Acknowledgement and Disclaimer

- Dr. Mary Hardy
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Objectives

- Explore the history of Chillies
- Review the pharmacology and physiology of Chillies
- Discuss the evidence-based use in medical practice and culinary medicine
- Learn about interesting uses of Chili Peppers

http://www.missouribotanicalgarden.org/PlantFinder/PlantFinderDetails.aspx?kempercode=a685
Chili vs Chillies?

- In the US, spellings with one "l" are preferred: chile or chili (plural: chiles or chilis)
- In the UK, Australia and some other English-speaking countries, two "l"'s are the norm: chilli and chillies
- I'm not sure how Canadians spell the word
- Perhaps we could solve the problem by saying "pepper" instead, which many Americans already do.
  - But of course, then some people would say that "pepper" is something else entirely: black/white pepper.
  - Or we could go with the genus name, Capsicum, which is used in the UK, especially for bell peppers, but actually covers the full range of chilli/es.

History of Chili Peppers(1)

- One of the earliest plants cultivated in the new world
- Considered to be the first spice to have been used by humans
- Evidence of use as food 8,000 yrs ago in Peru and domesticated in the Americas 6,000 years ago
- Columbus originally thought he had found the valuable spice pepper- what we call black pepper

http://www.missouribotanicalgarden.org/PlantFinder/PlantFinderDetails.aspx?kempercode=a685

History of Chili Peppers(2)

- January 1st should class as an important holiday (quite apart from being New Year’s Day!), because on that day in 1493, Christopher Columbus – on his first trip along the north coast of present-day Haiti – discovered a plant he assumed must be related to the common black pepper on account of the extraordinary spiciness of its fruit.
- Actually, this discovery wasn’t totally by chance, because one goal of the expedition – financed by the Spanish monarchy – was to locate a rich new source of pepper.
- Columbus called his new plant “red pepper”, although with some uncertainty

It was the French botanist Joseph Pitton de Tournefort (1656–1708) who later became the first to classify the supposed “red pepper” under the new genus Capsicum, where it became part of the nightshade family (solanaceae).
History of Chili Peppers

- The new plants that Columbus brought to Europe soon became widely distributed, even into Asia by Portuguese traders along the traditional “Spice Road”.
- Chile peppers journeyed from India, through central Asia and Turkey, to Hungary, where it became the national spice in the form of paprika.
- Capsicum was quickly integrated into regional cuisines of the Mediterranean countries, as well as North Africa and both the Near- and Far-East, whereas Central Europeans at first reacted skeptically to this new “pepper”, adopting the plants only as ornaments.
- Leonhart Fuchs made explicit reference to red pepper in his herbal book of 1543, noting that the seeds of the new Indian pepper “produced nearly all the effects, and had nearly all the virtues of real pepper.”
- Diego Alvarez Chance, a physician brought the first chile pepper to Spain and first wrote about their medicinal effects in 1494.

The Spice Route

Map showing the routes by which chilies travelled from the Americas to Africa and Eurasia. The tale begins with Columbus’ voyage of 1495 (green line), but the true spread of chilies occurred concurrent with the Portuguese voyages (red lines) from 1488 to 1549 as they traversed the globe from Africa through Arabia, India, the Spice Islands, China and Japan. Also shown (blue lines) are the ancient overland routes from India to China, the Spice route from Arabia to China and the trade route from Arabia to Central Europe.

Botanical Classification

<table>
<thead>
<tr>
<th>Kingdom</th>
<th>Plantae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Division</td>
<td>Magnoliophyta</td>
</tr>
<tr>
<td>Class</td>
<td>Magnoliopsida</td>
</tr>
<tr>
<td>Subclass</td>
<td>Asteridae</td>
</tr>
<tr>
<td>Order</td>
<td>Solanales</td>
</tr>
<tr>
<td>Family</td>
<td>Solanaceae</td>
</tr>
<tr>
<td>Genus</td>
<td>Capsicum</td>
</tr>
</tbody>
</table>

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Capsicum
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C. annuum  C. chinense  C. frutescens  C. baccatum  C. pubescens
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History of Chili Peppers(3)

- 35 species in the world; 25 or so in the US
- Earliest domestication and most common Chili is *Capsicum annuum* *(introduced in Europe in 16 AD)*
- Other independently created sps:
  - *C. chinense* (yellow lantern chili, habernaro, lowland Amazonia)
  - *C. pubesence* (the tree pepper – southern Andes)
  - *C. baccatum* (amarillo chili, lowland Bolivia)
  - *C. frutescense* (piri piri or tabasco chili, Caribbean)

Botany of Chili

- Hot pepper: *Capsicum annuum* group
- Solanaceae family
- Plant part used is the fruit
- Warm weather (tropical)
- Genus name comes from Greek kapto to bite
- 200 varieties in genus w/variable intensity of heat

Ripening of Chili: Color & Chemistry

http://www.missouribotanicalgarden.org/PlantFinder/PlantFinderDetails.aspx?permcode=6085

Carotenoids in Ripe and Unripe Peppers

<table>
<thead>
<tr>
<th>Carotenoid</th>
<th>Color</th>
<th>Bell pepper</th>
<th>Long cayenne</th>
<th>Golden wonder</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>unripe</td>
<td>ripe (green)</td>
<td>ripe (red)</td>
<td>ripe (red)</td>
</tr>
<tr>
<td>l-carotene (2)</td>
<td>yellow</td>
<td>13.4</td>
<td>11.6</td>
<td>28.3</td>
</tr>
<tr>
<td>Zeaxanthin (5)</td>
<td>orange</td>
<td>0.6</td>
<td>2.5</td>
<td>0.9</td>
</tr>
<tr>
<td>Antheraxanthin (6)</td>
<td>yellow</td>
<td>-</td>
<td>1.6</td>
<td>-</td>
</tr>
<tr>
<td>Violaxanthin (7)</td>
<td>yellow</td>
<td>13.8</td>
<td>9.9</td>
<td>25.9</td>
</tr>
<tr>
<td>Lutein (4)</td>
<td>orange</td>
<td>40.8</td>
<td>-</td>
<td>28.8</td>
</tr>
<tr>
<td>Capsanthin (8)</td>
<td>red</td>
<td>-</td>
<td>34.7</td>
<td>-</td>
</tr>
<tr>
<td>Capsorubin (16)</td>
<td>red</td>
<td>6.4</td>
<td>-</td>
<td>30.3</td>
</tr>
<tr>
<td>B-Cryptoxanthin (3)</td>
<td>orange</td>
<td>0.5</td>
<td>6.7</td>
<td>-</td>
</tr>
<tr>
<td>Capsanthin 5,6-epoxide</td>
<td>red</td>
<td>-</td>
<td>0.9</td>
<td>-</td>
</tr>
</tbody>
</table>

*All quantitative data reported as % of total carotene content

Anatomy of a Chile Pepper

Where Does the Hot Come From?

Figure 11. Where does the actual "hotness" (pungent spiciness) originate in peppers?

To measure the concentration of capsaicin, a solution of the chilli pepper’s extract is diluted in sugar water until the ‘heat’ is no longer detectable to a panel of tasters.

A rating of 0 Scoville Heat Units (SHUs) means that there is no heat detectable.

The Carolina Reaper (2,200,000 SHU) is the hottest pepper in the world – ranging from 1,500,000 Scoville Heat Units and peaking at 2,200,000 SHUs. The Scoville Scale is dominated early by chemical compounds such as Resiniferatoxin (16,000,000,000 SHU) – a chemical likely to cause chemical burns on contact with the skin.

The Bhut Jolokia Pepper, commonly known as a Ghost Pepper weighs in at a super hot 1,041,427 SHUs. Because it was the first chilli pepper to test at over 1 million Scoville Heat Units, it has enjoyed healthy popularity across the web.

# Scoville Heat Index
(Willbur L. Scoville, 1912)


# Nutritional Value

- Chillies are high in vitamin C (about twice that of citrus fruits) Even after cooking it only loses 30 percent of its vitamin C.
- Dried chillies are very high in vitamin A
- Red chillies are a great source of β-carotene.
- Chillies have antibacterial qualities, and contain bioflavinoids and anti-oxidants.
Other Nutritional Compounds

| Capsanthin | • Primary carotenoid (antioxidant) in red chili peppers, giving them their red color and typically accounting for up to 50 percent of the spice's antioxidant content. |
| Lutein     | • Most plentiful in immature (green) chili peppers, it has been shown to help maintain and improve eye health. |
| Volaxanthin | • It is the main carotenoid found in yellow chili peppers, which accounts for 37 to 68 percent of their total content. |
| Ferulic acid | • This compound has shown promise in protecting against diabetes, cancer and cardiovascular diseases |

Chile Pepper Leaf benefits

• Contain phytochemicals and phenolic acids - detoxifies enzymes, stimulates immune system, and reduces blood pressure.
• High antioxidant activity - reduces cancer risk, cataracts, cardiovascular diseases, and macular degeneration
• Clinical trials in humans prove that chili pepper leaves can lower LDL levels
• Also capable of alleviating chronic pain, control microbial contamination of food, and protect stomach lining from H.pylori infection.

• https://food.tv/facts/361578-chili-pepper-leaf-benefits#dOCCiDFLP7RAAGpB.99

Benefits of Chili/ Capsaicin

• Counter irritant treatment for pain
• Gastrointestinal benefits
  – Diabetic & Other neuropathic pain
  – Osteoarthritis & Chronic low back pain
  – Headache
• Metabolic management
  – Glucose control & Weight control
  – Gestational DM
Benefits of Chili/ Capsaicin

- Gastro-Intestinal Benefits
  - Dyspepsia & GERD
  - IBS
- Chronic non-allergic respiratory complaints
  - Idopathic rhinitis
  - Chronic unexplained cough
- Cancer Prevention

Pain Relief

Neuropathy
Fibromyalgia

How does Capsaicin work?

- Capsaicin exerts the effect through the capsaicin receptor, which is now known as vanillloid receptor (VR1) or transient receptor potential vanillloid sub family member1(TRPV1)
  - Bhaveetal., 2002; Caterina et al., 1999; Zygmunt et al., 1999
- TRPV1 is a non-selective cation channel activated by a wide range of stimuli including chemical substances and chemical factors, such as noxious heat, proton and vanilloids
  (Caterina et al., 1999; Cortright and Szallasi, 2009)
Mechanism of Pain Relief

- Transient receptor potential vanilloid 1 (TRPV1)
- Used to sense heat or warmth
- Capsaicin agonist reduces heat activation threshold
- Initial activation followed by long refractory state


Capsaicin & Fibromyalgia

- RCT severely affected FM pts (n=130) Usual trx vs Usual trx + 0.075% topical capsaicin
  - Applied to 18 tender points TID for 6 weeks
  - Low dose OTC strength of capsaicin cream
- Outcomes:
  - Primary standardized pain score
  - Secondary: Depression, FM, ADL scores, Additional pain measurements, typical FM symptoms

Casanueva B et al. Rheumatol Int, 2013; 33:2665-70

Capsaicin & Fibromyalgia

- Results: All improved
  - Myalgic Score (5.21 vs 3.8, p=0.02)
  - Global Subjective (22.8 vs 5%, p=0.001)
  - VAS scale of depression (5.63 vs 7.35, p=0.02)
  - FM Impact Questionnaire (67.89 vs 77.7, p=0.02)
  - Role Limit Due to Emotional problems (36.17 vs 17/2, p=0.05)
  - Fatigue Severity Scale (6.2 vs 6.6, p=0.004)
  - Pressure Pain Threshold (79.25 vs 56.71, p=0.004)

Casanueva B et al. Rheumatol Int, 2013; 33:2665-70
Capsaicin for Migraine Headaches

- 23 migraineurs w/pain @ pressure on scalp arteries, but w/o migraine were tested w/0.1% topical capsaicin or vaseline
- Those who responded with >50% relief (n=17) tested same substance during attack mild to mod intensity
- 11/17 showed >50% reduction w/cap
- 1 pt showed >50% reduction w/placebo
- Clinical conclusions & Limitations

Cianchetti C. In J Clin Pract 2010; 64: 457-9

Proving of Potentized Capscinoids

- Standard homeopathic proving of capsaicin & dihydrocapsaicin
- N= 22
  - 15 administered 30c combination of both capsinoids
  - 7 received placebo
- Produced symptoms of pain in various body locations in healthy volunteers


Metabolic Effects

Gestational Diabetes
Diabetes
Obesity
Effect of Capsaicin on Cardiometabolic Disease

Capsaicin as a Weight Loss Agent

- Effects on many functions related to weight loss have been tested
- Most data shows at best a small effect which may be dose limited
- Tolerance limited because of pain during ingestion
- Does decrease desire to eat after meal but effect not related to release of satiety hormones and is accentuated by increasing protein in meal.

Effects may not be solely related to capsaicin molecule.


Capsaicin vs Capsiate as Weight Loss Agent

- Intolerance for SE of capsaicin limits intake
- Capsiate is non-pungent capsaicin analogue produced from CH-19 Sweet pepper
- CH-19 Extract available commercially 1mg TID

Effect of Capsinoids on Energy Metabolism

- Dose ranging comparisons two capsinoids

Effect of Capsinoids on Substrate Oxidation

- Dose ranging comparisons two capsinoids

Capsaicin Glucose Absorption & Utilization

GTT in 15 healthy subjects. Glucose absorption increased significantly with an ED₅₀ dose of 400micrograms of capsaicin. Insulin & peptide C increased but not significantly. Glucagon increased sig with capsaicin suggesting a role for capsaicin sensitive neurons independent of insulin.

Red Pepper Thermogenesis & Appetite

- Prior studies red pepper on thermogenesis generally showed effect but dose of 10 gm was not well tolerated.
- RCX trial of 25 lean healthy young adults (13 spicy food eaters; 12 not)
- Standardized dose 1 gm, preferred amount (1.8 gm spicy eaters; 0.3 gm non-spicy) or P delivered in standardized meals
- Standardized dose was given orally in capsule or in meal


Red Pepper Thermogenesis & Appetite

- Red pepper powder
  - 1995ug/g capsaicin
  - 247 ug/g nordihydrocapsaicin
  - 1350 ug/g dihydrocapsaicin
  - Equivalent 53,800 Scoville Heat Units

- Outcomes
  - Postpandial energy expenditure
  - Core & skin temperature
  - Respiratory quotient


Red Pepper Thermogenesis & Appetite

Significant changes in energy expenditure for 270 min after a meal w/ 1 gm red pepper powder. Effect was more pronounced with oral intake than via capsule.

Red Pepper Thermogenesis & Appetite

Significant increase in core body temperature for 270 min after a meal w/ 1 gm red pepper powder. (p<0.05)


Red Pepper Thermogenesis & Appetite

Significant decrease in food preoccupation & cravings after a meal w/ 1 gm red pepper powder in red pepper naive group only. (p<0.05)


Metabolic Effects Hot Chili Meal in Overweight Subjects

- 34 overweight but not obese, healthy
- subjects (n= Male 16; Female 18) in South Africa; Normal glucose tolerance
- Single meal (HOT or CON) test followed by metabolic testing after washout crossover to other meal.
- Peri-peri (African bird’s eye chilli)
- Comparison of each patient to their own control meal.

Metabolic Effects Hot Chili Meal in Overweight Subjects


<table>
<thead>
<tr>
<th>Nutritional composition of the intervention (HOT) and control (CON) meals (per 280 g serving)</th>
<th>HOT</th>
<th>CON</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kJ)</td>
<td>2295</td>
<td>1874</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>47.4</td>
<td>47.0</td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>46.2</td>
<td>45.4</td>
</tr>
<tr>
<td>Of which total sugar (g)</td>
<td>9.5</td>
<td>10.1</td>
</tr>
<tr>
<td>Total fat (g)</td>
<td>20</td>
<td>10.7</td>
</tr>
<tr>
<td>Of which saturated fat (g)</td>
<td>4.7</td>
<td>3.0</td>
</tr>
<tr>
<td>Of which trans fat (g)</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Of which MUFA (g)</td>
<td>5.5</td>
<td>3.4</td>
</tr>
<tr>
<td>Of which PUFA (g)</td>
<td>9.7</td>
<td>3.6</td>
</tr>
<tr>
<td>Cholesterol (mg)</td>
<td>73</td>
<td>70</td>
</tr>
<tr>
<td>Dietary fibre (g)</td>
<td>3.1</td>
<td>3.1</td>
</tr>
<tr>
<td>Nt (%)</td>
<td>1060</td>
<td>912</td>
</tr>
</tbody>
</table>

*Parent chicken burger with 60 ml hot sauce.
*Plain chicken burger with 35 ml tomato sauce.

Table 3: Capsaicin analysis of the intervention (HOT) and control (CON) meals (absolute values)

<table>
<thead>
<tr>
<th>HOT</th>
<th>Start</th>
<th>End</th>
</tr>
</thead>
<tbody>
<tr>
<td>North-west capsaicin (mg/kg)</td>
<td>&lt;10</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Capsaicin (mg/kg)</td>
<td>14.7</td>
<td>13.0</td>
</tr>
<tr>
<td>Dihydrocapsaicin (mg/kg)</td>
<td>9.6</td>
<td>8.0</td>
</tr>
<tr>
<td>Total capsaicins (mg/kg)</td>
<td>24.3</td>
<td>23.0</td>
</tr>
<tr>
<td>Sober heat index</td>
<td>432</td>
<td>367</td>
</tr>
</tbody>
</table>

Start and end, beginning and end of the data collection phase of the study, respectively.


Capsaicin Chili in Gestational DM

- 44 women w/ gestational DM at 22-3wks gestation enrolled RDBPCT
- 0.625 gm chili powder BID at lunch & dinner (5 mg capsaicin/ day)
- Hot pepper used in study was Yanjiao
  - Botanical identification not certain
- Significant reductions in
  - 2 hr PPG
  - 2 hr Insulin
  - 2 hr post prandial HOMA-IR
  - Large for gestational age newborns

Table 2: General characteristics, clinical conditions, glucose metabolism, liver and kidney function, and lipids of women with GDM at the end of the trial.

<table>
<thead>
<tr>
<th>Capsaicin (n = 20)</th>
<th>Placebo (n = 22)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change</td>
<td>Change</td>
<td>Change</td>
</tr>
<tr>
<td>Glucose metabolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting plasma glucose (mmol/L)</td>
<td>5.16 ± 0.41</td>
<td>5.06 ± 0.39</td>
</tr>
<tr>
<td>Fasting serum insulin (IU/L)</td>
<td>1.01 (0.65, 1.51)</td>
<td>1.32 (0.79, 1.86)</td>
</tr>
<tr>
<td>Fasting HOMA-IR</td>
<td>0.40 (0.36, 0.44)</td>
<td>0.29 (0.26, 0.32)</td>
</tr>
<tr>
<td>2 h PC (mmol/L)</td>
<td>5.88 ± 0.02</td>
<td>6.01 ± 0.02</td>
</tr>
<tr>
<td>2 h-INS (IU/L)</td>
<td>0.04 (0.04, 0.05)</td>
<td>0.03 (0.03, 0.04)</td>
</tr>
<tr>
<td>3 h-INS/2h-INS</td>
<td>0.39 (0.35, 0.43)</td>
<td>0.46 (0.43, 0.49)</td>
</tr>
<tr>
<td>2 h-C-peptide (ng/mL)</td>
<td>2.04 ± 0.79</td>
<td>3.05 ± 0.79</td>
</tr>
</tbody>
</table>

Maternal and neonatal outcomes of the capsaicin and GOW trial.

<table>
<thead>
<tr>
<th>Capsaicin (n = 20)</th>
<th>Placebo (n = 22)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change</td>
<td>Change</td>
<td>Change</td>
</tr>
<tr>
<td>Pregnancy outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>2 (10.0)</td>
<td>4 (18.2)</td>
</tr>
<tr>
<td>IUGR</td>
<td>1 (5.0)</td>
<td>2 (9.1)</td>
</tr>
<tr>
<td>Macrosomia</td>
<td>1 (5.0)</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Polycythemia</td>
<td>1 (5.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>General delivery</td>
<td>4 (20.0)</td>
<td>4 (18.2)</td>
</tr>
<tr>
<td>GA</td>
<td>9 (45.0)</td>
<td>4 (18.2)</td>
</tr>
<tr>
<td>GA &gt; 41 wks</td>
<td>4 (20.0)</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>I-topi n = 14</td>
<td>3 (13.6)</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4 (20.0)</td>
<td>3 (13.6)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>2 (10.0)</td>
<td>2 (9.1)</td>
</tr>
</tbody>
</table>

*Data are presented as n (%). Abbreviations: GDM: gestational diabetes mellitus; IUGR: large for gestational age; GA: small for gestational age.
**Gastrointestinal Effects**

IBS
Nausea & Vomiting

**Beneficial Effects of Chili on Digestion**

- Prevention of gastric ulceration
- Regulation of GI acid & bicarbonate production
- Chemoprevention GI cancer
- Reduction GERD
- Inhibition of GI pathogens


**Effect of Red Pepper on IBS Symptoms**

TRPV1 receptor mediates visceral hypersensitivity and symptoms in IBS

- 50 pts w/ IBS after 2 wks washout were enrolled in RDBPCT.
- Red pepper powder (ground whole fruit) 150 mg (0.5 mg capsaicin) 2 enteric coated pills 1 ac breakfast & dinner
- Tolerability was problem. 6 dropouts & 8 pts required lower dose.

1Wouters et al. Gastroenterology 2016; 150: 875-87; 2Bortolotti & Porta. 2011; 56:3288-95
Effect of Red Pepper on IBS Symptoms

Capsicum Plaster Hand Acupuncture Point for PONV

- RDBPCT of 160 operative patients
- Capsaicin patch was applied to either k-d2 Korean acupuncture point or the Chinese pericardium 6 point bilaterally
- Treatment was initiated before induction of anesthesia for abd hysterectomy
- Removed 8hrs after surgery
- Outcomes within first 24 hours
  - Vomiting Rescue antiemetic use were significantly better in capsaicin groups
  - Patches were well tolerated


Capsicum Plaster Hand Acupuncture Point for PONV

<table>
<thead>
<tr>
<th>Table 2. Incidence of Nausea and Vomiting at 8 and 24 Hours After Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>PONV at 8 h postoperatively</td>
</tr>
<tr>
<td>Nausea, n (%)</td>
</tr>
<tr>
<td>Vomiting, n (%)</td>
</tr>
<tr>
<td>Rescue antiemetics, n (%)</td>
</tr>
<tr>
<td>PONV at 24 h postoperatively</td>
</tr>
<tr>
<td>Nausea, n (%)</td>
</tr>
<tr>
<td>Vomiting, n (%)</td>
</tr>
<tr>
<td>Rescue antiemetics, n (%)</td>
</tr>
<tr>
<td>Total fentanyl administered, μg (mean ± sd)</td>
</tr>
</tbody>
</table>

K-D2 = Korean hand acupuncture point located on the lateral distal phalanges of the index finger; Ps = Chinese point located two Chinese inches (1.5-2 cm) proximal to the distal wrist crease and lying between the tendons of the palmaris longus and the flexor carpi radialis; PONV = postoperative nausea and vomiting

* P < 0.01 versus the control group.

Effect of Capsaicin Load in Functional Dyspepsia

- 116 pts w/ UGI sx DBPCT; 73 pts at end of study dx w/ functional dyspepsia
- 750 mg capsule (97% capsaicin or placebo) single dose, two tests one week apart
- Sx dx capsaicin hypersensitivity & to correlate w/ functional dyspepsia vs other UGI disorders
- Results
  - 9 pts no sx
  - Half functional dyspepsia patient + for hypersensitivity
  - No correlation w/ dx or specific sx

Fuhrer M et al. Neurogastroenterol Motil 2011; 23:918-e397

Capsaicin & Risk of Gastric Cancer

- Gastric cancer rates vary 20X over world- effect of diet?
- Diet style associate w/ increased risk
  - Salty, smoked, pickled, preserved, nitrates
  - Cooked vs raw veggies
- Diet style associate w/ decreased risk
  - Fresh fruit & veggies
  - AO rich foods
- Capsaicin controversial
  - Reports of both carcinogenic & protective effects

Pabian N et al. J Gastrointest Canc 2014; 45:334-41
Cough Reduction & Capsaicin

- Chronic unexplained cough (n=24 + 15)
- 4 wks crossover RDBPCT
- Stepwise dose used
  - 1st 2 wks 0.4mg capsaicin 1 cap bid
  - 2nd 2 wks 0.4 mg 2 cap bid
- Cough sensitivity tested with capsaicin challenge
- Spirometry, standardized questionnaire & symptom diary


Results

- Cap challenge scores improved in both control & cough group after cap trx (pts p<0.020 cntrl p<0.0061)
- Cough sx scores improved after 4 wks (p<0.0030)

**Idiopathic Rhinitis & Capsaicin**

- Non-allergic, non-infectious rhinitis 10%
- 14 sx pts & 12 healthy control
- Intranasal capsaicin 5 doses throughout day (0.1mmol/L, 2 puffs ea nostril, 0.4ml per puff)
- Symptoms & receptor expression measured
- Non-toxic effects on cell culture nasal cells (no apoptosis, necrosis or morphology change)

*Van Gervan L et al. J Allergy Clin Immunol 2014; 133; 1332-9*

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**Idiopathic Rhinitis & Capsaicin**

- TPRV1 is upregulated in patients w/ IR
- Higher amount Substance P in nasal secretions
- Expression TPRV1 down regulated after capsaicin
- IR sx sig reduced after capsaicintrx in IR patients


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**Homeopathic Nasal Spray for Non-allergic Rhinitis**

42 subjects w/ symptomatic NAR in RCT to receive homeopathic nose spray (capsaicin + eucalyptol) BID or P continuously over 2wks. No sig ADE observed

Cancer Prevention

- The anticancer and chemo-preventive effects of capsaicinoids are closely related to their ability to prevent cell proliferation and migration and to induce cell apoptosis

- Capsaicin along with dihydrocapsaicin have been reported to repress the growth of various immortalized or malignant cell lines via induction of cycle arrest, apoptosis, autophagy, and/or via the inhibition of cellular metabolic activation (Choi et al., 2010; Ghosh and Basu, 2010; Oh et al., 2010; Oh et al., 2008; Thoennissen et al., 2010; Zhang et al., 2003).

Cancer Prevention...

- Capsaicin and dihydrocapsaicin may inhibit an isoform of cytochrome P450, an enzyme involved in metabolic activation as well as detoxification of many low-molecular-weight carcinogens (Singh et al., 2001)

- There is growing evidence that the induction of cellular apoptosis by capsaicin or dihydrocapsaicin is involved in the direct pathway (receptor-independent one) and the indirect pathway (receptor-dependent one). (Ziglioli et al., 2009)
Cancer Prevention...

- In the direct pathway, capsaicin induces apoptosis by interacting with caspases, particularly caspases 1 and 3. Whereas, in the indirect pathway, capsaicin needs to interact with TRPV-1, which leads to the intracellular calcium increase and consequently to the evidence of precocious and late elements of apoptosis (Ziglioli et al., 2009).
- Interestingly, it seems that capsaicin only selectively inhibits the growth or induces apoptosis of immortalized or malignant cell lines, but not of normal cell lines (Kim and Moon, 2004).

Other Interesting Uses

Industrial Uses

- **Cosmetic Industries:**
  - Antidandruf agent – *C. annuum* fruit extract
  - Cosmetic astringent - *C. annuum* fruit extract
  - Hair conditioners - *C. annuum* fruit extract
  - Skin Conditioning - *C. annuum* fruit extract
  - Skin protectant - *C. annuum* fruit extract
  - Lip Color, chap sticks, and nail colors

- **Liquor Industries:**
  - Liquor industry – hot and spicy adult beverages
Use as weapons

- **Chile Bombs**
  - Used in Africa and parts of India to ward off elephants from straying into human habitation
  - The Defense Research and Development Organization (DRDO) in India are working on a project to develop hand grenades and other repellents to deal with terrorists by using bhoot jolokia

- **Pepper Spray**
  - (OC Spray – Oleoresin Capsicum) – tears, pain, temporary blindness – sprays must contain 1.0% capsaicin and related capsaicinoids

- **PAVA spray**
  - another version of this spray is a synthetic analogue of capsaicin and used in UK

Summary

- Chile Peppers make you hot and sweaty even if you aren’t in menopause!

- Capsaicin has many health benefits but published clinical studies have been small with dropouts due to intolerance

- We all love Chile so go enjoy it if you can tolerate!

Questions & Thanks