Evidence for Health Benefits of Ginger and Turmeric

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Zingiberaceae family

Ayurvedic, Chinese, and Hindu medicine[1,2,3]

Ginger (*Zingiber officinale* Rosc.)

- Digestive disorders
- Nausea, morning sickness
- Arthritis
- Muscular discomfort
- Head aches
- Common cold
- Inflammatory conditions

Turmeric (*Curcuma longa L.*)

- Respiratory conditions
- Liver disorders
- Rheumatism
- Diabetic wounds
- Cough & sinusitis
- Anorexia
- Abdominal pain
- Sprains
- Swelling

1. Sharma H. Contemporary Ayurveda. 1998.
2. Araujo CC. Mem Inst Oswaldo Cruz, 2001, 96:723
3. Aggarwal BB, Expert Opin Investig Drugs, 2004, 13:1327.
4. Park KK. Cancer Letters, 1998, 129:139.

Ginger

(*Zingiber officinale* Rosc.)

Therapeutic Effects[1]

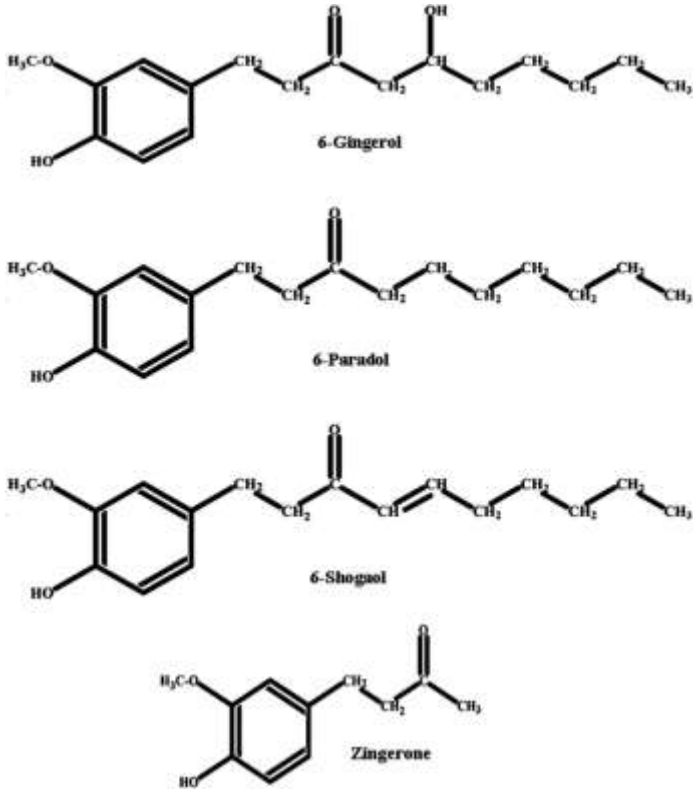
- Anti-oxidant[2]
- Anti-platelet[3,4]
- Anti-inflammatory[5,6]
- Anti-tumorigenic[7]
- Hypoglycemic[8,9]
- Hypocholesterolemic
- Analgesic[10]
- Anti-microbial activity[11, 12,13]

1. Ali et al., 2007
2. Cao et al., 1993
3. Nurtjahja-Tjendraputra et al., 2003
4. Thomson et al., 2002
5. Grzanna et al., 2004
6. Grzanna et al., 2005
7. Shukla et al., 2007
8. Kadnur & Goyal, 2005
9. Al-Amin et al., 2006
10. Pedov et al., 2002
11. Jagetia et al., 2003
12. Ficker et al., 2003
13. Mahady et al. 2003

Ginger

(*Zingiber officinale* Rosc.)

Non-volatile phytochemicals in ginger



Toxicity and safety of ginger

- Generally considered a safe herbal medicine.[1]
- Minor adverse effects in humans
  - 400 mg ginger 3x/day for 3 weeks – 1/12 report of mild diarrhea[2]
  - Heartburn
  - Gastric irritant (>6g per day)
- Evidence for early embryo loss in pregnant mice given ginger tea[3]

1. Weidner MS. J Ethnopharmacol, 2000. 73:513
2. Chrubasik S. Phytomedicine, 2005. 12:684
3. Wilkinson JM. Reprod Toxicol. 2000, 14:507

Turmeric

Curcuma longa L.

Therapeutic Effects

- Antioxidant[1-3]
- Anti-inflammatory[4]
- Anticarcinogenic[5]
- Antimicrobial[6]
- Hepatoprotective[7]
- Thrombosuppressive[8]
- Antiarthritic[9]
- Cardioprotective[10]

1. *Sharma O.* Biochem. Pharmacol. *1976*, 25(15), 1811.
2. Ruby AJ. Cancer Lett. 1995, 94(1), 79.
3. Sugiyama Y. Biochem. Pharmacol. 1996, 52(4), 519
4. Srimal RC. J Pharm Pharmacol. 1973, 25(6), 447.
5. Shishodia S. Curr Probl Cancer, 2007, 31(4):243.
6. Mahady G.B. Anticancer Res, 2001, 22(6C), 4179
7. Kiso Y. Planta Med. 1983, 49(3), 185.
8. Scrivastava R. Thromb Res. 1985, 40(3), 413.
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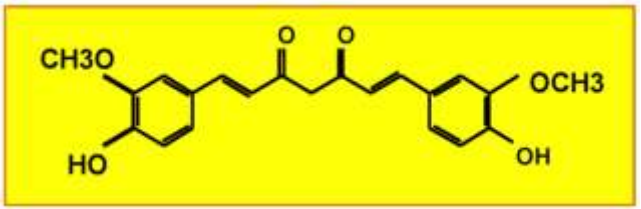
Turmeric

Curcuma longa L.



Curcumin identified as the active ingredient

3 major curcuminoids (3 – 5% of raw plant):

- Curcumin - Diferuloylmethane (77%)
- Demethoxycurcumin (17%)
- Bisdemethoxycurcumin (3%)

Molecular targets of curcumin[1]

- Transcription factors
- Inflammatory cytokines
- Enzymes
- Kinases
- Genes regulating cell proliferation and apoptosis

1. Goel A. Biochemical Pharmacology, 2008, 75:787

Transcription factors regulate the expression of genes contributing to tumorigenesis, inflammation, cell survival, cell proliferation, invasion, and angiogenesis:

- NF-κB
- AP-1
- STAT proteins
- PPAR-γ
- B-catenin

Curcumin inhibits activation of transcription factors

Transcriptional factors
- Activating protein-1↓
- β-Catenin↓
- CREB-binding protein↓
- Early growth response gene-1↓
- Electrophile response element↑
- Hypoxia inducible factor-1↓
- Notch-1↓
- Nuclear factor-kappa B↓
- Nuclear factor 2-related factor↑
- Peroxisome preoliferator-activated receptor-gamma↑
- Signal transducers and activators of transcription-1↓
- Signal transducers and activators of transcription-3↓
- Signal transducers and activators of transcription-4↓
- Signal transducers and activators of transcription-5↓
- Wilms' tumor gene 1↓

1. Goel A. Biochemical Pharmacology, 2008, 75:787

Example:

Inhibition of inflammatory cytokine expression effects on cancer cells and renal failure:

- Inhibition of TNF-a downregulates NF-κB required for COX-2 protein expression
- Inhibition of TNF- a and IL-1β in chronic renal failure mouse models slowing renal failure[2]

Curcumin inhibits expression of inflammatory cytokines

Inflammatory cytokines
- Interleukin-1↓
- Interleukin-2↓
- Interleukin-5↓
- Interleukin-6↓
- Interleukin-8↓
- Interleukin-12↓
- Interleukin-18↓
- Monocyte chemoattractant protein↓
- Migration inhibition protein↓
- Macrophage inflammatory protein↓
- Tumor necrosis factor alpha↓

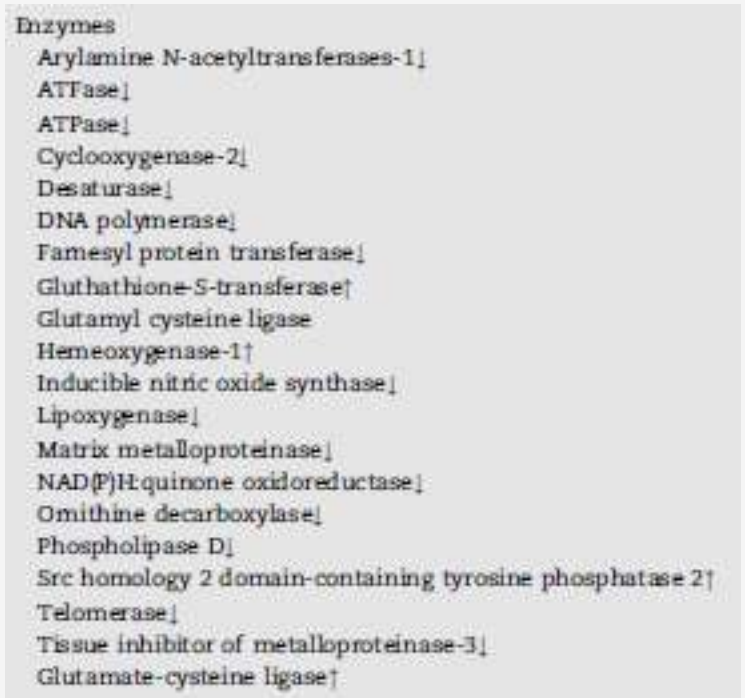
1. Goel A. Biochemical Pharmacology, 2008, 75:787
2. Ghosh SS. Am J Physiol Renal Physiol, 2011, 302:F439

Curcumin regulates activity of enzymes

Example:

Regulates activities of enzymes that control cell/tumor growth and proliferation:

- Blocks fibrosis in glomerulonephritis by upregulation of hemoxygenase-1
- Suppress tumor cell growth by inhibiting FPTase activity
- Inhibit tumor promotion by inhibiting xanthine oxidase activity, a cause of PMA-mediated tumor promotion.



1. Goel A. Biochemical Pharmacology, 2008, 75:787

Curcumin down regulates the activity of multiple kinases:

Example:

- Mitogen-activated protein kinase (ERK1/ERK2, JNK, & P38 MAPK)
- EGF receptor-kinase
- Completely inhibits phosphorylase kinase, protein kinase C(PKC) among others

Curcumin inhibits activation of kinases

Kinases
Autophosphorylation-activated protein kinase↓
Ca^{2+}-dependent protein kinase↓
EGF receptor-kinase↓
Extracellular receptor kinase↓
Focal adhesion kinase↓
IL-1 receptor-associated kinase↓
Janus kinase↓
c-jun N-terminal kinase↑
Mitogen-activated protein kinase↓
Phosphorylase kinase↓
Protamine kinase↓
Protein kinase A↓
Protein kinase B↓
Prorein kinase C↓
pp60c-src tyrosine kinase↓

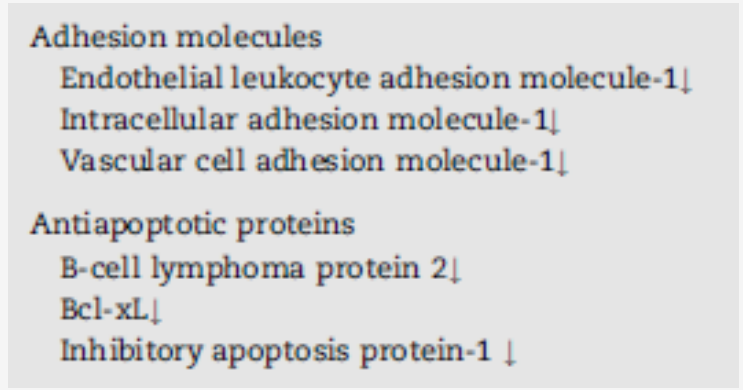
1. Goel A. Biochemical Pharmacology, 2008, 75:787

Curcumin impacts genes/pathways of apoptosis, cell invasion, and adhesion

Curcumin effects targets controlling cell adhesion, apoptosis, and invasion.

Example:

- Inhibits TNF- a induced expression of intracellular ICAM-1, VCAM-1 and E-selectin – adhesion molecules
- Anticancer effects via activation of p53 – intranuclear, tumor suppressor transcription factor.



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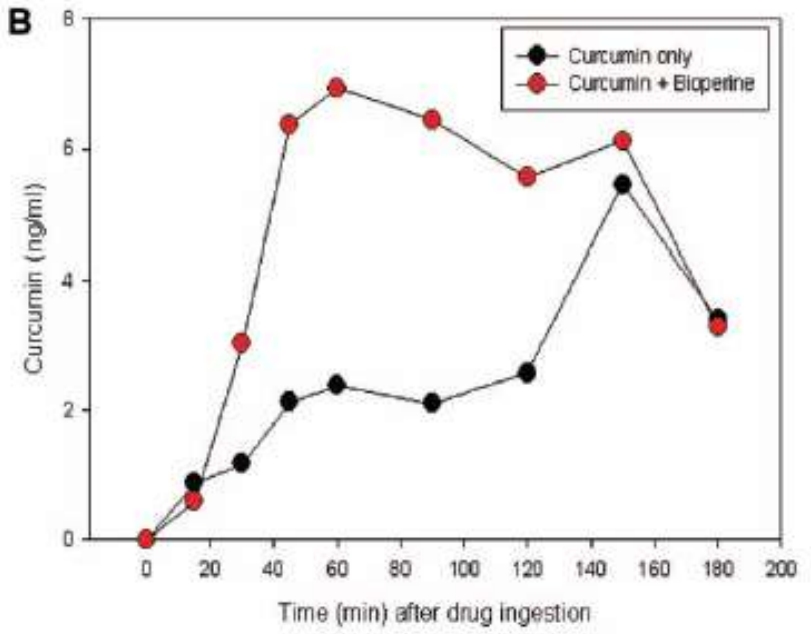
Curcumin: bioavailability and safety

Poor Bioavailability

- Poor absorption with a major route of elimination in feces (up to 75%)
- Rapid metabolism in intestine and liver to glucuronide conjugates
- Curcumin metabolites found in plasma in low nanomolar range (3.6 – 12g daily)
- Increased absorption and Inhibition of hepatic and intestinal glucuronidation when combined with piperine (2g/5mg).



Safety & Efficacy of curcumin in humans

- Doses up to 8 g daily for 3months – no toxicity[1]
- Studies testing maximal tolerated dose of curcumin up to 12g; minimal adverse side effects, including diarrhea, rash, headache
- Special formulations of curcuminoids – 3600 mg for 4 months – diarrhea, nausea, alkaline phosphatase elevations.[3]
- FDA has declared curcumin as "generally regarded as safe" GRAS.
- Clinical trials to assess optimal dose, disease targets, and interactions with other drugs.

1. Cheng, et al., 2001
2. Lao et al., 2006
3. Sahrma et al.,2004

Conclusions

- Ginger and turmeric have health benefits
- Multiple metabolic targets identified through research
- Generally safe, but toxicity of future formulations requires study