conventional medications (be especially wary if on anticoagulants)
- Monitor everything - glucose, A1C, BP, lipids, weight, renal, hepatic function
- Ask patients to stop a supplement 2 weeks before surgery
- Ask patients to inform you when they start/stop a supplement
- Support patients’ efforts at self-care



Asking the Right Questions: Patients

▶ Patients:

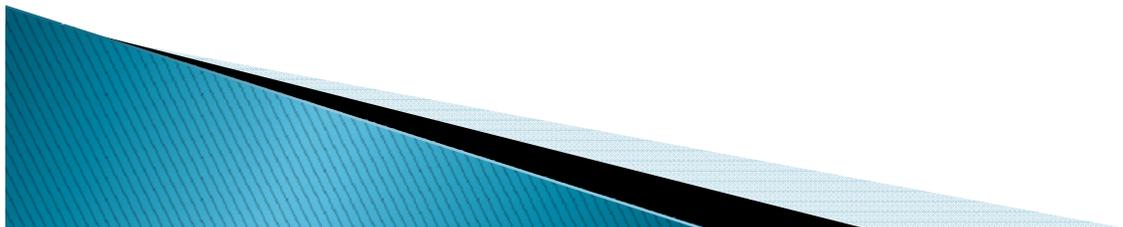
- Ask – why take this supplement?
- Check the USP (www.usp.org) website to evaluate products
- Check the “Tips for the Savvy Supplement User” website
- Tell your health care team when you start/stop a supplement
- Don’t stop conventional medications
- Don’t assume natural means safe (child safety)
- Don’t share the product
- Take only one new product at a time to determine response
- Don’t duplicate ingredients
- Stop the supplement 2 weeks before surgery
- Continue monitoring and healthy lifestyle options





Counseling Patients

- ▶ Be respectful of patients beliefs
- ▶ Provide evidence-based information
- ▶ Discuss target goals, evidence of benefit (or lack)
- ▶ Consider potential side effects; drug interactions
- ▶ Help patient evaluate whether brand is appropriate
- ▶ Emphasize role of conventional medications
- ▶ Be informed and supportive



Questions?

