Australian Ginger

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Health benefits of fresh and processed ginger: a critical review of the peer reviewed scientific literature

Stages 1-2: In-depth literature review – full report

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## Contents

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abstract &amp; Executive summary</td>
<td>3</td>
</tr>
<tr>
<td>Introduction &amp; Objectives</td>
<td>7</td>
</tr>
<tr>
<td>Methodology</td>
<td>8</td>
</tr>
<tr>
<td>Stage 1: Creating a framework</td>
<td>12</td>
</tr>
<tr>
<td>Stage 1 &amp; 2: Literature review &amp; In-depth literature review</td>
<td>13</td>
</tr>
<tr>
<td>Conclusions</td>
<td>60</td>
</tr>
<tr>
<td>Addendum: Considerations regarding commercial relevance</td>
<td>64</td>
</tr>
<tr>
<td>References</td>
<td>70</td>
</tr>
<tr>
<td>Glossary</td>
<td>71</td>
</tr>
</tbody>
</table>
Abstract & Executive summary

Ginger contains bioactive components including gingerols and shogaols, and has been shown to have considerable antioxidant, anti-inflammatory, anti-emetic, blood sugar and lipid lowering effects, and thus potential health benefits. Experiments demonstrate powerful antioxidant properties, which are thought to underlie ginger’s effects, though the bioavailability in humans is unconfirmed, and no definitive dosage has been defined.

To date clinical studies are minimal, and have concentrated on anti-emetic effects, however recent preliminary clinical studies have encouraging indications for a role for ginger in digestive and metabolic disorders.

The present paper reviews all of the available peer reviewed scientific literature on the many health benefits of ginger to determine the role fresh and processed Australian ginger plays in promoting good health. Discussions focus on the implications for the development of the Australian Ginger Industry.

Note: a glossary is provided at the end of this document

Executive summary

1. The active compounds in ginger
   - Gingerols are the major pungent bioactive compounds in fresh ginger roots, with the most abundant being [6]-gingerol. Shogaols are the dehydrated form of gingerols, and are found in processed (dried) ginger. [6]-shogaol is the most abundant. The mechanisms of actions of gingerols and shogaols are not well understood
   - Shogaols may be more powerful than gingerols, so processed ginger may be more powerful than fresh ginger. The preparation method used in scientific experiments can therefore influence the chemical composition and the potency of ginger’s effects

2. Dosage and toxicity
   - There is little evidence supporting ginger’s practical usefulness in humans, and no definitive dosage has been defined
   - Ginger appears to be a safe dietary supplement, including consumption in pregnancy. Reported adverse events are mild, infrequent gastrointestinal complaints (though pregnant women should be advised to use for a few days only as longer term effects of ginger have not been studied)

3. Ginger’s many health benefits are attributed to synergistic effects of more than one ‘pharmacological’ action (e.g. antioxidant, anti-inflammatory etc.)
   - This represents a challenge in that health benefits cannot be linked to a very specific pharmacological action e.g. ‘weight loss’ cannot be explained by ‘thermogenic effects’ alone, but also involves antioxidant action (e.g. speeding up the metabolism of fats), immune system mediation (e.g. inhibiting enzymes in carbohydrate metabolism) etc.
- This also represents an opportunity as it opens the scope for the way health benefits are phrased in the market, and the level of information communicated to the consumer. There is an opportunity to ‘cluster’ various health benefits and/or pharmacological actions in order to maximise the strength of the health claim and the scientific support.

- Ideally communication of the health benefits of ginger will link a pharmacological action to a health benefit as simply as possible, in language that will resonate with consumers.

**Figure 1.** shows the links between the pharmacological actions and health benefits of ginger.

**KEY:**

- **Red: health benefits** *(e.g. prevention of nausea, weight management)*
- **Blue: pharmacological actions** *(e.g. anti-inflammatory, antioxidant)*
- Size of bubble: importance of the pharmacological action or health benefit in relation to associated pharmacological actions or health benefits
  - The bigger the bubble the more important and all-encompassing the pharmacological action or health benefit is *(e.g. ‘antioxidant’ encompasses ‘free radical scavenging’; and ‘gastroprotection’ encompasses ‘easing digestive discomfort’)*
- **Darker shades: potential strength of opportunity**
  - The darker the shade of red or blue the more potential resonance with consumers AND the greater the support from scientific literature *(e.g. ‘eases digestive discomfort’ is a bigger opportunity than ‘relieves period pain’; and ‘thermogenic’ is a bigger opportunity than ‘speeds up gastric emptying’)*

**Figure 1. Links between pharmacological actions and health benefits**
Figure 1. shows that:

- **Antioxidant and anti-inflammatory actions** underlie all health benefits
- Three health benefits stand out as umbrella health benefits (i.e. big opportunities) that encompass related health benefits
  1. Gastroprotection
  2. Diabetes control
  3. Weight management
- **Controlling blood sugar** is a key action linking these three health benefits. It moderates the metabolism of fats, insulin sensitivity AND stomach contractions
- **Diabetes control** and **weight management** are both metabolism-related and therefore may be merged under the health benefit of ‘boosting metabolism’
- Antioxidant activity, specifically preventing the oxidation of lipids, supports the evidence for metabolism boosting
- **Thermogenic effects**, though clinical evidence is not yet strong, also potentially supports metabolism boosting

4. Clinical evidence is limited

- The clinical studies that are available have tended to be incomparable due to variations in dosage, treatment duration and preparation
- Currently the health benefits of ginger with the strongest clinical support are:
  - Anti-emetic activity – especially preventing nausea in early pregnancy
  - Pain relief in osteoarthritis and premenstrual pain
- Research into natural alternatives to current drug treatments is attracting attention, and recent clinical studies demonstrate preliminary support for:
  - Thermogenic and metabolism stimulating effects
  - Soothing sore muscles after exercise
- Key actions which underlie several health benefits (shown by in vitro and animal studies) are:
  - Controlling blood sugar and blood lipids
  - Antioxidant activity
  - Anti-inflammatory activity

5. Implications for shortlisting health benefits

- It is possible to cluster health benefits in order to maximise the weight of scientific support
- Ginger’s role as a general gastroprotective is promising:
  - Ginger has been shown to speed up digestive contractions, including stomach emptying time. Whilst the evidence is not strongly associated with relieving indigestion symptoms per se, these actions provide general benefits when linked to secondary protective roles
  - Ginger may provide a secondary gastroprotective role in type 2 diabetes. Ginger’s ability to control blood sugar is the link, which influences the stomach’s digestive contractions (including gastric emptying)
  - There is also an interesting link between ginger’s gastroprotective benefit for the stomach and the arteries, bridged by ginger’s antioxidant activity
Ginger has anti-emetic effects and can prevent nausea, protecting against stomach discomfort in early pregnancy and for motion sickness.

- Ginger’s role in managing metabolic conditions (diabetes and weight management) is promising
  - Ginger has been shown to stimulate digestion and metabolism. In vitro and animal studies indicate that ginger inhibits key enzymes controlling metabolism and lowers lipids which improves insulin sensitivity.
  - Combining the clinical literature for thermogenic effects, stimulating digestion, and the metabolism of fat may strengthen the case for ginger’s role in managing metabolic conditions.

- The next step in the review process is Stage 3 – Health benefits shortlist. In this stage Brand Story will narrow down a shortlist of health benefits proposed as the most valuable to the Australian Ginger Industry moving forward. Some initial considerations for commercial relevance of the scientific literature are discussed as an Addendum at the end of this document.
Introduction & Objectives

Introduction

Commonly known as ginger, *Zingiber officinale* has been used in Asian, Arabic and Indian cultures as a herbal medicine since ancient times. Ginger reached the west 2000 years ago as a preserved form and became so important to British food and medicine that the plant was transported to Australia on the First Fleet in 1788 (Ryder, 2014).

Ginger is valued for its rhizomes that can be consumed fresh or dried. The key active compounds of ginger that account for its anti-inflammatory, antioxidant, anti-emetic, and gastroprotective activities are gingerols, shogaols, and paradols.

Gingerols are the most abundant pungent compounds in fresh roots, and several gingerols of various chain-lengths [6 to 10] are present in ginger, with the most abundant being [6]-gingerol. Shogaols are the dehydrated form of gingerols, and are found in only small quantities in the fresh root and mainly in the dried and thermally treated roots, with [6]-shogaol being the most abundant (Zick et al, 2008).

The Australian Ginger Industry (AGI) needs to find ways to increase usage and consumption of fresh ginger amongst both current and infrequent users. One of the identified ways to encourage increased use is through the communication of health benefits.

In 2013 Brand Story conducted research on behalf of RIRDC and the AGI to understand the domestic market for Australian ginger. A key recommendation from this project was to develop compelling messages about the as yet unknown health benefits of ginger to motivate people to consume more fresh ginger.

The present project flows from the 2013 project, and this paper reports on the progress of the first 2 stages; the literature review and meta-analysis.

Overarching objectives:

1. Conduct a desktop review of the international peer reviewed scientific literature that has investigated Australian and non-Australian ginger to determine the role fresh and processed Australian ginger plays in promoting good health
2. Present the outcome of the review in a form the Australian Ginger Industry can easily understand and use to develop and/or add value to the ginger industry within the constraint of the *Australian New Zealand Food Standards Code*
Methodology

An iterative two stage approach:

**Stage 1 – Literature review**

**Part 1 Create a framework**

*Purpose: compile a list of all of the health benefits associated with ginger and establish rough categories as a framework to structure the full literature review*

- Computer search using the term ‘health benefits of ginger’
- Manual search using the references of articles and studies located through computer search
- Manufacturers of ginger preparations asked to contribute published and unpublished materials
- Collation and categorisation of the health benefits of ginger leading with ‘Effects of ginger’ as broad categories, then listing ‘Associated health benefits’ as sub-clusters

**Part 2 Literature review**

*Purpose: create a comprehensive library of the available literature across the breadth of health benefits associated with ginger*

- Literature search and collation of studies under each category as guided by the framework covering the full breadth of available research on the health benefits of ginger
- Focused on published research in peer reviewed Journals
- Examples of literature databases:
  - PubMed
  - The University of Sydney Library

*Note the literature on ginger is vast, especially for certain categories such as anti-emetic, and an effort has been made to provide as wide a library of studies as possible within the agreed timeframe.*

- **A filtering criteria** was established in order to shortlist health benefit categories and relevant studies for in-depth review. This part of the process was key and is explained below. The filtering criteria consisted of four components:

  1. **Focus on randomised controlled trials (RCTs)**

*Why?* RCTs are considered to be the most reliable form of scientific evidence in the hierarchy of evidence that influences healthcare policy and practice because they reduce false causality and bias. Results of RCTs may be combined in systematic reviews and meta-analyses which are increasingly being used in the conduct of evidence-based practice.
The randomised controlled trial and, especially, systematic reviews of several of these trials have been established as the gold standards for judging the benefits of treatments (e.g. see Barton, 2000 for a review of RCTs).

2. Considerations around ‘in vitro’ and animal studies

Why? Previous literature reviews have concluded that animal studies provide insufficient evidence on the relevance of findings to humans (Nicoll & Henein, 2009). In a systematic review Pound et al (2004) listed the methodological problems of animal experiments. The most important point Pound made was the uncertainty of the relevance of findings on animals to the human condition due to different digestive systems, lifespans and length of follow-up, dosages, and diseases being experimentally induced in animals.

Animal studies were key, however, for understanding the mechanisms of action of ginger, as many of these investigations tend to be too invasive or risky to carry out in humans.

‘In vitro’ studies involve using human cell cultures for experiments in test tubes in a laboratory, and have been used to identify individual components of ginger and explore their biological functions. These studies make up the bulk of literature for ginger’s antioxidant activity and were therefore important to include in the review.

Where animal and in vitro studies made up the bulk of the literature it was important to avoid over interpretation. Some categories such as ‘anti-cancer’ were not reviewed in depth for this reason.

3. Focus on health benefits that resonate with consumers

Why? Getting the focus right was important for helping to steer the AGI towards the health benefits most likely to motivate consumers to increase their consumption of ginger.

Previous market research by Brand Story (2013) indicated that consumers were most compelled by broader health and wellness benefits such as digestion enhancing, metabolism boosting – and particularly the ‘warming’ effects of ginger. In the scientific literature there appears to be a growing mass of research on the chemo-preventative effects of ginger, though it is not known whether such a specific benefit would appeal to the majority of Australians. Considerations such as these were a key part of the filtering process.

Figure 2 demonstrates the exercise Brand Story employed to highlight potential areas of opportunity. The two axes represent key dichotomies in the way health benefits might be perceived by consumers. These dichotomies are: General vs. Specific and Treatment vs. Prevention. Each type of health benefit tends to sit naturally in one of the four quadrants. Each quadrant was evaluated in terms of the ease of integrating ginger into the diet, the type of audience the health benefit might appeal to, and conduciveness to frequency of use.

The exercise indicated that the biggest area of opportunity is potentially around General health benefits that are either Treatment or Preventative based in nature.
(the top left and right quadrants). This aligned with Brand Story’s 2013 research on consumers, however it is important to note that the purpose of the exercise was as an evaluative guide rather than to rule out certain health benefits altogether.

**Figure 2. Opportunities map: evaluating potential areas of opportunity**

<table>
<thead>
<tr>
<th>General</th>
<th>Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>E.g. indigestion symptoms, joint pain</strong></td>
<td><strong>E.g. chemotherapy-induced nausea and vomiting</strong></td>
</tr>
<tr>
<td>✓ Ease: for chronic conditions where there is no ‘cure’ ginger may be a welcome contributor to symptom relief</td>
<td>✓ Ease: suggestive of bigger lifestyle changes and may be part of clinical intervention</td>
</tr>
<tr>
<td>✓ Audience: aligned with consumer trend for natural alternatives for healing the body</td>
<td>✓ Audience: niche (limited to people concerned about specific conditions)</td>
</tr>
<tr>
<td>✓ Frequency: potentially motivating for on-going symptoms with frequent or predictable episodes such as osteoarthritis/ muscular pain</td>
<td>✓ Frequency: could be on-going as part of a lifestyle program or intervention</td>
</tr>
<tr>
<td>! Caution: potentially less emotional and evidence may need to support ginger’s superiority over available clinical drugs</td>
<td>! Caution: lack of immediate gratification risks loss of motivation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Specific</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>E.g. maintaining or enhancing general digestion</strong></td>
<td><strong>E.g. colorectal cancer, nausea in pregnancy</strong></td>
</tr>
<tr>
<td>✓ Ease: supports existing lifestyle and may align well with mainstream behavioural goals such as weight loss</td>
<td>✓ Ease: potential for lack of motivation to try an alternative to clinical drugs if seeking immediate relief or treatment for a life-threatening condition</td>
</tr>
<tr>
<td>✓ Audience: very broad; could include athletes, mothers, and sufferers of general digestive disorders, including nausea</td>
<td>✓ Audience: potentially niche (limited to sufferers of specific conditions)</td>
</tr>
<tr>
<td>✓ Frequency: potentially habitual</td>
<td>✓ Frequency: not necessarily conducive to frequent use or purchase of fresh ginger products if symptoms treating are sporadic</td>
</tr>
<tr>
<td>! Caution: could general prevention be too fluffy?</td>
<td>! Caution: risky attempting to base claims on serious conditions such as cancer that involve several interacting pharmacological actions</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Specific</th>
<th>Prevention</th>
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<tbody>
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<tr>
<td>! Caution: could general prevention be too fluffy?</td>
<td>! Caution: lack of immediate gratification risks loss of motivation</td>
</tr>
</tbody>
</table>

4. **Previous literature reviews**

**Why?** The most recent existing literature reviews were reviewed as a starting point in order to establish studies that have already been evaluated and the conclusions that have already been drawn. Recent reviews also indicated gaps in the science and established where clinical research has been lacking. It was then possible to evaluate the research that has been conducted since the last literature reviews, building on previous conclusions.

**Stage 2 – In-depth literature review**

*Note: the in-depth review replaces the originally labelled ‘meta-analysis’. This amendment to the methodology was based on there being few clinical studies and considerable variation in the dosages and treatment durations, making the studies difficult to combine and compare.*

**Purpose:** evaluate the literature within shortlisted categories to determine the strength of the support for the health benefits that represent the biggest opportunities.

- Shortlisted categories for in-depth review were:
  - Anti-emetic - pharmacological action
  - Gastroprotection - health benefit
  - Weight management - health benefit
  - Antioxidant - pharmacological action
  - Controls blood glucose and lipids - pharmacological action

- The most recent full papers per shortlisted category were purchased and reviewed

- Qualitative analysis carried out based on study narratives, including:
- Evaluation of the methodological quality of shortlisted studies, giving consideration to whether data is *in vitro* (using human cell cultures in the lab) or *in vivo* (in the human body), and the consistency of sample sizes, dosages, and outcome measures
- Implications for the AGI in the context of the project objectives
The health claims associated with ginger are extensive and come from many sources. To date little of the information about ginger has been aggregated in any comprehensive fashion (Ryder, 2014).

Figure 3 attempts to categorise the health benefits of ginger as a starting point for reviewing the literature.

Note that there is some overlap between the categories. This is because ginger may have beneficial effects towards several diseases through its multiple ‘pharmacological’ actions – “ginger may have beneficial effects toward cardiovascular disease through its actions counteracting inflammation, hyperlipidemia, platelet aggregation, and hypertension” (Singletary, 2010).

**Figure 3. Health benefits of ginger; and a framework for reviewing the literature**

<table>
<thead>
<tr>
<th>Broad clusters: Pharmacological actions and general health benefits</th>
<th>Sub clusters: Associated health benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gastroprotection</strong> General health benefit</td>
<td>Helps break down high protein foods like meat and beans</td>
</tr>
<tr>
<td></td>
<td>Relieves stomach upsets, indigestion, spasms, diarrhea, flatulence, IBS</td>
</tr>
<tr>
<td></td>
<td>Increases appetite</td>
</tr>
<tr>
<td></td>
<td>Alleviates colic in babies</td>
</tr>
<tr>
<td></td>
<td>Prevents gastric ulcers</td>
</tr>
<tr>
<td></td>
<td>Treatment for Crohn’s disease/ ulcerative colitis</td>
</tr>
<tr>
<td></td>
<td>Helps protect the stomach from the toxic effects of alcohol, NSAIDs and MSG</td>
</tr>
<tr>
<td><strong>Anti-emetic (nausea)</strong> Pharmacological action</td>
<td>Relieves morning sickness</td>
</tr>
<tr>
<td></td>
<td>Relieves chemotherapy related nausea</td>
</tr>
<tr>
<td></td>
<td>Relieves motion sickness</td>
</tr>
<tr>
<td></td>
<td>Prevents postoperative nausea</td>
</tr>
<tr>
<td><strong>Controls blood glucose and lipids</strong> Pharmacological action</td>
<td>Helps prevent ‘bad’ LDL cholesterol</td>
</tr>
<tr>
<td></td>
<td>Improves circulation</td>
</tr>
<tr>
<td></td>
<td>Improves energy production in the heart</td>
</tr>
<tr>
<td></td>
<td>Reduces risk of coronary artery and cardiovascular disease</td>
</tr>
<tr>
<td></td>
<td>Helps combat diabetes and insulin resistance</td>
</tr>
<tr>
<td></td>
<td>Lowers blood pressure/ prevents thrombosis</td>
</tr>
<tr>
<td><strong>Weight management</strong> General health benefit</td>
<td>Increases basal metabolic rate</td>
</tr>
<tr>
<td></td>
<td>Helps curb obesity</td>
</tr>
<tr>
<td><strong>Antioxidant</strong> Pharmacological action</td>
<td>Slows aging</td>
</tr>
<tr>
<td><strong>Anti-inflammatory</strong> Pharmacological action</td>
<td>Relieves joint pain, rheumatism in arthritis,</td>
</tr>
<tr>
<td></td>
<td>Reduces toothache, headaches, fever</td>
</tr>
<tr>
<td></td>
<td>Soothes sore muscles after exercise</td>
</tr>
<tr>
<td></td>
<td>Reduces risk of colorectal cancer</td>
</tr>
<tr>
<td><strong>Anti-cancer</strong> General health benefit</td>
<td>Chemopreventative</td>
</tr>
<tr>
<td></td>
<td>Suppresses growth of cancerous cells</td>
</tr>
<tr>
<td><strong>Anti-infection</strong> Pharmacological action</td>
<td>Fights infections</td>
</tr>
<tr>
<td></td>
<td>Anti-malaria and yellow fever</td>
</tr>
<tr>
<td><strong>Miscellaneous:</strong> • Effects on cognitive function • Effects on respiratory system</td>
<td>Memory boosting</td>
</tr>
<tr>
<td></td>
<td>Benefits conditions like Alzheimer’s/ Dementia</td>
</tr>
<tr>
<td></td>
<td>Alleviates asthma and breathlessness</td>
</tr>
<tr>
<td></td>
<td>Alleviates symptoms of the common cold</td>
</tr>
<tr>
<td></td>
<td>Relieves depression, mental stress, exhaustion, dizziness and anxiety</td>
</tr>
<tr>
<td></td>
<td>Increases testosterone levels, aphrodisiac, removes impotency, treats premature ejaculation</td>
</tr>
</tbody>
</table>

These categories were used as a framework for guiding the literature review.
In vitro research has revealed that ginger comprises hundreds of compounds and metabolites, many of which have not been studied in detail. The most extensively studied bioactive components include ‘gingerols’ and ‘shogaols’, especially [6]-gingerol and [6]-shogaol (Bode & Dong, 2011).

Literature reviews have concluded that in general preclinical data and preliminary findings suggest a variety of potential health benefits of ginger, although clinical trials supporting these benefits are relatively few (European Medicines Agency, 2012; Singletary, 2010).

Interest in the scientific research community has increased markedly over the last few years in determining the role of natural compounds in preventing disease, though many of the studies are descriptive and observational rather than mechanistic in nature.

There is currently a lack of standardisation of ginger supplements, and a lack of understanding on the mechanisms of the action of ginger and its constituents and on the effects of consumption over a long period of time (Bode & Dong, 2011). However, despite the need for more studies on how ginger exerts its positive effects in the human body, no recent studies appear to have found any adverse effects of consuming ginger.

“In spite of the lack of specific mechanistic information, use of ginger appears to be safe and its effects are mighty and amazing in its many applications” (Bode & Dong, 2011).

Contents

Shortlisted categories for in-depth review
1. Gastroprotection
2. Anti-emetic
3. Controls blood glucose and lipids
4. Weight management
5. Antioxidant
6. Anti-inflammatory

Other categories
7. Anti-cancer
8. Anti-infection
9. Miscellaneous

Previous literature reviews
Shortlisted categories for in-depth review

1. **Gastroprotection** *(general health benefit)*

Ginger was mentioned in the first century by the Greek philosopher Dioscorides to have *digestive properties*, for stimulating the gut and as profitable for the stomach. Ginger has been an integral ingredient for managing digestive disorders and has been used to relieve gas and bloating and to prevent nausea and vomiting, motion sickness, stomach ache, stomach ulcers, bacterial dysentery and indigestion.

The stomach is an important organ for sustenance and healthy living. It is also very sensitive and there is a need for effective alternative natural approaches that are without side effects.

In a recent literature review Haniadka et al (2013) summarised the various gastroprotective effects of ginger and concluded that; “*ginger has the potential [as a] non-toxic broad spectrum gastroprotective agent when gaps existing in knowledge are bridged*”. It must be noted that their statement is drawn from preclinical evidence and further clinical studies are required before firm conclusions can be drawn.

The European Medicines Agency (2012) reviewed the available literature and reported that “*powdered ginger in single dosages of 1000-2000mg seems to modify gastric muscular contractions and increase gastric emptying*”. However the relevance of these findings regarding health benefits to humans is still unclear.

Gastroprotection: Summary of the literature

The gastroprotective health benefits of ginger can be divided into three groups:

1. **Indigestion** *(relieving gas, bloating and stomach discomfort)*
2. **Stomach ulcer** *(protecting the stomach against stresses, such as chemical and bacterial toxins)*
3. **Hyperglycemia** *(relieving diabetes-related stomach discomfort)*

1. **Indigestion**

- **Flatulence**: in a clinical study Lohiriwat et al (2010) found that ginger enhances relaxation of the lower esophageal sphincter, decreasing esophageal contraction velocity, which possibly mediates the anti-flatulence effects of ginger.

- **Gastric emptying**: a recent RCT demonstrated that ginger speeds up gastric emptying in patients with functional dyspepsia (Hu et al, 2011). However this study did NOT find that ginger impacts on the size of the ‘fundus’ (upper part of the stomach associated with reflux and bloating), regulation of hunger or post-meal blood glucose – and importantly, *despite more rapid emptying, ginger had no effect on gastrointestinal symptom scores in the patients* (i.e. no perceivable benefit). This could have been because the researchers did not specifically select patients with delayed gastric emptying (which about 40% of patients with functional dyspepsia suffer from). So the *use of ginger as a treatment for digestive discomfort is not clear*, and further studies are required of longer treatment.

- Ginger has also been shown in several *in vitro* and animal studies to be protective against chemotherapy drug and induced stomach discomfort and delayed gastric emptying time (Haniadka et al, 2013).

- **Nausea and vomiting** *(see ‘Anti-emetic’ category)*
2. Stomach ulcer

- Stomach ulcers associated with the use of aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) to relieve pain and inflammation is a major problem. Studies have shown a 15-30% prevalence of ulcers in the stomachs of patients taking NSAIDs regularly (Zaman et al, 2014). Stomach ulcers can also be caused by stress and by pathogenic bacteria in the gut such as Helicobacter pylori, which causes an overproduction of acid in the stomach. Scientists now know there is more to treating stomach ulcers than controlling the secretion of acid and that understanding the role of immune system receptors and responses are also important. Numerous animal studies have investigated the anti-ulcer efficacy of ginger (most recently; Zaman et al, 2014) as an alternative to anti-ulcer drugs.

- Recent results from animal studies (Zamal et al, 2014) indicate that ginger root extract has the potential to prevent the gastric damage resulting from NSAIDs. NSAIDs act by inhibiting the ‘cyclooxygenase’ pathway - the drawback being that the gastro-protective functions of ‘prostaglandins’ (which maintain gastric mucosal integrity) are inhibited at the same time. Ginger shows promise as a gastroprotective agent.

- In a literature review Haniadka et al (2013) document numerous animal studies that have shown gastroprotective efficacy of ginger against various ulcer-inducing stresses including: indomethacin (an anti-inflammatory and pain relief for gout and rheumatoid arthritis), aspirin, reserpine (an alkaloid compound used for hypertension), hypothermic restraint, pyloric ligation (a stomach binding method used in experiments), ethanol (alcohol), swim stress (causes an increase of acid in the lumen), acetic acid (e.g. in vinegar – in experiments it is used to induce blood clotting and inhibit certain enzyme activity), and Helicobacter pylori infection. These stresses generate free radicals, deplete antioxidant enzyme activity and inhibit mucus release. Pretreatment with ginger extract (at doses ranging from 100 – 1000mg) may be effective in decreasing gastric acid secretion and increasing mucus wall thickness in rats, thereby protecting against (induced) gastric stresses.

3. Hyperglycaemia

- Indigestion and other stomach ailments are common in people with diabetes, and affect the quality of life (Haniadka et al, 2013). One human trial indicated that ginger could play a beneficial role in the management of diabetes by mediating stomach complications associated with ‘hyperglycemia’ (Gonlachanvit et al, 2003).

- In people with diabetes the degree of glycaemic control can influence the magnitude of ‘gastric motor’ dysfunction (stomach contractions in digestion). In hyperglycaemia the emptying of the stomach is delayed. In an RCT with healthy volunteers, Gonlachanvit et al (2003) demonstrated a beneficial role of ginger in mediating these effects.
Gastroprotection: Possible mechanisms
The mechanisms are not well understood. Two key mechanisms of gastro protection are possibly by:

1. Inhibition of the ‘proton pump’ (pumps protons out of the cells and into the stomach cavity, making the stomach very acidic)
2. Growth of ‘Helicobacter pylori’ (a type of bacteria that causes infection in the stomach)

Some of ginger’s broad mechanisms of action described in Haniadka et al’s (2013) review are listed below. Note these are all based on in vitro and animal studies.

- **Antioxidant**
  - Scavenging for ‘free radicals’
  - Preventing oxidative damage to lipids (which prevents plaques forming in the arteries). On this Haniadka et al note that it is possible that ginger; “...mediates its protective effects on both stomach and vascular system through this mechanism and offers additional benefit to the individual”
  - Enhances antioxidant defense systems

- **Anti-inflammatory**
  - Suppresses the production of prostaglandin (by inhibiting enzymes COX-1, COX-2 and the biosynthesis of leukotriene by inhibiting 5-LOX – involved in immune responses)
  - The phytochemicals 8-paradol and 8-shogaol have strong inhibitory effects on COX-2
  - Ginger’s phytochemicals also decrease pro-inflammatory cytokines (important in cell signaling)

- **Modulates receptors in the nervous system** (e.g. serotonin, which is integral to intestinal contractions and digestion)

- **Modulates gut detoxifying enzymes**

- **Stimulates the secretion of mucin** (which acts as a buffer for the cell walls)

Specific mechanisms: (see Haniadka et al, 2013) for a detailed discussion and references)

- **In functional dyspepsia:**
  - Ginger decreases pressure on lower esophagus, reducing intestinal cramping, preventing indigestion, flatulence and bloating
  - Note: Hu et al (2011) did NOT demonstrate any modulation of gut-derived hormones that are known to effect gastric motility – including motilin (clearing out the gut), ghrelin (hunger), or GLP-1 (glucose)

- **In stomach ulcer:**
  - Suppressed gastric acid secretion increases mucus thickness, protecting cell walls
  - The protective action against toxins could be due to inhibition of ‘5-LOX’
- Anti-spasm activity could prevent gastric damage and ulcers by reducing the gastric emptying time, thereby decreasing the contact time of acidic gastric contents with the mucosa
- Enhanced antioxidant enzyme activity has also been suggested
- A ‘thromboxane synthetase’ inhibition (blood clotting) may also play a role

**In hyperglycemia:**
- Ginger prevents the production of prostaglandin

**Gastroprotection: Recommendation**
- The scientific evidence is unable to provide firm conclusions on ginger’s role as a treatment for gastric disorders
- Ginger as a general gastroprotective agent falls within the identified area of opportunity for engaging consumers – as a general preventative; enhancing digestive well-being
- There is an interesting link between ginger’s gastroprotective benefit for the stomach and the arteries, bridged by ginger’s antioxidant activity that is worth exploring. This link may add clout to the evidence for ginger as a general gastroprotective
- Ginger has also been shown to help in controlling blood sugar, which has both benefits to the stomach and a secondary protective role in diabetes. The scientific literature is not strong but it may add strength to the growing body of clinical evidence for a role of ginger in managing diabetes (e.g. Mahluji et al, 2013; Li et al, 2012 – see Blood glucose and lipids category)
- The anti-ulcer effect of ginger is not recommended for taking further at this stage as studies are all based on animals

**Library 1. Studies on the gastroprotective effects of ginger**

<table>
<thead>
<tr>
<th>Study design/subjects</th>
<th>Findings</th>
<th>Reference</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Rats                  | Dose: ginger (200mg/kg or 400mg/kg) or omeprazole (10mg/kg)  
Promising result: ginger root extract significantly inhibited the gastric damage induced by indomethacin and its efficacy as a gastroprotective agent was comparable to that of omeprazole  
Cond: ginger root is a promising gastroprotective agent | Zaman et al (2014) | Full paper reviewed  
Anti-ulcer  
Animal study |
| Ethanol (alcohol)-induced ulcers in male Wistar rats | Dose: oral ginger essential oil (GEO) 100, 500 and 1000 mg/kg body weight  
Promising results:  
- Ethanol-induced lesions such as dead tissue, erosion and hemorrhage of the stomach wall were significantly reduced  
- Oxidative stress produced by ethanol was significantly reduced  
Cond: GEO can reduce the gastric ulcer in rat stomach | Liu et al (2014) | Anti-ulcer  
Animal study |
| Literature review    | Promising result: free radical scavenging, antioxidant activity and inhibition of lipid peroxidation might have contributed to the observed gastroprotective effects | Haniadka et al (2013) | Full paper reviewed  
Gastroprotection |
<p>| RCT / 40 Iraqi        | Dose: mebeverine vs. powder capsule containing | Sahib (2013) | IBS |</p>
<table>
<thead>
<tr>
<th>Study Type</th>
<th>Study Details</th>
<th>Results</th>
<th>Caveats</th>
</tr>
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<tbody>
<tr>
<td><strong>Clinical study</strong></td>
<td><strong>14 healthy young men</strong></td>
<td><strong>Dose:</strong> 1g dried ginger powder suspended in 100ml water&lt;br&gt;&lt;br&gt;<strong>Promising result:</strong> showed greater likelihood of gastric gas expulsion or anti-flatulent effect</td>
<td><strong>Aspirin-induced gastric ulcer rat model</strong>&lt;br&gt;&lt;br&gt;<strong>Dose:</strong> group 1: 3 mL of 1% carboxymethylcellulose in water&lt;br&gt;group 2: ginger powder (200 mg/kg body weight) suspended in 3 mL of 1% carboxymethylcellulose in water&lt;br&gt;group 3: aspirin (200 mg/kg body weight) suspended in 3 mL of 1% carboxymethylcellulose in water&lt;br&gt;group 4: aspirin together with ginger powder suspended in 3 mL of 1% carboxymethylcellulose in water&lt;br&gt;&lt;br&gt;<strong>Conclusion:</strong> ginger powder prevents the aspirin induced gastric ulcer formation by reducing mucosal INOS activity and the plasma levels of inflammatory cytokines but does not affect gastric juice or acid production or mucosal PGE2 content&lt;br&gt;&lt;br&gt;<strong>Protective effect of ginger against gastric ulcers may be attributable to both gingerol and shogaols</strong></td>
</tr>
<tr>
<td><strong>RCT</strong> / 11 patients with functional dyspepsia</td>
<td><strong>Dose:</strong> 8 hour fast followed by 3x 1.2g ginger root powder capsules or placebo, followed by after 1 hour 500ml low-nutrient soup&lt;br&gt;&lt;br&gt;<strong>Promising results:</strong>&lt;br&gt;- Gastric acid more rapid after ginger than placebo&lt;br&gt;- More antral contractions after ginger than placebo&lt;br&gt;&lt;br&gt;<strong>Discouraging results:</strong>&lt;br&gt;- No differences in dimensions of the 'fundus' (upper part of the stomach), plasma concentrations of motilin (the 'housekeeper of the gut': it improves movement in the small intestine and clears out the gut to prepare for the next meal), ghrelin (the 'hunger hormone') or GLP-1 (regulation of glucose post-meal)&lt;br&gt;&lt;br&gt;<strong>Caveats:</strong>&lt;br&gt;- Did not specifically include patients with delayed gastric emptying&lt;br&gt;- Low-nutrient soup only induced modest changes in bloating and fullness – future study might benefit from a higher calorie/lipid dense meal to provoke more symptoms, from which it might be possible to demonstrate an improvement with ginger&lt;br&gt;- Observation was limited to 90 min of gastric emptying, and a single dose of ginger would not have been adequate for treatment of dyspepsia symptoms in patients with functional dyspepsia, especially as this disease is chronic and recurrent</td>
<td><strong>Hu et al (2011)</strong>&lt;br&gt;&lt;br&gt;<strong>Full paper reviewed</strong>&lt;br&gt;&lt;br&gt;<strong>In Haniadka et al (2013)</strong>&lt;br&gt;&lt;br&gt;<strong>Gastric motility and functional dyspepsia Clinical study</strong></td>
<td></td>
</tr>
<tr>
<td><strong>RCT</strong> / 1 patients with functional dyspepsia</td>
<td><strong>Dose:</strong> combination of Mentha longifolia (mint), Cyperus rotundus (nut grass) and ginger – assessed before and after 8 weeks of treatment&lt;br&gt;&lt;br&gt;<strong>Promising result:</strong> patients with IBS showed significant improvement in symptoms after 8 weeks of treatment with a herbal combination of nut grass, mint and ginger&lt;br&gt;&lt;br&gt;<strong>Caveat:</strong> combined effect with other herbs</td>
<td><strong>(combined effects) Clinical study</strong></td>
<td></td>
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<tr>
<td>Study Type</td>
<td>Intervention</td>
<td>Outcome</td>
<td>Result</td>
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<tr>
<td>RCT/ 32 ARDS patients (adult respiratory distress syndrome)</td>
<td>Dose: placebo 1g coconut oil/ 120mg ginger extract</td>
<td>Promising results:</td>
<td>Ginger group had significantly higher nutritional intake during first 8 hours than control group.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Amount of intensive care/ ventilator free days was higher in the ginger group</td>
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<tr>
<td></td>
<td></td>
<td>Mechanism: benefits were ascribed to a reduction in delayed gastric emptying by ginger</td>
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<tr>
<td>Ulcer-induced rat experiment</td>
<td>Dose: 2x 100mg and 200/kg body weight 2x daily for 14 days</td>
<td>Promising results:</td>
<td>Ginger group had significantly higher nutritional intake during first 8 hours than control group.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Amount of intensive care/ ventilator free days was higher in the ginger group</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Mechanism: benefits were ascribed to a reduction in delayed gastric emptying by ginger</td>
<td></td>
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<tr>
<td>RCT / 24 healthy volunteers</td>
<td>Dose: 8 hour fast followed by 3x 1200mg capsules ginger or placebo, followed by after 1 hour 500ml low-nutrient soup</td>
<td>Promising result: ginger accelerated gastric emptying and stimulated antral contractions in healthy volunteers</td>
<td></td>
</tr>
<tr>
<td>RCT/ 22 healthy and hyperglycaemic volunteers</td>
<td>Dose: 1g ginger root powder</td>
<td>Promising result: prevented the induction of slow wave dysrhythmias induced by hyperglycemic clamping (which delays gastric emptying)</td>
<td></td>
</tr>
<tr>
<td>RCT/ 12 healthy volunteers</td>
<td>Dose: 200mg ginger rhizome extract</td>
<td>Promising results:</td>
<td>Increase in interdigestive antral motility Improved gastroduodenal motility in the fasting state and after a standard meal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Note: did not measure gastric emptying</td>
<td></td>
</tr>
<tr>
<td>RCT/ 16 healthy volunteers</td>
<td>Dose: 1g (2 capsules) powdered ginger root or placebo</td>
<td>Measure: oral paracetamol absorption model</td>
<td>Discouraging result: ingestion of ginger did NOT effect gastric emptying. The anti-emetic effect of ginger is NOT associated with an effect on gastric emptying</td>
</tr>
</tbody>
</table>

**Full references**


2. **Anti-emetic (pharmacological action)**

In “Ginger in Australian Food and Medicine” Leonie Ryder (2014) documents ginger’s history of use as a treatment for stomach disorders, indigestion and nausea since it was brought to Australia from Britain in 1788 (Ryder, 2014). Ryder says; “The obsession with digestion [in Australia] is illustrated clearly in domestic medicine text...”.

Whether ginger is truly efficacious for indigestion and nausea is still a matter of debate and dependent on the context in which it is used for treatment - i.e. following pregnancy, surgery, cancer, motion sickness etc. As the mechanisms behind any anti-emetic action of ginger is not well characterised, and dosages, latency and length of response periods vary across the studies reviewed, existing literature reviews (e.g. Viiljoen et al, 2014; Singletary, 2010) have concluded that further human trials are needed before recommendations can be made.

The literature on ginger’s anti-emetic effects appears to be by far the most extensive. Additional RCTs to those included in Library 2 can be found in the literature reviews listed in the table.
Anti-emetic: Summary of the literature
The anti-emetic health benefits of ginger can be divided into four groups:

1. Early pregnancy
2. Post-operative
3. Motion sickness
4. Chemotherapy

1. Early pregnancy
   - Evidence is some of the strongest (European Medicines Agency, 2012; Singletary, 2010). Singletary’s conclusion has continued to be supported by the most recent literature reviews of RCTs; e.g. Viljoen et al (2014) found promising results for ginger as a harmless alternative option for women suffering nausea and vomiting in early pregnancy. However, the review caveat this statement due to the limited number of good quality studies and quality of evidence.
   - The European Medicines Agency (2012) reviewed 10 RCTs. In 5 studies ginger was compared to placebo, and in 4 studies ginger was compared to vitamin B6. Different measurement scales were used, though most used validated scales (Rhode’s Index/VAS). Dosages and treatment periods were reasonably consistent: between 1000 and 1500 mg for 3-4 days. Most studies demonstrated that ginger was better or similar to vitamin B6 in relieving nausea and vomiting, though vitamin B6 may not be the best comparator as its efficacy is uncertain. The conclusion was that there is sufficient scientific documentation to claim efficacy of ginger root in the prevention of pregnancy-induced nausea and vomiting.

2. Post-operative
   - Most research has been gynecological and results are not consistent (European Medicines Agency, 2012; Singletary, 2010), possibly due to large inconsistencies in the dosages across the studies reviewed (0.3g/d – 2g/d)
   - The European Medicines Agency (2012) reviewed 8 RCTs and concluded that there is sufficient scientific documentation to claim efficacy of ginger root in the prevention of post-operative nausea and vomiting.

3. Motion sickness
   - Studies are quite dated, and there is a lack of consistent beneficial effect of ginger for use on motion sickness (Haniadka et al, 2013; Singletary, 2010)
   - The European Medicines Agency (2012) reviewed 8 RCTs. Five of the studies induced motion sickness (e.g. rotating chair), while only 2 examined the efficacy in a real life situation. In 5 studies ginger was superior to the placebo in preventing motion sickness and as effective as other commonly used agents. Although the effect size was generally small the conclusion was that the scientific evidence does demonstrate an effect of ginger in preventing motion sickness.
4. Chemotherapy

- There is limited evidence from animal models that ginger has anti-emetic activity in reducing the adverse effects of agents used in chemotherapy, and results from human studies are mixed (Singletary, 2010). The most recent literature reviews of human trials (Haniadka et al, 2013; Marx et al, 2013) concluded that the area of chemoprevention research is the most conflicting.

- The European Medicines Agency (2012) reviewed 4 RCTs, two of which did not demonstrate an effect of powdered ginger taken in connection with chemotherapy, and one (promising study) had dubious methodology. The conclusion was that there is insufficient evidence to claim an effect of ginger on chemotherapy-induced nausea and vomiting.

Anti-emetic: Possible mechanisms

Further research is needed to confirm whether ginger acts on the gastrointestinal tract (as suggested by Lumb, 1993) or on the central nervous system.

- In humans ginger may block production of gastric ‘prostaglandins’ (mediators that regulate the contraction and relaxation of smooth muscle tissue) and decrease plasma vasopressin release (a hormone) induced by circular vection (the illusion of self-motion induced by rotating visual or auditory stimuli).

- In animals ginger constituents may block ‘5-HT3 receptors’ (serotonin receptors that modulate the release of neurotransmitters), as well as having an effect on other peripheral receptors involved in smooth muscle contraction in the gastrointestinal tract.

- NK1 antagonist (specifically related chemotherapy), antihistaminic and prokinetic effects (enhances gastrointestinal motility by increasing the frequency of contractions in the small intestine or making them stronger, but without disrupting their rhythm).

- Ginger juice produces anti-motion sickness action possibly by central and peripheral anticholinergic and antihistaminic effects (Qian & Liu, 1992). Some researchers hypothesise that ginger ameliorates the nausea associated with motion sickness by preventing the development of gastric dysrhythmias and the elevation of plasma vasopressin (Lien et al, 2003).

Anti-emetic: Recommendation

- The anti-emetic effect of ginger has received much attention by research, with promising results.

- The literature indicates that anti-emetic effects should be developed as a potential health benefit for engaging consumers - especially as it falls within the identified area of opportunity: a general prevention for nausea (the evidence is less strong for vomiting). However the literature does not support ginger’s efficacy as a broad spectrum anti-emetic.

- Ginger as an alternative prevention for nausea in early pregnancy appears to be receiving the most attention recently and should be considered for shortlisting. Ginger’s role in preventing motion sickness is also an area with strong support and should be considered, though clinical studies are quite old.
### Library 2. Studies on the anti-emetic effects of ginger

<table>
<thead>
<tr>
<th>Study design/subjects</th>
<th>Findings</th>
<th>Reference</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Literature review and meta-analysis (12 RCTs)</td>
<td></td>
<td>Viljoen et al (2014)</td>
<td>FIND FULL PAPER</td>
</tr>
<tr>
<td>Data sources: RevMan5 software (Cochrane Collaboration) used for analysis</td>
<td>Dose: &lt;1500mg daily</td>
<td></td>
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<tr>
<td></td>
<td>Promising results:</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>• Significantly improved the symptoms of nausea when compared to placebo</td>
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<td></td>
<td>• No risk for abortion compared to placebo, or vitamin B6. No sig risk for heartburn or drowsiness</td>
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<tr>
<td></td>
<td>Discouraging result: did NOT significantly reduce the number of vomiting episodes</td>
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<tr>
<td></td>
<td>Conc: (with caveats) ginger could be considered a harmless and possibly effective alternative option for women suffering nausea and vomiting in pregnancy</td>
<td></td>
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<tr>
<td>Literature review (4 RCTs)</td>
<td></td>
<td>Ding et al (2013)</td>
<td>Pregnancy</td>
</tr>
<tr>
<td>Data sources: CINAHL, the Cochrane Library MEDLINE and TRIP</td>
<td>Promising results:</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>• All studies found orally administered ginger to be more effective than placebo in reducing the frequency of vomiting and intensity of nausea</td>
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<tr>
<td></td>
<td>• Adverse effects generally mild and infrequent</td>
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<tr>
<td>RCT/ pregnant women</td>
<td>Dose: 250mg ginger 4x daily/ 40mg vitamin B6 4x daily</td>
<td>Haji Seid Javadi et al (2013)</td>
<td>Pregnancy</td>
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<tr>
<td></td>
<td>Promising result: ginger reduced nausea the same as vitamin B6</td>
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<tr>
<td></td>
<td>Discouraging result: vomiting was greater reduced by vitamin B6 (but not significant)</td>
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<tr>
<td>Literature review</td>
<td>Discouraging result: anti-emetic effects were inconclusive</td>
<td>Haniadka et al (2013)</td>
<td>Broad anti-emetic</td>
</tr>
<tr>
<td>Norwegian Mother and Child Cohort study – population based/ 68,522 women</td>
<td>Promising result: the use of ginger during pregnancy was not associated with increased risk</td>
<td>Heitmann et al (2013)</td>
<td>Pregnancy (safety)</td>
</tr>
<tr>
<td>RCT/ 239 women who underwent elective cesarean section at term</td>
<td>Dose: 2x capsules of 1g powdered ginger – 1x capsule half-hour before induction of anesthesia and 1x capsule 2h after surgery</td>
<td>Kalava et al (2013)</td>
<td>Postoperative Gynaecology</td>
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<tr>
<td></td>
<td>Promising results:</td>
<td></td>
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<tr>
<td></td>
<td>• Intraoperative incidence of nausea was 52% and 61%, ginger versus placebo</td>
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<td></td>
<td>• Number of episodes of intraoperative nausea was less in the ginger group compared to placebo</td>
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<td></td>
<td>• Incidence of intraoperative vomiting was 27.35% in the ginger group and 36.59% in the placebo group (but insignificant)</td>
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<td></td>
<td>• Fewer episodes of vomiting during surgery in the ginger group compared to placebo (but insignificant)</td>
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<td></td>
<td>Discouraging results:</td>
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<tr>
<td></td>
<td>• No statistical difference in the incidence of nausea and vomiting assessed at 0, 2, 2 ½ and 24h after surgery</td>
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<td></td>
<td>• No differences in post-operative pain or pruritus</td>
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<td></td>
<td>Conc: dry powdered ginger reduced the number of episodes of intraoperative nausea compared to a placebo, but it had no effect on incidence of nausea, vomiting, or pain during and after an elective cesarean section performed under combined spinal epidural anesthesia</td>
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<td></td>
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<tr>
<td>Literature review</td>
<td>Discouraging result: mixed support of ginger as an anti-</td>
<td>Marx et al (2013)</td>
<td></td>
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<tr>
<td>Study Design</td>
<td>Sample</td>
<td>Treatment</td>
<td>Outcome</td>
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<tr>
<td>RCT/ 76 patients</td>
<td>Chemo patients</td>
<td>Dose: 0.3-1g ginger daily along with 5-HT(3) receptor antagonist anti-emetic on day 1 of all cycles</td>
<td>Promising result: supplementation with ginger reduced the severity of acute chemotherapy-induced nausea</td>
</tr>
<tr>
<td>RCT/ children &amp; young adults 8-21y</td>
<td>Chemo patients</td>
<td>Dose: ginger powder or starch: patients weighing 20-40 kg received 1000mg per day (6x 167mg capsules)/ patients weighing over 40 kg received 2000mg per day (3x 400mg capsules) from days 1-3 of the chemo cycle</td>
<td>Measure: Edmonton’s Symptom Assessment Scale</td>
</tr>
<tr>
<td>RCT/ 70 pregnant women &gt;20 weeks</td>
<td>Chemo patients</td>
<td>Dose: 250mg ginger root powder capsules 4x daily for 4 days/vitamin B6/ placebo: lactose</td>
<td>Measure: 100mm VAS</td>
</tr>
<tr>
<td>RCT/ 644 patients receiving chemo for breast, GI &amp; lung cancer</td>
<td>Chemo patients</td>
<td>Dose: 0.3-1g ginger daily</td>
<td>Promising result: helped reduce nausea in chemo patients (assessed on 7-point scale) significantly better than standard anti-nausea drugs and placebo</td>
</tr>
<tr>
<td>RCT/ 126 pregnant women &lt;16 weeks</td>
<td>Chemo patients</td>
<td>Dose: 325mg powdered ginger capsules/ 12.5mg vitamin B6 3x 4x per day for 4 days</td>
<td>Measure: Rhode’s Index</td>
</tr>
<tr>
<td>RCT/ 170 pregnant women &lt;16 weeks</td>
<td>Chemo patients</td>
<td>Dose: 0.5g ginger powder/ 50mg dimenhydrinate 2x daily for 1 week</td>
<td>Measure: 100mm VAS</td>
</tr>
<tr>
<td>Mode of action study</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>RCT/ 60 inpatients</td>
<td>Chemo patients</td>
<td>Dose: 1.5g powdered ginger (3 capsules of 0.5g)</td>
<td>Promising result: significant efficacy compared to placebo in prevention of nausea in inpatients who underwent laparoscopic operations for non-cancer gynaecological conditions 6 hours post-op (assessed by Visual Analogue Scores)</td>
</tr>
<tr>
<td>Literature review</td>
<td></td>
<td>Dose: at least of 1g of ginger</td>
<td></td>
</tr>
<tr>
<td>Literature review</td>
<td>Promising results</td>
<td>Caveat</td>
<td>Data sources</td>
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<tr>
<td>and meta-analysis (5 RCTs)</td>
<td>Promising results:</td>
<td>Caveat: studies did not report amount or quality of active ingredients</td>
<td>Medline, IPA, CINAHL, Cochrane CENTRAL, Healthstar, Current</td>
</tr>
<tr>
<td>Literature review</td>
<td>Promising results:</td>
<td>Caveat: inconsistent outcome measures and different control groups (i.e. placebo and reference drug) in the RCTs</td>
<td>MEDLINE, EMBASE, and the Cochrane-Library (24 trials of patients)</td>
</tr>
<tr>
<td>Literature review</td>
<td>Promising results:</td>
<td>Caveat: specific profile for each extract used in the studies is not known</td>
<td>Literature review (6 RCTs)</td>
</tr>
<tr>
<td>Literature review</td>
<td>Promising results:</td>
<td>Caveat: studies did not report amount or quality of active ingredients</td>
<td>RCT/48 gynecologic cancer patients receiving cisplatin – based chemo</td>
</tr>
<tr>
<td>Literature review</td>
<td>Promising results:</td>
<td>Caveat: more women were aware that they were allocated to ginger than to vitamin B6</td>
<td>RCT/291 women 8-16 weeks pregnant</td>
</tr>
<tr>
<td>Literature review</td>
<td>Promising results:</td>
<td>Caveat: did not appear to increase the rates of major malformations above the baseline rate of 1% to 3%</td>
<td>RCT/187 pregnant women in first trimester Compared with women exposed to nonteratogenic</td>
</tr>
</tbody>
</table>

In European Medicines Agency (2012), Bode & Dong (2011) and Singletary (2010)
<table>
<thead>
<tr>
<th>Study Type</th>
<th>Participants</th>
<th>Intervention</th>
<th>Outcome Measures</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT/120 women &gt;20 weeks pregnant</td>
<td>120 women</td>
<td>125mg ginger extract capsules (equiv. 1.5g dried ginger) 4x daily for 4 days</td>
<td>Rhode’s Index</td>
<td>Promising result: nausea experience score was significantly less in the ginger group compared to placebo group after the first day of treatment (which continued for 4 days). Discouraging result: no significant effect observed for vomiting.</td>
</tr>
<tr>
<td>RCT/70 women &gt;17 weeks pregnant</td>
<td>70 women</td>
<td>250mg capsule powdered ginger 4x daily for 4 days</td>
<td>100mm VAS</td>
<td>Promising results: After 4 days, the proportion of women vomiting in the ginger group was significantly less than placebo. Fewer vomiting incidents in the ginger group compared to placebo. At follow-up visit, 28/32 women in the ginger group reported improved symptoms compared to 10/35 in the placebo group.</td>
</tr>
<tr>
<td>Literature review (6 RCTs)</td>
<td></td>
<td></td>
<td></td>
<td>Promising results: Collectively, a study each on seasickness, morning sickness, and chemotherapy-induced nausea favoured ginger over placebo. 2/3 studies on post-operative nausea &amp; vomiting suggested ginger was superior to placebo and equally effective as metoclopramide. Concl: a promising anti-emetic, but clinical data insufficient to draw firm conclusions.</td>
</tr>
<tr>
<td>RCT/120 female outpatients</td>
<td>120 female outpatients</td>
<td>2x capsules of 0.5g ginger and 0.5ml saline (through IV)/2 capsules 0.5g and 1.25mg droperidol</td>
<td></td>
<td>Discouraging results: no significant differences in the incidence of nausea and vomiting frequency between the 4 study groups.</td>
</tr>
<tr>
<td>RCT/28 volunteers</td>
<td>28 volunteers</td>
<td>Powdered ginger root 500 or 1000mg/fresh ginger root 1000mg</td>
<td>Number of timed head spins in a rotating chair</td>
<td>Discouraging results: ginger does not possess anti-motion sickness activity, nor does it alter gastric function during motion sickness. Caveat: non-blinded and experimentally induced nausea.</td>
</tr>
<tr>
<td>RCT/80 naval cadets who were “unaccustomed to sailing in heavy seas”</td>
<td>Naval cadets</td>
<td>1g powdered ginger/ placebo: lactose</td>
<td></td>
<td>Promising result: ginger root reduced the tendency to vomiting and cold sweating significantly better than the placebo. Discouraging result: no difference between ginger and placebo in severity of nausea.</td>
</tr>
</tbody>
</table>

**Literature databases used:** Medline, Embase, Biosis, CISCOM, Cochrane Library.
RCT/ 36 men and women reporting “very high susceptibility to motion sickness”

**Dose:** 2x 940mg gelatin capsules of powdered ginger/100mg dimenhydrinate/placebo: powdered chickweed (taken 25mins before induced nausea)

**Promising result:** ginger observed to be more effective than the antihistamine dimenhydrinate and a placebo in reducing induced motion sickness

**Caveat:** experimentally induced nausea (rotating chair)

**Mowrey & Clayson (1982)**

**In European Medicines Agency (2012) and Bode & Dong (2011)**

**Motion sickness Clinical study**

---

**Full references**

- Wilkinson, J.M. 'What do we know about herbal morning sickness treatments? A literature survey.' Midwifery. 2000b;16(3):224-8
- Grontved, A., Brask, T., Kambskard, J. and Hentzer, E. Department of Oto-Rhino-Laryngology, Svedborg Hospital, Denmark. 'Ginger root against seasickness. A controlled trial on the open sea'. ACTA OTOLARYNGOL (Stockh) 1988, 105 (1-2):45-49
3 Controls blood glucose and lipids *(pharmacological action)*

In terms of ginger’s effects on the blood, the evidence is strongest regarding the role of ginger in the treatment and prevention of diabetes mellitus (type 2 diabetes).

Approximately 3.61 million Australians have diabetes or pre-diabetes, and 366 million people have diabetes worldwide (Australian Diabetes Council, 2014). Diabetes can lead to a number of complications including cardiovascular diseases and neuronal injury induced by ‘hyperglycemia’ *(an excess of glucose – sugar - in the blood)*.

Diabetes is a metabolic disorder of lipids *(fat/ cholesterol)* and carbohydrate.

Cardiovascular diseases are the leading cause of death in diabetic patients. ‘Dyslipidemia’ *(abnormal amount of cholesterol and fat in the blood)* is the most important modifiable risk factor for atherosclerosis *(fatty arteries)* in diabetic patients. Insulin sensitivity can control blood sugar and moderate diabetes-related dyslipidemia.

Effective control of hyperglycaemia in diabetic patients is critical but side effects of the presently available hyperglycaemia drugs have impeded their usefulness as anti-diabetic agents. This has led to continuous effort to explore effective agents for the control of diabetes.

**Controls blood glucose and lipids: Summary of the literature**

- Up until very recently there have been few clinical studies
- Preliminary clinical trials showed that ginger improved lipid profiles in diabetic patients (Andallu et al, 2003)
- Data from recent clinical trials have demonstrated the ‘anti-hyperglycemic’ effect of ginger (Arablou et al, 2014; Mahluji et al, 2013; Li et al, 2012). However the research is inconsistent with regard to ginger’s effect on blood lipids *(e.g. HDL and LDL cholesterol)*
- Arablou et al (2014) investigated the effect of ginger on glycaemic status, lipid profile, and inflammatory markers in patients with type 2 diabetes, and found that ginger reduced fasting blood glucose and insulin, and increased insulin sensitivity. These findings support those of Mahluji et al (2013), who also found that ginger reduced insulin, though the two studies did not align on whether ginger lowers fasting blood glucose. This difference may be attributable to the longer duration of Arablou et al’s study
- Consistent with Arablou et al; Alizadeh et al (2008) also found that ginger had no effect on the HDL and LDL cholesterol ratio but did have an effect on *total* cholesterol in hyperlipidemic patients
- Bordia et al (1997) found NO significant changes in blood lipids in patients with diabetes
- It should be noted that the recent clinical evidence is hugely encouraging compared to earlier studies that led previous authors of literature reviews to conclude *(e.g. Li et al, 2012; European Medicines Agency, 2012)* that there is insufficient evidence to document an effect of ginger on blood glucose
In vitro studies indicate that ginger has insulin sensitising and glucose uptake enhancing effects (e.g. Rani et al, 2012; Kato et al, 2006). A number of studies have demonstrated that ginger possessed prominent lipid lowering effects, and subsequently increased insulin sensitivity (see Li et al, 2012).

Animal studies have had conflicting results. In type 2 diabetes-induced rats the majority of studies demonstrated protective effects of ginger in the development of various parameters of metabolic syndrome, and concurred that ginger is effective in decreasing serum TG (which is consistent with the findings of Arablou et al, 2014). In normal animals the findings were less consistent (see Li et al, 2012 for a full review).

Diabetic complications

Animal and in vitro studies have demonstrated the protective potential of ginger for diabetic complications (see Li et al, 2012 for a full review). These include protective effects on the:

- Liver
- Kidney
- Central nervous system
- Eye

Other effects on the blood

Blood clotting (antiplatelet activity)

- There are only a few small non-methodologically sound investigations in this area and more clinical studies are needed to test the effects of ginger on blood clotting biomarkers (European Medicines Agency, 2012; Singletary, 2010).
- Caution when taking ginger and other herbal extracts has been suggested because of an apparent association of ginger with reported incidences of increased risk of bleeding following surgery or if taken with anticoagulant drugs such as Warfarin (Kruth et al, 2004) - however, the data are not conclusive.
- Possible mechanisms of action: Inhibition of the formation of ‘thromboxane B2’ (a precursor to platelet aggregation) and inhibition on platelet COX enzyme.
- The 8-gingerol and 8-paradol may be the major active principles that inhibit platelet aggregation.

Blood pressure (hypertension)

- Ginger possibly lowers blood pressure by inhibiting voltage-dependent calcium channels, and by stimulating muscarinic receptors – however research is based on animal studies and the exact mechanism needs to be better defined as individual gingerols and shogaols constituents of ginger appear to exhibit dissimilar actions with regard to blood vessel reactivity.
Controls blood glucose and lipids: Possible mechanisms

- **Inhibits enzymes in carbohydrate metabolism**
  - The key enzymes controlling carbohydrate metabolism associated with hyperglycemia and type 2 diabetes are *α-amylase* and *α-glucosidase*. A recent *in vitro* study demonstrated that the action of ginger against these two enzymes correlated with the phenolic contents of gingerol and shogaols.

- **Inhibits prostaglandin E2 (PGE2) enzyme activity**
  - PGE2 is involved in inflammatory responses. Chronic low grade inflammation and activation of the immune system are closely involved in the pathogenesis of diabetes.

- **Increases insulin release and sensitivity**
  - Gingerols, shogaols, paradols and zingerones may increase GLUT4 protein insulin receptors (*i.e. insulin regulated glucose transport*), improving B-cells function in humans (Mahluij et al, 2013).
  - *In vivo* (in animals), the underlying mechanism may involve interaction with the 5-HT3 receptors (serotonin).
  - Reduction of ‘ChREBP’ (*carbohydrate-responsive element-binding protein*) gene expression in the liver, decreasing fat accumulation in the liver and improving insulin resistance.

- **Improves lipid profiles**
  - Excessive free fatty acid and fatty acid oxidation inhibits glucose transport into peripheral tissues (*which limits glucose metabolism*).
  - Increased liver cholesterol ‘7 α-hydroxylase’ enzyme activity, and the conversion of cholesterol into bile acids; resulting in reduced cholesterol concentration.
  - Increases LDL particle size and reduces uptake of oxidized LDL by macrophages (*cells that remove dying or dead cells; very important in chronic inflammation*).

**Controls blood glucose and lipids: Recommendation**

- The most recent literature review represents, bar two studies, the most up to date status of the evidence on ginger’s role in blood glucose control. There is strong scientific support.

- Diabetes has reached an epidemic scale worldwide, including in Australia, therefore treating or preventing diabetes and blood glucose problems may be positioned in the ‘General’ realm of opportunity areas for the AGI.

- Diabetes is associated with obesity and related to weight management. These are topical issues associated with metabolism, and likely to resonate with consumers. It is recommended that ginger’s effects on blood glucose and lipids be shortlisted for communications, as key actions relating to metabolic conditions.
**Library 3. Studies on the effects of ginger on blood glucose and lipids**

<table>
<thead>
<tr>
<th>Study design/subjects</th>
<th>Findings</th>
<th>Reference</th>
<th>Comments</th>
</tr>
</thead>
</table>
| **RCT/ 70 type 2 diabetic patients** | Dose: 1600mg ginger vs. 1600mg wheat flour daily (one capsule before dinner/ one after dinner) for 12 weeks  
Promising result: ginger can reduce blood glucose and insulin levels, improve insulin sensitivity, reduce serum cholesterol and TG and decrease inflammation by reducing CRP and PGE2 levels  
(CRP= C-reactive protein - rises in response to inflammation and is a cardiovascular risk factor)  
(PGE2= prostaglandin enzyme - involved in relaxing smooth muscles)  
(no differences in HDL, LDL and TNFa between groups)  
Concl: ginger improved insulin sensitivity, some functions of lipid profile in type 2 diabetes patients – ginger can be considered an effective treatment for prevention of diabetes complications. | Arablou et al (2014) | Full paper reviewed  
Diabetes complications  
Clinical study |
| **RCT/ 64 type 2 diabetic patients** | Dose: 2g/d for 2 months  
Promising result: ginger significantly lowered levels of insulin, HOMA, TG and LDL  
(no difference in FPG, HbA1c, total cholesterol and HDL)  
Concl: ginger may be considered a useful remedy to reduce the secondary complications of type 2 diabetes – further studies required with large doses of ginger and longer duration of intervention | Mahluji et al (2013) | Full paper reviewed  
Diabetes complications  
(preliminary) Clinical study |
| **Literature review** | Promising result: ginger shows effective glycaemic control properties in diabetes mellitus  
- The prominent lipid lowering effects of ginger contribute to improving insulin resistance  
- A protective effect of ginger against diabetic complications is an important aspect of its benefits  
Safety: sufficient acute and chronic toxicity studies have demonstrated the broad safety of ginger as a complementary hyperglycemic control agent  
Mechanisms: associated with the inhibition of key enzymes controlling carbohydrate metabolism and increased insulin release/ sensitivity, resulting in enhanced glucose uptake in peripheral adipose and skeletal muscle tissues | Li et al (2012) | Full paper reviewed  
Diabetes complications |
| **Mode of action study - antioxidant and anti-diabetic potential** | Promising result: the anti-diabetic effect of ginger was experimentally proven  
Mechanism: initiated by antioxidant, anti-glycation and potential to express or transport Glut4 receptors from internal vesicles | Rani et al (2012) | In Li et al (2012)  
Diabetes complications  
in vitro |
| **RCT/ 32 obese men** | Concl: progressive resistance training for 10 weeks significantly reduces chronic low grade inflammation, insulin resistance, body composition, and therefore has been an effective therapeutic devise to reduction cardiovascular risk factors in obese individuals  
Ginger supplementation can also decrease chronic low grade inflammation in obese men  
More research is required to elicit the effect of this supplement on cardiovascular risk factors in humans | Atashak et al (2011) | Obesity complications  
– resistance training  
Animal study |
<p>| <strong>Diabetic rats</strong> | Dose: distilled water (as vehicle) or 200 mg/kg body weight of ginger rhizome powder for 28 days | Madkor et al (2011) | In Li et al (2012) |</p>
<table>
<thead>
<tr>
<th>Study Type</th>
<th>Results</th>
<th>Conclusions</th>
</tr>
</thead>
</table>
| Diabetes complications Animal study | **Promising result:** Increased production of insulin, enhanced antioxidant defense system and decreased lipid peroxidation  
**Concl:** BUT garlic appears to have more impact than ginger and turmeric in alleviating the risks of the metabolic syndrome and cardiovascular complications |  |
| Diabetic rats       | **Promising result:** ginger decreased blood glucose significantly  
- Marked decrease in antioxidant marker enzymes, superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GR), reduced glutathione (GSH) and increase in malondialdehyde (MDA) observed  
- Decreased activities of antioxidant enzymes in diabetic rats were augmented on oral administration of ginger  
- Ginger depleted the MDA level, which was earlier increased in the diabetic rats  
**Concl:** results suggest that ginger has a neuroprotective effect by accelerating brain antioxidant defense mechanisms and down regulating the MDA levels to the normal levels. Thus, **ginger may be used as therapeutic agent in preventing complications in diabetic patients** | Shanmugam et al (2011) |
| Rats on a high fat diet | **Promising results:**  
- Effect of ginger on reduction of blood glucose and insulin  
**Mechanisms:**  
- Mediation through 6-gingerol and 6-shogaol  
- Effected the up-regulation of liver LDL receptor expression and down-regulation of liver 3-hydroxy-3-methylglutaryl coenzyme A expression | Nammi et al (2009) |
| Literature review    | Trials in humans have been few and generally used a low dose with inconclusive results  
**Promising results:** anti-platelet activity of doses of 5g or more  
**Concl:** more standardized human trials needed | Nicoll & Henein (2009) |
| Diabetic mice       | **Dose:** 100mg/kg body weight  
**Positive results:**  
- [6]-gingerol decreased fasting blood glucose and improved glucose tolerance  
- Lowered plasma triglyceride, total cholesterol, free fatty acid, LDL and plasma insulin levels | Singh et al (2009) |
| RCT/ hyperlipidemic patients | **Dose:** 3g ginger powder per day (6 capsules) for 45d  
**Promising result:** significant lipid-lowering effect compared to placebo, including total serum cholesterol  
**Mechanisms:** inhibits the biosynthesis of cholesterol in the liver  
**Caveat:** did not control for diet and physical activity | Alizadeh et al (2008) |
| Combined high fat diet/ STZ-induced type 2 diabetic animal model | **Dose:** 8 groups including: Control, Diabetic Control, Ginger Low, Ginger High, "Low" and "High" indicate addition of 0.5% and 2.0% freeze-dried ginger powder in the diets. 4 wks. feeding  
**Positive result:** better glucose tolerance and enhanced serum insulin concentration observed in ginger treated rats  
**Concl:** suggests **ginger is insulinotropic rather than hypoglycemic** | Islam & Choi (2008) |
<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Dose</th>
<th>Promising Results</th>
<th>Conclusion</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Al-Amin et al (2006)</td>
<td>Clinical study</td>
<td>500 mg/kg, intraperitoneally</td>
<td>Ginger was effective in lowering serum glucose, cholesterol and triacylgllycerol levels</td>
<td>Ginger possesses hypoglycaemic, hypcholesterolaemic and hypolipidaemic potential. Additionally, raw ginger is effective in reversing the diabetic proteinuria observed in the diabetic rats. Thus, ginger may be of great value in managing the effects of diabetic complications in human subjects.</td>
<td>Diabetes complications Animal study</td>
</tr>
<tr>
<td>Li et al (2012)</td>
<td>Animal study</td>
<td>4ml kg(-1) daily for 6 weeks (fresh squeezed juice)</td>
<td>Significant increase in insulin levels and decrease in fasting glucose levels</td>
<td></td>
<td>Blood glucose Animal study</td>
</tr>
</tbody>
</table>

**Streptozotocin-induced type I diabetic rats**

**Dose:** aqeous extract of raw ginger administered daily (500 mg/kg, intraperitoneally) for a period of 7

**Promising results:**
- Ginger was effective in lowering serum glucose, cholesterol and triacylglycerol levels
- Reduction in urine protein levels
- Ginger-treated diabetic rats also sustained their initial weights during the treatment period
- Ginger decreased both water intake and urine output in the STZ-induced diabetic rats

**Concl:** results indicate that raw ginger possesses hypoglycaemic, hypcholesterolaemic and hypolipidaemic potential. Additionally, raw ginger is effective in reversing the diabetic proteinuria observed in the diabetic rats. Thus, ginger may be of great value in managing the effects of diabetic complications in human subjects.

**Obese rats**

**Promising result:** ginger reduced blood sugar and insulin

**Goyal & Kadnur (2006)**

**Diabetic rats**

**Dose:** 800 mg/kg ethanolic extract

Morphine (10 mg/kg), diclofenac (100 mg/kg) and chlorpropamide (250 mg/kg) were used as reference drugs for comparison

**Promising results:**
- Decreased fasting blood glucose level after 1 hour treatment
- Findings indicate ginger possesses analgesic, anti-inflammatory and hypoglycaemic properties; and thus lend pharmacological support for uses of ginger in the management of painful, arthritic inflammatory conditions, and control of type 2 diabetes mellitus in some rural Africa communities

**Ojewole, 2006**

**Hypertension patients**

**Dose:** 1g ginger powder

**Promising result:** ginger may have a synergistic effect on antiplatelet aggregation in hypertensive patients

**Young et al (2006)**

**Rats, rabbits and guinea-pigs**

**Dose:** crude extract of ginger; (0.3-3 mg/kg)

**Promising result:** a dose-dependent fall in arterial blood pressure of anesthetised rats

**Mechanism:** blockade of voltage-dependent calcium channels

**Ghayur & Gilani (2005b)**

**Cardiovascular**

**Animal study**

**Rats**

**Promising result:** ginger lowers blood cholesterol and blood glucose levels

**Mechanism:** vasodilator (widening of blood vessels) effects may be caused by gingerols and shogaols

**Ghayur et al (2005)**

**Cardiovascular**

**Animal study**

**RCT/ 12 healthy males**

**Dose:** 25mg Warfarin alone or after 5 days pretreatment with 3.6g powdered ginger extract

**Discouraging result:** no significant effect on clotting status

**Jiang et al (2005)**

**Blood clotting Clinical study**

**Streptozotocin-induced type I diabetic rats**

**Dose:** 4ml kg(-1) daily for 6 weeks (fresh squeezed juice)

**Promising results:**
- Significant increase in insulin levels and decrease in fasting glucose levels
- A decrease in serum cholesterol, serum triglyceride and blood pressure

**Akhani et al (2004)**

**Blood glucose Animal study**
**BUT:** In normal animals rats fed fresh squeezed ginger juice for 6 weeks neither blood insulin, cholesterol or triglyceride were affected

**Mechanism:** 5-HT receptors (serotonin)

**Case study/ 76 year old white European woman**
Ginger may react with phenprocoumon (anticoagulant) resulting in elevated platelet inhibition (bleeding)


**Adverse event:** ginger - phenprocoumon

**Mode of action study - effect of ginger extracts on the adipocyte differentiation (using cultured mouse 3T3-L1 preadipocytes)**

**Promising result:** in geriol-treated cells; insulin-sensitive glucose uptake was increased

**Mechanism:** [6]-gingerol promoted glucose uptake in insulin responsive 3T3-L1 adipocytes

**Concl:** expected that ginger enhances insulin-sensitivity, and improves chronic disease, such as diabetes

**Sekiya et al (2004)**

**In Li et al (2012)**

**Blood lipids**

**In vitro**

**RCT/ diabetic patients**

**Dose:** 3g dry ginger powder in divided dose for 30 days

**Promising result:** reduction in blood glucose, triglyceride, total cholesterol, LDL, and VLDL cholesterol

**Andallu et al (2003)**

**In Li et al (2012)**

**Clinical study**

**Mode of action study - ability of synthetic gingerols (G1-G7) to inhibit human platelet activation compared to aspirin**

**Promising results:**

- Gingerols inhibited the AA-induced platelet release reaction in a similar dose range as aspirin
- Gingerols were also effective inhibitors of AA-induced human platelet aggregation

**Mechanism:** via an effect on cyclooxygenase (COX) activity in platelets: gingerols (G3-G6) potently inhibited COX activity in rat basophilic leukemia (RBL-2H3) cells

**Concl:** results provide a basis for the design of more potent synthetic gingerol analogues, with similar potencies to aspirin, as platelet activation inhibitors with potential value in cardiovascular disease

**Koo et al (2001)**

**In Bode & Dong (2011)**

**Cardiovascular**

**In vitro**

**Atherosclerotic mice**

**Promising result:** found to inhibit LDL (bad cholesterol) oxidation in apolipoprotein (proteins that transport lipids through the lymphatic and circulatory systems)


**In Bode & Dong (2011)**

**Blood lipids**

**Animal study**

**RCT/ healthy individuals/ 10 coronary artery disease (CHD) patients/ patients with non-insulin-dependent diabetes mellitus**

**Dose:** 4g daily for 3 months

**Promising results for platelet aggregation:** significantly reduced platelet aggregation in CHD patients

**Discouraging result for glucose:** no changes in blood glucose or blood lipid levels

**Bordia et al (1997)**

**In Li et al (2012)**

**Blood clotting**

**Clinical study**

**Full references**

- Islam, M.S. and Choi, H. ‘Comparative effects of dietary ginger (Zingiber officinale) and garlic (Allium sativum) investigated in a type 2 diabetes model of rats.’ J Med Food, 2008; 11:152–159
4 Weight management (general health benefit)

Ginger has been purported to warm up the body and increase metabolism and fat burning - in traditional Chinese medicine, ginger is classified as a warming remedy releasing exterior conditions (European Medicines Agency, 2012).

This was the most compelling health benefit of ginger in a focused market research study with consumers (Brand Story, 2013).

There is increasing pressure on governments to address the growing global obesity epidemic, and losing weight is a topic that is likely to resonate with a wide range of people.

Evidence from the animal literature supports the use of ginger as a functional dietary agent for weight management and prevention of metabolic disorders but research in humans is limited. Nevertheless, the available literature provides intriguing implications for the role of ginger in weight management in humans.

Weight management: Summary of the literature

- Preliminary clinical evidence for thermogenic and satiety-inducing effects of ginger in humans was provided in a (albeit small) pilot study by Mansour et al (2012) who found that a daily dose of ginger tea containing 2g dried ginger powder resulted in 43 extra calories burned on a daily basis and increased satiety in overweight men. However, this study cannot be generalised to women and further clinical studies are needed to determine the complex mechanisms involved in energy balance.

- Only one small study conducted before 2012 specifically investigated the thermogenic properties of ginger in humans (Henry & Piggott 1987), and it did NOT demonstrate any effects of ginger on the metabolism. However a limitation of the study was that it used fresh ginger in a sauce, which has not been proven to contain shogaols.

- The prevailing view is that obesity results from a small sustained positive energy balance and it has been proposed that modest diet and/or physical activity adjustments are sufficient to reverse the epidemic and that these minor changes will be more simply implemented and sustained in the long-term than radical dietary or behavioral modifications. Consequently, growing attention is being placed on the manipulation of foods with bioactive ingredients that may influence energy balance modestly by altering energy expenditure, substrate oxidation, and appetitive sensations (Ludy et al, 2011).
This is good news for ginger because as Beattie (2012) aptly put; “in our Western society… it’s difficult to get people to change their diet. The issue is that the amount of ginger a person would have to eat; 25g-50g of ginger a day, would blow your head off”. Recommendations to increase consumption of bioactive food ingredients (like ginger) may be made, but if they are not implemented (i.e. because the food isn’t palatable), there will be no impact on health. The situation regarding ginger and weight loss is one where there is a need for additional clinical trials to determine not just the efficacy of ginger, but also the dosage and format of ginger that can be translated into a relevant and accessible weight loss aid that consumers will engage with

Weight management: Possible mechanisms

- Effects ‘ghrelin’ levels (the ‘hunger hormone’)
  - Mansour et al (2012) found increased ghrelin levels after ginger, which (according to hormone data) should have resulted in increased appetite and food consumption, but instead participants reported decreased appetite and less prospective food intake. The opposite was found in animal studies. As this is confusing further studies are needed to determine the complexity of the satiety response

- Activates the ‘transient-receptor potential vanilloid uncoupling pathway’ (which detects and regulates body temperature) – implicated in the thermogenic effect of capsaicin
  - Mansour et al (2012) did NOT find this effect however

Weight management: Recommendation

- At present there is limited clinical evidence for the thermogenic effects of ginger.
- There are however, a number of studies on the thermogenic properties of capsaicin, which is contained in ginger and other spices such as chili peppers. Ludy et al (2011) critically evaluated current knowledge on the thermogenic and appetitive effects of capsaicin from foods, and concluded that: “Evidence indicates that capsaicin and capsiate both augment energy expenditure and enhance fat oxidation, especially at high doses. Purposeful inclusion of these compounds in the diet may aid weight management, albeit modestly.”
- The concept of warming up the body has potential to engage consumers with ginger – it is recommended that this continue to be explored within the broader context of ginger’s role in weight management, which in turn links in to ginger’s potential role in blood glucose management and speeding up the metabolism of fats (see Blood glucose and lipids category)
**Library 4. Studies on the weight management effects of ginger**

<table>
<thead>
<tr>
<th>Study design/subjects</th>
<th>Findings</th>
<th>Reference</th>
<th>Comments</th>
</tr>
</thead>
</table>
| 40 male albino rats fed high fat diet | **Dose:** ginger (5% ginger powder) for 4 weeks, and orlistat (pharmaceutical agent promoting weight loss)  
**Promising result:** ginger reduced body weight without inhibiting pancreatic lipase level, or affecting bilirubin concentration, with positive effect on increasing peroxisomal catalase level and HDL-cholesterol | Mahmoud & Elnour (2013) | Anti-obesity  
Animal study |
| RCT/ 10 (overweight) men aged 19-50y (39y on average), with BMI 27 (on average) | **Dose:** hot ginger tea with 2g dissolved ginger powder  
**Promising results:**  
- Significant effect of ginger on thermic effect of food  
- Lower hunger  
- Lower prospective food intake  
- Greater fullness  
**Discouraging results:**  
- No effect on total resting energy expenditure  
- No effects on glucose, insulin or inflammatory markers | Mansour et al (2012) | Thermogenic  
Small clinical pilot study |
| Weaning mice | **Dose:** a high-fat diet containing 6-gingerol (HFG), zerumbone (HFZ) for 6 weeks/ vs low fat diet control  
**Promising result:** increased adiposity in the ginger group compared with the control group was significantly reduced without food intake being affected | Beattie (2011) | Anti-obesity  
Animal study |
| Rats | **Promising results:** rats consuming a high fat diet with ginger for 6 weeks had lower weight gain, glucose, insulin, total cholesterol, low-density lipoprotein cholesterol, triglycerides, free fatty acids and phospholipids compared to rats fed the high-fat diet without ginger | Nammi et al (2009) | Anti-obesity  
Animal study |
| Rats | **Dose:** a single injection of [6]-gingerol (2.5 or 25 mg/kg)  
**Promising results:**  
- A rapid, marked drop in body temperature in a dose-related manner, with no change in physical activity  
- Significant decrease in metabolic rate observed immediately after injection although heat-loss responses underwent no alteration  
**Concl:** [6]-gingerol modulates or interferes with the mechanisms underlying body temperature regulation, while other bioactive constituents of ginger may counteract the hypothermic effect of [6]-gingerol | Ueki et al (2008) | Thermogenic  
Animal study |
| Rats | Gingerols ([6, 8, 10]-gingerols) and shogaols ([6, 8, 10]-shogaols) having different alkyl carbon chain lengths were targeted  
**Results:**  
- All the gingerols and shogaols increased intracellular calcium concentration in rat transient receptor potential vanilloid subtype 1 (TRPV1)-expressing HEK293 cells via TRPV1.  
- The shogaols were more potent than the gingerols  
- [10]-Shogaol induced nociceptive responses via TRPV1 in rats following subcutaneous injection into the hind paw; capsaicin (CAP) and [6]-shogaol were observed to have similar effects  
- Adrenal catecholamine secretion, which influences energy consumption, was promoted in rats in | Iwasaki et al (2006) | Thermogenic  
Animal study |
<table>
<thead>
<tr>
<th>Literature review</th>
<th>Promising results:</th>
<th>Concl: gingerols and shogaols activated TRPV1 and increased adrenaline secretion. [10]-shogaol is the only non-pungent compound among the gingerols and shogaols, suggesting its usefulness as a functional ingredient in food</th>
</tr>
</thead>
<tbody>
<tr>
<td>Westerterp-Plantenga et al (2006)</td>
<td>Consumption of spiced foods including ginger leads to greater thermogenesis and in some cases to greater satiety. Spicy food ingredients have the potential to produce significant effects on metabolic targets such as satiety, thermogenesis, and fat oxidation. Concl: thermogenic ingredients may be considered as functional agents that could help in preventing a positive energy balance and obesity.</td>
<td>Full paper reviewed</td>
</tr>
<tr>
<td>Eldershaw et al (1992)</td>
<td>Rat hind limbs perfused with [6]-gingerol showed increased heat production that was associated with increased oxygen consumption and lactate efflux. Mechanism: thermogenesis was at least partly associated with vasoconstriction independent of adrenergic receptors or secondary catecholamine release. BUT in contrast, LARGER DOSES of ginger components inhibited oxygen consumption which was attributed to disruption of mitochondrial function.</td>
<td>In Bode &amp; Dong (2011) and Singletary (2010)</td>
</tr>
</tbody>
</table>

**Full references**

- **Mahmoud, R.H. & Elnour, W.A.** ‘Comparative evaluation of the efficacy of ginger and orlistat and liver peroxisomal catalase enzyme in male albino rats’. European Review for Medical and Pharmacological Sciences. 2013; 17:75-83

5 Antioxidant (pharmacological action)

It has been widely speculated that ginger might be beneficial to human health because it exerts antioxidant activity (Soilova et al, 2007). The presence of oxidative stress is associated with numerous diseases, and a common mechanism often put forth to explain the actions and health benefits of ginger is associated with its antioxidant properties (Bode & Dong, 2011).

So far more than 40 antioxidant compounds are detected in ginger (Arablou et al, 2014; Shirdel et al, 2009).

Rehman et al (2011) report recent research that ranked ginger very highly compared to a number of high antioxidant foods such as berries, walnuts, sunflower seeds, and pomegranate – this is a compelling area of research given the increasing links being made between antioxidants and “superfoods” in the consumer world.

Several studies have recognised opportunities for ginger in the consumer market. Soilova et al (2007) recognised that ginger has potential as a natural antioxidant in food processing (as a disease preventative in relation to the oxidation of fats, and to enhance digestion by preventing the disruption to bile production caused by oxidation of fats). Beverages produced by lactic fermentation of ‘Zingiberaceae’ plants were found to retain antioxidant activity (Singletary, 2010) – however, none of the literature available at the time of Singletary’s (2010) literature review demonstrated antioxidant efficacy followed by consumption of ginger by humans.

Tapsell et al (2006) pointed out the potential for ginger to play an important role in the prevention of diseases such as heart disease: “The antioxidant properties of herbs and spices are of particular interest in view of the impact of oxidative modification of low-density lipoprotein cholesterol in the development of atherosclerosis” (Tapsell et al, 2006).

There is strong in vitro evidence that ginger contains high antioxidant levels. However there is a need for clinical studies to confirm the health benefits to humans.

Antioxidant: Summary of the literature

- Studies are largely based on measuring antioxidant activity in vitro or in animal studies, so the benefits in the human body is not known.

Antioxidant: Possible mechanisms

- Hydrogen atom or electron donation and capture of free radicals (damaged cells)
- Inhibits lipid peroxidation (when free radicals "steal" electrons from the fatty acids in cell membranes, resulting in cell damage)
Antioxidant: Recommendation

- It is recommended that ginger’s powerful antioxidant properties are used to support shortlisted health benefits, since antioxidant actions underlie many of the health benefits of ginger.

**Library 5. Studies on the antioxidant effects of ginger**

<table>
<thead>
<tr>
<th>Study design/subjects</th>
<th>Findings</th>
<th>Reference</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 male rats</td>
<td>Promising results: ginger has protective nutraceutical capacity to help in overcoming induced oxidative stress</td>
<td>Rasyidah et al (2014)</td>
<td>Toxicity - testicular Animal study</td>
</tr>
<tr>
<td>RCT/ 60 trained Iranian females aged 13-25</td>
<td>Dose: 3g ginger/ cinnamon powder every day for 6 weeks Discouraging result: no change in MDA level, body composition or exercise performance</td>
<td>Mashhadi et al (2013)</td>
<td>Exercise (combined effects) Clinical study</td>
</tr>
<tr>
<td>Measurement study – 2 varieties</td>
<td>Measured antioxidant activity of methanol extracts from leaves, stems and rhizomes of 2 ginger varieties – Halia Bentong and Halia Bara Result: Halia Bara had higher antioxidant activities and total contents of phenolic and flavonoid compared to Halia Bentong. Concl: validated the medicinal potential of the leaves and young rhizome of ginger, and the positive relationship between total phenolics content and antioxidant activities in ginger</td>
<td>Ghasemzadeh et al (2010)</td>
<td>In vitro</td>
</tr>
<tr>
<td>Literature review – effects of heat</td>
<td>Concl: the effects of γ-radiation or heat processing on antioxidants, or the vitamin content in herbs and spices is still lacking, which makes the direct assessment of the effect of treatment on the antioxidant status of herbs and spices practically impossible However, the changes in composition observed to date suggest that they have only a small effect on the behavior of herbs and spices in a real food matrix</td>
<td>Polovka &amp; Suhaj, (2010)</td>
<td>Effects of heat processing</td>
</tr>
<tr>
<td>Measurement study - antioxidant activity and total phenols</td>
<td>Promising results: * Ginger shown to have high polyphenol content with very good scavenging of DPPH (one of the tests used to prove ability of the components of ginger to act as donors) * The extract can be used as an antioxidant at an earlier stage of fat oxidation - the properties of ginger compared to synthetic antioxidant determined it’s potential as a natural preservative, applicable in the food and pharmaceutical industries Mechanism: hydrogen atom or electron donation and capture of free radicals</td>
<td>Stoilova et al. (2007)</td>
<td>Full paper reviewed In vitro</td>
</tr>
</tbody>
</table>
Anti-inflammatory (pharmacological action)

One of the many health benefits attributed to ginger is its ability to decrease inflammation, swelling, and pain. Anti-inflammatory conditions are high on the global health agenda because they are responsible for a long list of debilitating chronic diseases such as osteoarthritis, inflammatory bowel disease, some respiratory disorders, and even some cancers and cardiovascular disease.

Patients with chronic and painful diseases often seek alternative therapy, and currently ginger is one of the most popular herbal medications for inflammatory diseases (Zamal et al, 2014).

Bode & Dong (2011) and Singletary (2010) found that the majority of scientific evidence seems to suggest that ginger and its various components have anti-inflammatory effects both in vitro and ex vivo, but found the data supporting ginger as an effective anti-inflammatory agent in humans to be contradictory and incomplete.

**Anti-inflammatory: Summary**

The anti-inflammatory health benefits of ginger can be divided into three groups:

1. **Osteoarthritis**
2. **Premenstrual pain**
3. **Muscle soreness after exercise**

---

**Full references**

1. Osteoarthritis
   - Clinical studies evaluating the efficacy of ginger in alleviating the symptoms of arthritis/joint pain provide mixed results (Terry et al, 2011; Singletary, 2010), and the form and dose of ginger most advantageous for treatment is unclear.
   - The European Medicines Agency (2012) reviewed 4 RCTs on the efficacy of oral administration of ginger in osteoarthritis. Dosages were around 500-1000mg daily, administered for 3-12 weeks. Three studies demonstrated beneficial effects, however studies were hampered by high dropout rates, relatively short treatment periods and short or no wash-out periods. The conclusion aligned with previous literature reviews in that the scientific evidence is insufficient to claim efficacy of ginger in osteoarthritis.
   - Recently two clinical trials HAVE demonstrated promising results for ginger in reducing pain in osteoarthritis (e.g. Therkelson, 2014; Niempoog et al, 2012).
   - There is a recent focus on gastropathy in osteoarthritis, which is a frequent complication caused by taking drugs such as Ibuprofen to cope with the pain of the inflamed joints (e.g. Drozdov et al, 2012) – this and further studies could be potential support for the role of ginger as a broad digestive enhancer.

2. Premenstrual pain
   - Post 2011 there appear to be more promising results for the efficacy of ginger in reducing premenstrual pain (e.g. Jenabi, 2013; Halder, 2012; Rahnama et al, 2012).

3. Muscle soreness after exercise
   - Two clinical trials demonstrated specific links between ginger constituents and analgesic properties for pain related to eccentric exercise (e.g. Black et al, 2010; Black & O’Connor, 2010), though the evidence is weak.

Anti-inflammatory: Possible mechanisms
   - Inhibition of arachidonic acid metabolism (a polyunsaturated fatty acid present in animal fats that is important in metabolism, especially in the synthesis of prostaglandins and leukotrienes) via COX-2 pathways (for prostaglandins) and lipoxygenase products (for leukotrienes).
   - Inhibition of ‘cyclooxygenase’ (an enzyme responsible for formation of important biological mediators called prostanoids), ‘nitric oxide synthase’ (an enzyme that helps modulate insulin secretion) and ‘lipoxygenase’ activity (enzyme activity regulating fats) and suppression of prostaglandin synthesis and interference in ‘cytokine’ signaling (immune function).

Anti-inflammatory: Recommendation
   - Recent clinical studies are promising regarding health benefits specific to osteoarthritis and premenstrual pain, but the clinical literature is unable to support ginger’s efficacy as a broad spectrum anti-inflammatory.
   - Osteoarthritis and premenstrual pain technically fall into the ‘Specific Treatment’ space, which was not identified as the biggest area of opportunity. However, chronic...
Recent literature on the potential role for ginger to soothe the muscles after exercise is a compelling area that ties in with issues such as weight management which are topical. This is worth considering in the shortlisting process.

Ginger’s anti-inflammatory properties underlie many of its health benefits and could provide powerful support for health claims – e.g. supporting ginger’s role in gastroprotection, where immune system receptors (that mediate inflammatory responses in the stomach) are involved in the mechanisms of action.

**Library 6. Studies on the anti-inflammatory effects of ginger**

<table>
<thead>
<tr>
<th>Study design/subjects</th>
<th>Findings</th>
<th>Reference</th>
<th>Comments</th>
</tr>
</thead>
</table>
| RCT /70 adults with chronic osteoarthritis | Dose: topical ginger compress for 7 days (with option to continue for 24 weeks)  
Measure: self-completed questionnaire for 3 weeks and 4 weekly for 24 weeks  
Promising results:  
- Scores in pain, fatigue, global effect and functional status reduced by 48%, 49%, 40% and 31%  
- Health satisfaction improved 80% dissatisfied to 70% satisfied  
Concl: topical ginger has potential to relieve symptoms, improve overall health, and increase independence of people with chronic osteoarthritis | Therkleson (2014) | Osteoarthritis Clinical study |
| RCT/ 70 female students in Iran | Dose: ginger capsule for 3 days in first menstrual cycles  
Measure: visual analogue scale/ 5-point Likert scale  
Promising results:  
- Ginger reduced pain greater than placebo  
- Ginger group reported improved nausea symptoms | Jenabi (2013) | Premenstrual pain Clinical study |
| RCT/ 43 patients | Dose: 340mg ginger extract/ 100mg diclofenac daily for 4 weeks  
Measure: ‘severity of dyspepsia assessment’ (SODA) form/ biopsy  
Promising results:  
- Ginger slightly lowered SODA pain - though not dyspepsia  
- Mucosa-protective; biopsy showed increased levels of gastric mucosa  
Concl: ginger combination is as effective and more safe than diclofenac in treating osteoarthritis | Drozdov et al (2012) | Gastropathy in osteoarthritis Clinical study |
| RCT/ 75 nursing students in Pune, Maharashtra | Dose: 1g ginger powder 2x per day with warm water after a meal during first 3 days menstruation  
Measure: severity of symptoms on 5-point Likert scale  
Promising result: ginger powder has efficacy superior to progressive muscle relaxation | Halder (2012) | Premenstrual pain Clinical study |
| RCT/ 50 patients | Dose: combination 4% ginger and plai extract in a gel compared to 1% solution of diclofenac – for 6 weeks  
Measure: Knee Injury and Osteoarthritis Outcome Score  
Promising results:  
- Both treatments significantly improved knee joint | Niempoog et al (2012) | Osteoarthritis Clinical study |
<table>
<thead>
<tr>
<th>Study Type</th>
<th>Participants</th>
<th>Dose</th>
<th>Measure</th>
<th>Promising Results</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT</td>
<td>120 students</td>
<td>500 mg capsules ginger root powder/placebo 3x/d for 5 days</td>
<td>verbal multidimensional scoring system and a visual analogue scale</td>
<td>Treatment of premenstrual pain in students with ginger had a significant effect on relieving intensity and duration of pain</td>
<td>Rahnama et al (2012) Premenstrual pain Clinical study</td>
</tr>
<tr>
<td>RCT</td>
<td>60 patients treated 208 migraine attacks</td>
<td>feverfew/ginger/placebo treatment at earliest recognition of migraine (over 1 month)</td>
<td>Promising results: At 2 hours 32% subjects receiving active medication were pain free. Safe, apart from some oral numbness and nausea</td>
<td>Cady et al (2011) Migraine Combined effects - feverfew</td>
<td></td>
</tr>
<tr>
<td>Literature review</td>
<td>8 clinical RCTs</td>
<td>ginger reduces subjective pain reports in some conditions such as osteoarthritis</td>
<td>Promising result: ginger may attenuate the day-to-day progression of muscle pain</td>
<td>Terry et al (2011) Osteoarthritis</td>
<td></td>
</tr>
<tr>
<td>RCT</td>
<td>27 participants</td>
<td>2g ginger/placebo 24h and 48h after exercise</td>
<td>ginger may attenuate the day-to-day progression of muscle pain</td>
<td>Black &amp; O’Connor (2010) Muscle pain by eccentric exercise Clinical study</td>
<td></td>
</tr>
<tr>
<td>2x RCTs</td>
<td>34 and 40 volunteers</td>
<td>2g raw and heated ginger for 11 days</td>
<td>both reduced pain due to induced inflammation Heating had no effect</td>
<td>Black et al (2010) Muscle pain by eccentric exercise Clinical study</td>
<td></td>
</tr>
<tr>
<td>Literature review</td>
<td>4 RCTs</td>
<td>ginger root on osteoarthritis</td>
<td>Promising result: ginger extract alleviated the symptoms of acetic acid-induced ulcerative colitis</td>
<td>El-Abhar et al (2008) Bowel disease Animal study</td>
<td></td>
</tr>
<tr>
<td>Clinical trial</td>
<td>150 students with premenstrual pain</td>
<td>250mg of capsules ginger root powder/ 250mg mefenamic acid/ 400mg Ibuprofen</td>
<td>ginger decreased severity of premenstrual pain as effectively as mefenamic acid and Ibuprofen (but not greater)</td>
<td>Ogoli et al (2009) Premenstrual pain Clinical study</td>
<td></td>
</tr>
<tr>
<td>Rats</td>
<td></td>
<td></td>
<td>ginger extract alleviated the symptoms of acetic acid-induced ulcerative colitis</td>
<td>El-Abhar et al (2008) Bowel disease Animal study</td>
<td></td>
</tr>
<tr>
<td>Literature review</td>
<td>3 RCTs</td>
<td>ginger was well tolerated compared to Ibuprofen</td>
<td>ginger was well tolerated compared to Ibuprofen</td>
<td>Leach &amp; Runar (2008) Osteoarthritis</td>
<td></td>
</tr>
<tr>
<td>RCT</td>
<td>59 patients 60y+</td>
<td>aromatic oil massage 6x in 2-3 weeks (1% ginger and 0.5% orange oil in olive oil)/ placebo: olive oil only</td>
<td>WOMAC</td>
<td>Yip &amp; Tam (2008) Osteoarthritis</td>
<td></td>
</tr>
<tr>
<td>Case Study</td>
<td>Promising result:</td>
<td>ginger massage intervention demonstrated a better outcome in physical functioning compared to placebo at 1 week BUT not after 4 weeks</td>
<td>Lantz et al (2007)</td>
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<tr>
<td>Mode of action experiment</td>
<td>Promising result:</td>
<td>compounds found in ginger are capable of inhibiting PGE2 production and may act at several sites</td>
<td>Lantz et al (2007)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case Study</td>
<td>Promising result:</td>
<td>migraine ceased within 30mins, with no side effects after 500-600mg of powdered ginger mixed with water</td>
<td>Muhammed &amp; Prakash, 2007</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCT/ 20 patients</td>
<td>Promising result:</td>
<td>ginger was as effective as placebo during first 12 weeks, but at the end of 6 months the ginger extract showed superiority over placebo</td>
<td>Wigler et al (2003)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rats</td>
<td>Promising result:</td>
<td>high doses of ginger effective in lowering serum cholesterol when given orally or intraperitoneally BUT: no effect on serum triglyceride levels</td>
<td>Thomson et al (2002)</td>
<td></td>
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</tr>
<tr>
<td>RCT/ 261 patients</td>
<td>Promising result:</td>
<td>experience of pain on standing was moderately less in the ginger group</td>
<td>Bliddal et al (2000)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCT/ 56 patients</td>
<td>Promising result:</td>
<td>powdered ginger reduced pain and swelling in ¾ RA patients and all patients with muscular discomfort (over period ranging 3m – 2.5y)</td>
<td>Srivastava &amp; Mustafa (1992)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCT/ 56 patients (28 with RA)</td>
<td>Promising result:</td>
<td>powdered ginger reduced pain and swelling in ¾ RA patients and all patients with muscular discomfort (over period ranging 3m – 2.5y)</td>
<td>Srivastava &amp; Mustafa (1992)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case study</td>
<td>Dose: 500-600mg powdered ginger at onset of migrane attack</td>
<td>Promising result: relief of symptoms within 30mins</td>
<td>Mustafa &amp; Sribastava, 1990</td>
<td>In European Medicines Agency (2012). Migraine Clinical study</td>
<td></td>
</tr>
</tbody>
</table>

Full references

- Yip, Y.B. and Tam, A.C. ‘An experimental study on the effectiveness of massage with aromatic ginger and orange essential oil for moderate-to-severe knee pain among the elderly in Hong Kong’. Complement Ther Med. 2008 Jun;16(3):131-8


Other categories

7 Anti-cancer (general health benefit)

Research into cancer prevention has attracted a lot of attention in recent years (Bode & Dong, 2011).

Mounting evidence suggests that cancers are not an inevitable consequence of aging but are preventable diseases. In a review of the literature, Kaefer & Milner (2011) state that “without question, evidence exists that multiple processes, including proliferation, apoptosis, angiogenesis, and immunocompetence, can be influenced by one or more spices” and that spices may be factors in the diet that may lower cancer risk and affect tumor behavior.

In vitro studies have shown anti-cancer effects, and animal studies have been mixed with regard to anti-cancer effects in the colon, bladder, and lung (Singletary, 2010).

Recently there have been several clinical trials on the benefits of ginger in treating colorectal cancer (e.g. Citronberg et al, 2013; Jiang et al, 2013; Zick et al, 2011), but the benefits for treating or preventing cancer in humans remains inconclusive and requires further study.

Little is known about the precise mechanisms of action (European Medicines Agency, 2012).

Anti-cancer: Summary

- **Tumor inhibition:** *In vitro* and *in vivo* (animals) studies have demonstrated tumor inhibition activity. But little is known about the mechanism
- **Tumour prevention:** non clinical animal studies *in vivo* demonstrated tumour preventative effects
- **Chemoprevention:** Oxidative stress and inflammation are considered to play an important role in tumor development – pro-inflammatory cytokines, chemokines and iNOS are considered potential molecular targets for chemoprevention (European Medicines Agency, 2012)


Anti-cancer: Possible mechanisms

- Antioxidant activity and the ability to induce ‘apoptosis’ (*death of cells*), decrease proliferation (*rapid production of cells*), cause cell-cycle arrest, and suppress activator protein 1 (AP-1) (*regulates gene expression*) and NF-κB/COX-2 signaling pathway (*regulation of the immune response, the cell proliferation and cell death*)

Anti-cancer: Recommendation

- Anti-cancer activity was allocated a category of its own due to the specific pharmacological actions of ginger on preventing tumour growth. There are many different types of cancer however, and further clinical research is needed before any broad conclusions can be drawn about ginger as a general anti-cancer agent
There are some recent promising indications that ginger has a role to play in the treatment of colorectal cancer, though further study is required before any assertions can be made, since cancer is such a serious disease.

It may be less risky to associate ginger with the prevention of cancer since research already shows that one third of cancer deaths in Australia may be prevented by modifying the diet and other lifestyle factors (Cancer Council, 2014).

Anti-cancer falls outside the key identified areas of opportunity – i.e. being a ‘Specific’ condition. As a ‘Preventative’ for cancer ginger is unlikely to enhance well-being at the moment.

Not recommended for shortlisting.

<table>
<thead>
<tr>
<th>Library 7. Studies on the anti-cancer effects of ginger</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study design/subjects</td>
</tr>
<tr>
<td>-----------------------</td>
</tr>
</tbody>
</table>
| RCT (pilot study)/ 20 people at increased risk of colorectal cancer | Dose: 2g ginger daily for 28 days  
Promising result: ginger may reduce proliferation in the normal appearing colorectal epithelium and increase apoptosis and differentiation relative to proliferation  
Concl: a larger study needed to further investigate | Citronberg et al (2013) | Colorectal cancer Clinical study |
| RCT/ 30 people at normal risk and 20 people at increased risk | Dose: 2g ginger daily for 28 days  
Discouraging result: ginger did not alter 15-PGDH protein expression in in either increased or normal risk participants  
Concl: further study needed with larger sample and longer ginger intervention to examine the ability of ginger to impact tissue levels of prostaglandin | Jiang et al (2013) | Colorectal cancer Clinical study |
| Mice given human prostate cancer xenografts | Promising results:  
- Whole ginger extract exerts significant growth-inhibitory and death-inductive effects in a spectrum of cancer cells  
- No toxicity in normal, rapidly dividing tissues such as gut and bone marrow | Karna et al (2012) | Prostate cancer First report to demonstrate in-vitro and in vivo (animal) anti-cancer activity |
| Literature review - pre-clinical studies | Promising result: the mechanisms seem to offer promise for cancer prevention but further clinical studies are needed to access the efficacy and safety  
| | Promising result: antiproliferative effect of steamed ginger at 120 degrees for 4h was 1.5 and 2-fold higher than dried and fresh ginger | Cheng et al (2011) | Chemoprevention In vitro |
| Literature review | Concl: overall, while the anticancer findings of ginger are intriguing and several processes may be associated with the observed responses, additional studies are needed to clarify the underlying mechanisms and to determine overall benefits to humans | Kaefer & Milner (2011) | Anti-cancer |
| Mice given human prostate cancer xenografts | Promising result: whole ginger extract reduced growth and progression of prostate cancer xenografts by 56%  
Mechanism: decreased concentration of gingerol and increased levels of shogaols | Karna et al (2011) | Prostate cancer First study to show anti-cancer activity Animal study |
| RCT/ 30 healthy volunteers | Dose: 2g ginger/ d for 28 days  
Promising result: ginger has the potential to decrease eicosanoid levels  
<p>| In vitro experiment | Promising result: [6] gingerol effective in suppression in | Jeong et al | In Bode &amp; Dong |</p>
<table>
<thead>
<tr>
<th>Study Type</th>
<th>Mode of action study</th>
<th>Literature review</th>
<th>Male Wistar rats</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Promising result: ginger inhibited growth and modulated secretion of angiogenic factors in ovarian cancer cells: treatment resulted in inhibition of NF-KB activation and diminished secretion of VEGF and IL-8</td>
<td>Mechanism: the anticancer properties of ginger are attributed to the presence of certain pungent vallinoids, viz. [6]-gingerol and [6]-paradol, as well as some other constituents like shogaols, zingerone etc.</td>
<td>Promising result: ginger supplementation suppressed colon carcinogenesis in the presence of procarcinogen DMH and cancer incidence significantly increased whereas enzymic and non-enzymic antioxidant concentrations decreased as compared to control rats</td>
</tr>
<tr>
<td></td>
<td>Mechanism: NF-KB can be constitutively activated in epithelial ovarian cells and may contribute towards increased transcription and translation of angiogenic factors. [6]-shogaol found to be the most effective</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Inhibition of tumor development – ovarian cancer in vitro</td>
<td>Colon cancer</td>
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<td></td>
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<td></td>
<td>Animal study</td>
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</tbody>
</table>

**Full references**

8 Anti-infection (pharmacological action)

Note this section is closely linked with ginger’s role as a general gastroprotective agent.

The gingerols in ginger have been reported in in vitro studies to suppress the growth of a variety of infectious bacteria (Singletary, 2011).

Singletary (2011) reported that commercial ginger paste demonstrated antimicrobial activity toward E. coli in laboratory butter and ground beef, and that gingerols have been shown to inhibit growth of H pylori and enhance the effectiveness of drugs targeting this bacterium.

Ginger may therefore have a role in combating H pylori related gastrointestinal diseases, and potentially have a role in food processing.

Other research in this area evaluated by Singletary (2011) includes two animal studies showing that ginger is able to protect mice against infections caused by several microbes, and several studies with mixed results on ginger’s anti-fungal and anti-viral activity.

Anti-infection: Recommendation

- The mechanisms of action have not been examined sufficiently in humans or animals. However ginger may have a role in combating bacterial infections that cause gastrointestinal upsets, and the (albeit limited) scientific evidence in this area may add weight to the gastroprotective health benefits of ginger

<table>
<thead>
<tr>
<th>Library 8. Studies on the anti-microbial effects of ginger</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study design/ subjects</td>
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<tr>
<td>------------------------</td>
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<tr>
<td></td>
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<tr>
<td></td>
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<tr>
<td>In vitro study - analysis of the essential oils (micro dilution technique)</td>
</tr>
<tr>
<td>Investigated humor and cell-mediated immune responses/ mice previously immunized with sheep red blood cells (SRBCs)</td>
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<tr>
<td></td>
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</tbody>
</table>
**Full references**


9 **Miscellaneous (health benefits)**

**Alleviates respiratory conditions/ allergies**

- Bode & Dong (2011) documented that components of ginger are reported to contain potent compounds capable of suppressing allergic reactions and might be useful for the treatment and prevention of allergic diseases (e.g. Chen et al, 2009). Shariatpanahi et al (2013) and Ghayur et al (2008) reported that ginger has positive effects on breathing mechanics.

**Improves brain functioning**

- Ginger has been shown to alleviate anxiety by activating 5-hydroxytryptophan 1A receptors in the brain, which helps to increase serotonin levels, and ginger may also have beneficial effects in treating dementia, including Alzheimer’s disease (see Bode & Dong, 2011)

**Miscellaneous: Recommendation**

- Studies are more sporadic in these areas and the literature is limited for supporting health benefits for respiratory conditions and brain functioning.
- Not recommended for shortlisting.

<table>
<thead>
<tr>
<th>Study design/ subjects</th>
<th>Findings</th>
<th>Reference</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT/ 32 patients with acute</td>
<td>Dose: high protein enteral diet enriched with</td>
<td>Shariatpanahi</td>
<td>Respiratory</td>
</tr>
</tbody>
</table>

**Library 9. Studies on the miscellaneous effects of ginger**
<table>
<thead>
<tr>
<th>Condition</th>
<th>Study Design</th>
<th>Dose</th>
<th>Promising Result</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory disease (ARDS)</td>
<td>Clinical study</td>
<td>Ginger or placebo (measures taken on days 0, 5 and 10)</td>
<td>et al (2013)</td>
<td>Clinical study</td>
</tr>
<tr>
<td>RCT/ 60 healthy middle aged women</td>
<td>Promising result: ginger may be beneficial for gas exchange and could decrease duration of mechanical ventilation and length of stay in intensive care unit</td>
<td>400 and 800mg ginger extract for 2 months</td>
<td>Saenghong et al (2012)</td>
<td>Memory Clinical study</td>
</tr>
<tr>
<td>Rat basophilic leukemia (RBL-2H3) cells incubated with five compounds of ginger</td>
<td>A study on five pure phenolic compounds (1–5) isolated from the rhizomes of ginger and investigated for their anti-allergic potency</td>
<td>Ginger harbors potent compounds capable of inhibiting allergic reactions and may be useful for the treatment and prevention of allergic diseases</td>
<td>Chen et al (2009)</td>
<td>Allergies Animal study</td>
</tr>
<tr>
<td>Mouse lung slices</td>
<td>Promising result: ginger extract inhibits airway contraction and associated calcium signaling, possibly by blocking plasma membrane calcium channels - reiterating the effectiveness of ginger in treating respiratory illnesses</td>
<td>Ginger extract inhibits airway contraction and associated calcium signaling, possibly by blocking plasma membrane calcium channels - reiterating the effectiveness of ginger in treating respiratory illnesses</td>
<td>Ghayur et al (2008)</td>
<td>Respiratory In vitro</td>
</tr>
<tr>
<td>In vitro study</td>
<td>Promising result: a unique combination of muscarinic, possible Ca(++) antagonist and BuChE inhibitory activities of dried ginger, indicating its benefit in dementia, including Alzheimer’s disease</td>
<td>Ginger extract inhibits airway contraction and associated calcium signaling, possibly by blocking plasma membrane calcium channels - reiterating the effectiveness of ginger in treating respiratory illnesses</td>
<td>Ghayur et al (2008)</td>
<td>Dementia In vitro</td>
</tr>
<tr>
<td>RCT/ 92 patients</td>
<td>Promising result: ginger significantly reduced dyspnoea, wheezing, chest tightness, nocturnal cough and asthma spray use compared to placebo</td>
<td>Ginger significantly reduced dyspnoea, wheezing, chest tightness, nocturnal cough and asthma spray use compared to placebo</td>
<td>Rouhi et al (2006)</td>
<td>Asthma Clinical study</td>
</tr>
</tbody>
</table>

**Full references**


**Previous literature reviews**
Summary of existing literature reviews on the general health benefits of ginger

Note existing reviews on the full range of health benefits of ginger only include literature up to 2012. Newer studies have been reviewed under each relevant category

- Variations in dosages, latencies and follow up periods after treatment have led to inconsistent study results. All previous literature reviews agree on a need for more clinical trials to confirm suggestive evidence, define dosage, and understand mechanisms of action

- Safety: ginger appears to be safe, including in pregnancy. Reported adverse events are mild, infrequent gastrointestinal complaints (though safety studies on pregnant women have been small with short treatment durations so pregnant women should be advised to use for a short term – i.e. a few days only)

  There are 2 (unconvincing) case reports suggesting an interaction between ginger and anti-coagulant (blood thinning) drugs. Animal studies show that ginger can block blood platelets from sticking together and cause bleeding. (There has been no reported bleeding in people taking ginger, but to be on the safe side people would be best advised not to take ginger with blood thinners - Hornick & Yarnell, 2006)

- Mechanisms: support for ginger as a useful preventative agent due to its powerful impact as an antioxidant. It is unconfirmed however whether ginger’s antioxidant constituents are bioavailable in humans once ingested and whether they can affect markers of oxidative stress in humans

  The reviews also support anti-inflammatory, immuno-modulatory, anti-lipidemic, and anti-hyperglycaemic activity in in vitro experiments

- Anti-emetic: conclusions are very promising. Ginger as an alternative treatment for women suffering nausea in early pregnancy is the most strongly supported by clinical evidence. There is also plausible clinical evidence for a role of ginger in ameliorating post-operative nausea and vomiting and motion sickness (though people would be advised not to take ginger pre-operation as this goes against pre-operation fasting protocol)

- Gastroprotective: recent reviews suggested a potential gastroprotective role for ginger, though clinical trials in humans are unable to confirm this and the demonstrated effects are attributed to animal studies

  Animal studies indicate that ginger increases gastric emptying, which serves dual protective roles for the stomach (against toxins), and in diabetes-related stomach disorder

- Osteoarthritis: some suggestive evidence from recent clinical trials for benefits with respect to pain relief, though previous reviews concluded that the evidence is insufficient (due to inferior scientific quality)

- Blood clotting, blood pressure, blood glucose and blood lipids: benefits have been shown in in vitro and animal studies, but no firm conclusions about the health benefits to humans can be based on these studies

- Anti-tumour: animal studies have demonstrated effects which indicate tumour suppression and preventative potential, however there is little clinical evidence supporting ginger’s practical usefulness in humans
There is some suggestion that because ginger and its constituents concentrate in the gut, this may support a possible role in colon cancer prevention

- **Thermogenic**: insufficient evidence

### Library 10. Studies on general health benefits of ginger

<table>
<thead>
<tr>
<th>Study design/subjects</th>
<th>Findings</th>
<th>Reference</th>
<th>Notes</th>
</tr>
</thead>
</table>
| Literature review of RCTs | Promising results:  
- Anti-emetic: most animal studies demonstrate that ginger root increases gastric emptying and gastrointestinal transit – suggests a role in treatment and prevention of nausea  
- Anti-inflammatory: *in vitro* and animal studies demonstrate that ginger has anti-inflammatory effects  
- Antioxidant: capabilities *in vitro* and in whole animals  
- Blood clotting: effects shown *in vitro* only  
- Anti-cancer: *in vitro* and *in vivo* animal studies suggest tumor suppression and preventative potential  
- Anti-infection: *in vitro* antibacterial, antifungal, antiviral and anthelmintic properties  

Discouraging results:  
- Blood glucose: most studies show reduced plasma concentration of lipids, glucose and insulin in experimentally induced hyperlipidemic and hyperglycemic whole animals, BUT clinical evidence is insufficient  
- Cardiovascular: insufficient evidence  
- Thermogenic: insufficient evidence  
- Analgesic: insufficient evidence  

Toxicology:  
- Studies inadequate but indicate that dosages are very high with no cause for major concerns  

<table>
<thead>
<tr>
<th>Reference</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>European Medicines Agency (2012)</td>
<td>Full paper reviewed</td>
</tr>
</tbody>
</table>

| Literature review | Promising results:  
- Gastroprotective/ anti-nausea: ginger is probably fairly effective in alleviating nausea and vomiting associated with a variety of conditions  
- Although the mechanism is not clear, ginger appears to have no adverse side effects and never seems to worsen nausea and vomiting  
- Ginger and its constituents accumulate in the gastrointestinal tract, which supports the many observations of ginger’s effectiveness as an anti-nausea agent and as a possible colon cancer-preventing compound  
- Anti-oxidant: potent in vitro and ex vivo, but data are not obvious for in vivo application and specific targets and mechanisms are lacking  
- Anti-inflammatory: appears to exert effects by suppressing COX-2 with subsequent inhibition of prostaglandin and leukotriene biosynthesis  
- Nausea/ vomiting: clinical data undoubtedly indicate that ginger is at least as effective, and may be better, than vitamin B6 in treating vomiting and nausea associated with pregnancy, chemotherapy, and some types of surgery – but mechanisms are lacking. No indication of adverse side effects or worsening illness in pregnant women or patients  
- Anti-cancer: a direct protein target has been identified in colon cancer  
- Blood lipids: appears to reduce cholesterol and |
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Bode &amp; Dong (2011)</td>
<td>Full chapter reviewed</td>
</tr>
<tr>
<td>Literature review</td>
<td>Promising results:</td>
</tr>
<tr>
<td>-------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td><strong>Discouraging results:</strong></td>
<td>Pain and swelling: data supporting the effectiveness in associated with arthritis are conflicting</td>
</tr>
<tr>
<td>Specific biological targets are largely unknown and remain to be determined</td>
<td><strong>Anti-inflammation mechanism:</strong> inhibition of prostaglandin and leukotriene biosynthesis and suppression of 5-lipoxygenase</td>
</tr>
<tr>
<td><strong>Literature review</strong></td>
<td><strong>Describes the role of ginger in reducing the extent of cardiovascular disorders, diabetes, and digestive problems</strong> – recommends further research to be carried out for meticulousness</td>
</tr>
<tr>
<td><strong>Chemoprevention mechanism:</strong> inhibition of NF-κB activation via impairing nuclear translocation</td>
<td><strong>Literature review</strong></td>
</tr>
<tr>
<td><strong>Anti-inflammation mechanism:</strong> inhibition of prostaglandin and leukotriene biosynthesis and suppression of 5-lipoxygenase</td>
<td><strong>Butt &amp; Sultan (2011)</strong></td>
</tr>
<tr>
<td><strong>Literature review</strong></td>
<td><strong>Promising results:</strong></td>
</tr>
<tr>
<td>Powerful antioxidant: inhibits the production of free radicals and enhances the body’s internal production of antioxidants</td>
<td><strong>Concl:</strong> a wide range of medicinal uses and can be used as single drug or compound drug to treat different ailments. It can be used as preventive medicine due to its potential against oxidative stress</td>
</tr>
<tr>
<td><strong>Literature review</strong></td>
<td><strong>Promising results:</strong></td>
</tr>
<tr>
<td><strong>Nausea and vomiting:</strong> support for alleviating effects following pregnancy, surgery, cancer therapy, and motion sickness</td>
<td><strong>Anti-oxidant:</strong> cell studies show antioxidant properties – but NOT yet known if bioavailable in humans once ingested and whether can affect markers of oxidative stress in human in vivo</td>
</tr>
<tr>
<td><strong>Inflammation/pain:</strong> suggestive evidence</td>
<td><strong>Antimicrobial:</strong> preliminary data for antimicrobial potential – BUT little evidence supporting practical usefulness in humans</td>
</tr>
<tr>
<td><strong>Anti-oxidant:</strong></td>
<td><strong>Cardiovascular:</strong> animal studies: may have beneficial effects towards cardiovascular disease (inflammation, hyperlipidemia, platelet aggregation, and hypertension)</td>
</tr>
<tr>
<td><strong>Literature review</strong></td>
<td><strong>Promising results:</strong></td>
</tr>
<tr>
<td>A renewed interest in ginger at the time of study</td>
<td>The main pharmacological actions of ginger and compounds isolated include immuno-modulatory, anti-tumorigenic, anti-inflammatory, anti-apoptotic, anti-hyperglycemic, anti-lipidemic and anti-emetic actions</td>
</tr>
<tr>
<td>Ginger is a strong anti-oxidant substance and may either mitigate or prevent generation of free radicals</td>
<td><strong>In Bode &amp; Dong (2011)</strong></td>
</tr>
<tr>
<td>A safe herbal medicine with only few and insignificant adverse/side effects</td>
<td><strong>Concl:</strong> more studies required in animals and humans on the kinetics of ginger and its constituents and on the effects of their consumption over a long period of time</td>
</tr>
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<td><strong>Promising results:</strong></td>
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</tr>
</tbody>
</table>
Literature review

Promising results:
- Ginger constituents DO interfere with the inflammatory cascade and vanilloid receptor
- Exerts in vitro antioxidative, antitumorogenic and immunomodulatory effects, and is an effective antimicrobial and antiviral agent
- Animal studies: effects on gastrointestinal tract, cardiovascular system, experimental pain and fever, antioxidative, antilipidemic and antitumor effects

Discouraging results:
- No postoperative anti-emetic effectiveness, or motion sickness or nausea/vomiting effects
- Unconfirmed if clinically useful to alleviate osteoarthritic/other pain

Concl:
- Pregnancy-related nausea and vomiting is the only clinical evidence available
- The most relevant human pharma studies require a confirmatory study to exclude interaction of ginger preparations with platelet aggregation
- Pharmacokinetic data only available for [6]-gingerol and zingiberene
- Preclinical safety data do not rule out potential toxicity, which should be monitored especially following ginger consumption over longer periods

Chrubrasik et al (2005)

<table>
<thead>
<tr>
<th>Literature review</th>
<th>Promising results:</th>
<th>Discouraging results:</th>
<th>Concl:</th>
</tr>
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</tr>
</tbody>
</table>

Full references

- **Bode** and Z. Dong. ‘The amazing and mighty ginger’. Oxidative stress and disease. 2011. 131-156 *(cited in Herbal Medicine, Ch.7)*
Conclusions

1. Ginger’s many health benefits are attributed to synergistic effects of more than one ‘pharmacological’ action (e.g. antioxidant, anti-inflammatory etc.)
   - This represents a challenge in that health benefits cannot be linked to a very specific pharmacological action e.g. ‘weight loss’ cannot be explained by ‘thermogenic effects’ alone, but also involves antioxidant action (e.g. *speeding up the metabolism of fats*), immune system mediation (e.g. *inhibiting enzymes in carbohydrate metabolism*) etc.
   - This also represents an opportunity as it opens the scope for the way health benefits are phrased in the market, and the level of information communicated to consumers. There is an opportunity to ‘cluster’ various health benefits and/or pharmacological actions in order to maximise the strength of the health claim and the scientific support
   - Ideally communication of the health benefits of ginger will link a pharmacological action to a health benefit as simply as possible, in language that will resonate with consumers

*Figure 1.* shows the links between the pharmacological actions and health benefits of ginger

**KEY:**
- **Red:** health benefits (e.g. *prevention of nausea, weight management*)
- **Blue:** pharmacological actions (e.g. *anti-inflammatory, antioxidant*)
- **Size of bubble:** importance of the pharmacological action or health benefit in relation to associated pharmacological actions or health benefits
  - The bigger the bubble the more important and all-encompassing the pharmacological action or health benefit is (e.g. ‘antioxidant’ encompasses ‘free radical scavenging’; and ‘gastroprotection’ encompasses ‘easing digestive discomfort’)
- **Darker shades:** potential strength of opportunity
  - The darker the shade of red or blue the more potential resonance with consumers AND the greater the support from scientific literature (e.g. ‘eases digestive discomfort’ is a bigger opportunity than ‘relieves period pain’; and ‘thermogenic’ is a bigger opportunity than ‘speeds up gastric emptying’)

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C1 RIRDC Literature review - Health benefits of ginger 140808
Figure 1. Links between pharmacological actions and health benefits

Figure 1. shows that:

- **Antioxidant** and **anti-inflammatory** actions underlie all health benefits
- Three health benefits stand out as umbrella health benefits (i.e. big opportunities) that encompass related health benefits:
  1. Gastroprotection
  2. Diabetes control
  3. Weight management
- **Controlling blood sugar** is a key action linking these three health benefits. It moderates the metabolism of fats, insulin sensitivity AND stomach contractions
- **Diabetes control** and **weight management** are both metabolism-related and therefore may be merged under the health benefit of ‘boosting metabolism’
- Antioxidant activity, specifically preventing the oxidation of lipids, supports the evidence for metabolism boosting
- **Thermogenic effects**, though clinical evidence is not yet strong, also potentially supports metabolism boosting

2. Clinical evidence is limited

- The clinical studies that are available have tended to be incomparable due to variations in dosage, treatment duration and preparation
- Currently the health benefits of ginger with the strongest **clinical support** are:
  - Anti-emetic activity – especially preventing nausea in early pregnancy
  - Pain relief in osteoarthritis and premenstrual pain
- Research into natural alternatives to current drug treatments is attracting attention, and recent clinical studies demonstrate preliminary support for:
3. Processed ginger is more potent than fresh ginger

- The challenge is to develop communications that encourage consumers to integrate more regular consumption of processed (i.e. dried) and fresh ginger into their dietary regime. However, fresh and processed ginger are chemically different and do not contribute the same or equal health benefits.
- The evidence suggests that the shogaols in processed ginger have a more powerful impact than fresh ginger.
- The majority of clinical studies have used powdered ginger. Clinical trials that have observed thermogenic effects (Mansour et al, 2012; Westerterp-Plantenga et al, 2006) and digestion stimulating effects (Hu et al, 2011; Wu et al, 2008; Micklefield et al, 1999) are attributed to dissolved powdered ginger or capsules of powdered ginger. The only available published clinical study using fresh ginger (30g) as part of a meal did NOT show a significant effect of ginger on the metabolic rate.

Some initial considerations for commercial relevance of the scientific literature are discussed as an Addendum at the end of this document.

4. Implications for shortlisting health benefits

- It is possible to cluster health benefits in order to maximise the weight of scientific support.
  - Ginger’s role as a general gastroprotective is promising:
    - Ginger has been shown to speed up digestive contractions, including stomach emptying time. Whilst the evidence is not strongly associated with relieving indigestion symptoms per se, these actions provide general benefits when linked to secondary protective roles.
    - Ginger may provide a secondary gastroprotective role in type 2 diabetes. Ginger’s ability to control blood sugar is the link, which influences the stomach’s digestive contractions (including gastric emptying).
    - There is also an interesting link between ginger’s gastroprotective benefit for the stomach and the arteries, bridged by ginger’s antioxidant activity.
    - Ginger has anti-emetic effects and can prevent nausea, protecting against discomfort in early pregnancy and for motion sickness.
- Ginger’s role in managing metabolic conditions (diabetes and weight management) is promising.
Ginger has been shown to **stimulate digestion** and **metabolism**. *In vitro* and animal studies indicate that ginger inhibits key enzymes controlling metabolism and lowers lipids which improves insulin sensitivity.

Combining the clinical literature for thermogenic effects, stimulating digestion, and the metabolism of fat may strengthen the case for ginger’s role in managing metabolic conditions.

- Ginger’s role as a general body stimulant, digestive enhancer, gastroprotector, and aid in metabolic conditions such as weight loss and diabetes are areas recommended for further exploration in Stage 3 – health benefits shortlist.

5. **Next steps**

- **Stage 3 – Health benefits shortlist**:
  - Brand Story to provide a shortlist (via summary Word document) of health benefits proposed as the most valuable for future development.
  - Revisiting the original opportunities map (*figure 2*): the model originally used to identify potentially fertile market development ground for ginger will provide a useful tool for shortlisting health benefits.
  - Brand story will plot health benefits, including potential clusters of health benefits (*such as managing metabolic conditions*), on the original opportunities map in order to determine how the health benefits align with previously identified opportunity areas (*i.e. General preventative or treatment*).
  - This exercise will start the ball rolling for discussions on narrowing down the shortlist of health benefits of most value to the development of the Australian Ginger Industry.

- **Stage 4 – Industry workshop**:
  - Brand Story to arrange a workshop to debrief the review findings (via PowerPoint) and ensure that the outputs relating the health benefits of ginger are easy to understand and communicate.

- **Stage 5 – Further substantiation of health benefit claims**:
  - To be discussed at the workshop.
Addendum: Considerations regarding commercial relevance

Caveats in the scientific literature

Caveats
The scientific literature that supports health benefits associated with ginger is caveated by the fact that the dosages used across the studies varied considerably:
- In clinical studies dosages range considerably from 500mg to 2000mg per day
- Oral vs. intravenous administration changes the way the ginger is metabolised (i.e. in the gut vs. in the brain/immune system)
- Scientific studies are largely based on powdered ginger, administered orally in capsules
- Studies have tended to focus on the most abundant compounds; [6]-gingerol and [6]-shogaol
- Dosages used in clinical studies are much lower than dosages used in animal studies

Considerations
This raises some key considerations for the commercial relevance of health claims based on the literature:
- Can support for health benefits based on processed ginger also support the consumption of fresh ginger?
- What should be the recommendation regarding the amount of ginger to consume to get the health benefits?
- What are the commercial restrictions?

Stage 3 – Health benefits shortlist will need to factor in the implications of these caveats and considerations for commercial relevance in order to answer the present objectives:

1. ...determine the role fresh and processed Australian ginger plays in promoting good health
2. ...use [the scientific literature] to develop and/or add value to the ginger industry within the constraint of the Australian New Zealand Food Standards Code

The usefulness of gingerols vs. shogaols in humans

The composition of ginger
- Gingerols are the most abundant pungent compounds in fresh roots, and several gingerols of various chain-lengths [6 to 10] are present in ginger, with the most abundant being [6]-gingerol
- Shogaols, the dehydrated form of gingerols, are found in very small quantities in the fresh root and mainly in the dried and thermally treated roots, with [6]-shogaol being the most abundant (Barceloux, 2013; Ok & Jeong, 2012; Zick et al, 2008)
- Ginger also contains about 1-3.5% essential oil following steam distillation. There is a current consumer trend for essential oils, however the variety of the compounds
in the essential oil depends on the extraction process, the strain and whether the ginger is fresh or dried

Although gingerols and shogaols are the major bioactive compounds present in ginger, their mechanisms of actions and the relationship between their structural features and the activity have not been well studied (Ok & Jeong, 2012).

- **No research has examined the ‘pharmacokinetics’** *(how drugs move within the body)* of the ginger constituents [6]-, [8]-, [10]-gingerol and [6]-shogaol in humans (Barceloux, 2013; Zick et al, 2008)

- Only a handful of studies in rats have examined the **absorption, bioavailability, metabolites** and **elimination** of ginger constituents. Only two of the pungent components [6]-gingerol and zingerone, have been investigated, and in two of these studies [6]-gingerol was administered as an intravenous bolus, which is unlikely to be reflective of oral dosing (see Zick et al, 2008)

- Studies on the pharmacokinetics of ginger tend to be **narrated through a specific lens**; e.g. in relation to anti-cancer efficacy (Zick et al, 2008). It is therefore difficult to assert with conviction what practical usefulness ginger has in humans wanting to consume ginger for general well-being (i.e. general digestive enhancement)

- [6]-gingerol has been found to possess various ‘pharmacological’ effects *(understanding the properties of drugs and their actions)* including anti-inflammatory, pain relief, reducing fever, chemopreventative, developing new blood vessels, and antioxidant (Ok & Jeong, 2012)

- [6]-shogaol has biological effects such as antibacterial and antioxidant properties **in vitro and in vivo (animals)**

**Gingerols vs. shogaols in the body**

- **Shogaols may increase ginger’s pungency** *(Mansour et al, 2012; Ok & Jeong, 2012; Hoffman, 2003)*. Recent studies have shown that shogaols are more potent than their corresponding gingerols in anti-inflammatory, antioxidant and chemopreventative effects (Barceloux, 2013; Ok & Jeong, 2012; Dugasani, et al. 2010)

- The preparation method used in scientific experiments can therefore influence the chemical composition and the potency of ginger’s effects.

- Until very recently studies on ginger have focused on the gingerols due to their abundance rather than the shogaols

- Ok & Jeong (2012) investigated the effects of temperature and pH on [6]-shogaol. This study has implications for how to maximise the usefulness of dried ginger in the food processing and nutraceutical industries

- Shogaols revert to gingerols in the acidic conditions of the stomach – so dehydration of gingerol to shogaol may not reduce the bioavailability of gingerol (Barceloux, 2013)

- The contribution of gingerols and [6]-shogaol to pharmacological effects is complex. It is suggested that the effect of dried ginger is **dose-dependent** (Barceloux, 2013)
Dosage and format

Commonly used dosages

- The most commonly used dosage in clinical trials appears to be between \textit{0.5g and 2g ginger per day}. This is also considered to be the safe upper limit recommended for use in early pregnancy (Singletary, 2010; Marcus, 2005; Friedman, 2000)

- **Typical daily doses** of fresh ginger is about \textit{2-4g} (1 inch/ 2.5cm rhizome) or \textit{0.5g-1g} (about a level teaspoon) powdered dry rhizome in 3-4 divided doses (Barceloux, 2013)

- An examination of the concentrations of gingerols and [6]-shogaol in 10 different ginger-root dietary supplements purchased randomly from a variety of pharmacies and health food stores found these active components to vary extensively (Schwertner et al, 2006). In addition, the suggested serving size ranged from about \textit{250 mg to 4.8 g/day}

- Various sources attempt to advise on dosages - e.g. The Natural Medicines Comprehensive Database \textit{(recognized as the scientific gold standard for evidence-based information, last reviewed Aug 2014)} has recorded the following dosages as having been studied in scientific research:
  
  - For morning sickness: 250mg 4x daily
  - For post-operative nausea and vomiting: 1-2g of powdered ginger root 1 hour before anaesthesia \textit{(note: this goes against pre-operation fasting protocol)}
  - For arthritis: dosages have varied depending on the product taken

Toxicity and cautions

**Toxicity**

- Currently the benefit/ risk balance is in favour for the oral use of \textit{powdered ginger} extract

- Zick et al (2008) reported that ginger and its constituents at doses up to \textit{2g daily} demonstrate low levels of toxicity and high levels of tolerability in humans with only mild gastrointestinal complaints being reported

- Slight side effects WERE reported in 30 RCTs reviewed by the European Medicines Agency (2012). Effects tended to be \textit{mild gastrointestinal complaints}, and may have been due to the study medication rather than the ginger dose

- HOWEVER, it is unclear if low toxicity is due to poor oral bioavailability or a high degree of safety of pungent ginger constituents

- \textit{No dose-response studies have been performed} (European Medicines Agency, 2012), and there is limited data on the toxicity of ginger exceeding typical therapeutic amounts (Barceloux, 2013) – though it was suggested by Bordia et al (1997), in a clinical trial with patients with coronary artery disease, that \textit{10g powdered ginger} produced no adverse effects
Three key cautions:

1. There is an association of ginger with reported incidences of increased risk of bleeding following surgery or if taken with anticoagulant drugs such as Warfarin (Kruth et al, 2004) - however, the data are not conclusive

2. Use for more than a few days in early pregnancy is not advised as clinical studies have been short in duration

3. Consuming ginger before surgery goes against fasting surgery protocol

Commercially approved products containing ginger

- The German Commission E approves the use of ginger for dyspepsia, nausea and vomiting of pregnancy and the prevention of motion sickness. Ginger is approved by the General Sale list of Medicines Control Agency of the UK, and as a safe dietary supplement in the US

- In Australia there are four key observations around dietary supplement products:

  1. Ginger dietary supplement products tend to contain a combination of ingredients, such as honey and other herbs and spices. Ginger-only products are for anti-nausea (e.g. preventing motion sickness) and general gastrointestinal comfort (including anti-nausea and stimulating digestion)

  2. Marketers tend to cluster health benefits in order to make claims that have some grounding in science. Products for “detox” and “probiotic liquid”, are able to be clustered under the broader umbrella of digestive health, with ginger’s contribution being eliminating gas and bloating. Within the aggregated health benefits of several ingredients, ginger is associated with; “supporting complex digestion”, a “soothing, comfortable and balanced digestive process”, “weight loss without calorie reduction”, “strengthening nutrient digestion”, “balancing immunity”, “untangling the knots in your stomach”... Marketing language is focused on warming, supporting, soothing, and maximising

  3. The guidelines around dietary supplement products containing ginger appear to allow health claims to be marketed based on one or two studies (note based on internet search) - e.g. Exercise and muscle pain (suggested dosage: 1x 1g capsule 2x daily with food). However, the clinical studies showing promising results for ginger’s efficacy in soothing sore muscles after exercise are recent, and so inconsistent:

<table>
<thead>
<tr>
<th>RCT/ 27 participants</th>
<th>Dose: 2g ginger/placebo 24h and 48h after exercise</th>
<th>Black &amp; O’Connor (2010)</th>
<th>Muscle pain by eccentric exercise Clinical study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Discouraging result: overall ginger had no effect on muscle pain, dysfunction or metabolic rate compared with placebo 45mins after ingestion</td>
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<tr>
<td></td>
<td>Promising result: ginger may attenuate the day-to-day progression of muscle pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2x RCTs/ 34 and 40 volunteers</td>
<td>Dose: 2g raw and heated ginger for 11 days</td>
<td>Black et al (2010)</td>
<td>Muscle pain by eccentric exercise Clinical study</td>
</tr>
<tr>
<td></td>
<td>Promising result: both reduced pain due to induced inflammation</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Heating had no effect</td>
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</table>

4. Not all products indicate the dosage required

Overall no definitive dose or format has been defined
Addendum library. Pharmacological effects of ginger

<table>
<thead>
<tr>
<th>Study design/ subjects</th>
<th>Findings</th>
<th>Reference</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Purpose</strong>: optimisation of extraction conditions for [6]-shogaol (by modulating temperature and pH)</td>
<td>Results:</td>
<td>Od &amp; Jeong (2012)</td>
<td>Full paper reviewed</td>
</tr>
<tr>
<td></td>
<td>The highest production of [6]-shogaol was achieved at 80 degrees extraction after drying at the same temperature – 7-fold compared to the lowest producing process; freezing and extracting at room temp</td>
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<td></td>
<td>Adjustment of pH for the [6]-shogaol richest extract also affected the chemical composition of ginger – the yield of [6]-shogaol was maximised at the most acidic condition of pH1</td>
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<td></td>
<td>Concl: could be useful in food processing or nutraceutical industries</td>
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<td><strong>Purpose</strong>: To examine and compare the antioxidant and anti-inflammatory activities of gingerols and their natural analogues to determine their structure-activity relationship and molecular mechanisms</td>
<td>Results:</td>
<td>Dugasani et al (2010)</td>
<td>In vitro</td>
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<td></td>
<td>Scavenging of 1,1-diphenyl-2-picyrhydrazil (DPPH), superoxide and hydroxyl radicals</td>
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<td></td>
<td>Inhibition of N-formyl-methionyl-leucyl-phenylalanine (f-MLP) induced reactive oxygen species (ROS) production in human polymorphonuclear neutrophils (PMN)</td>
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<td>Inhibition of lipopolysaccharide induced nitrite and prostaglandin E(2) production in RAW 264.7 cells</td>
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<td><strong>Purpose</strong>: 27 healthy volunteers</td>
<td></td>
<td>Zick et al (2008)</td>
<td>Full paper reviewed</td>
</tr>
<tr>
<td><strong>Pharmacokinetic study/27 healthy volunteers</strong></td>
<td>Dose: [6], [8], [10]-gingerol and [6]-shogaol</td>
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<td>Clinical study</td>
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<td></td>
<td>and their conjugate metabolites at 6 dose levels: 100mg – 2000mg powder capsules administered orally</td>
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<td>Results:</td>
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<td></td>
<td>Unclear if gingerols/ shogaols are conjugated (combined) to glucuronides in the intestinal mucus, liver or both</td>
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<td>The difference in time to maximum concentration and elimination between orally administered [6]-gingerol in rats and humans could be due to differences between species or differences in dose – the dose given to rats was equivalent to a human dose of 583mg of [6]-gingerol – MUCH higher than 43mg; the maximum that humans were given in Zick’s study</td>
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<td>All the in vitro studies required higher concentrations of free ginger to elicit activity than found in Zick’s study (e.g. for ovarian cancer a certain concentration of [6]-gingerol has been shown to be needed to activate the mechanism for growth</td>
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</tbody>
</table>
Ginger conjugates may be more biologically active than the parent compound. No adverse effects found up to 2g – all toxicities reported were consistent with previous clinical research (gas and bloating). Apart from (6)-gingerol the analytes were NOT well absorbed – though unlikely, this could be explained by the lack of stability of gingerols and shogaols in the blood during storage and analysis. No pharmacokinetic model was able to be constructed due to low absorption (and therefore nothing to calculate the 'elimination half-life' from).

Full references

Additional peer reviewed literature (studies on safety, methodological considerations, and non-ginger-specific research)


Non peer reviewed resources

- Leonie, A. Ryder: Ginger in Australian Food and Medicine. 2014. Ch.9, 181-205
- Nutrition Today: [http://journals.lww.com/nutritiontodayonline/pages/default.aspx](http://journals.lww.com/nutritiontodayonline/pages/default.aspx)
Glossary

- **Anti-emetic**: anti-nausea and vomiting
- **Clinical trial**: any research study that assigns human participants to one or more health-related interventions to evaluate the effects on health outcomes
- **Cyclooxygenase pathway**: the enzyme activity responsible for the formation of prostaglandins
- **Cytokine**: small proteins that are released by cells and affect the behavior of other cells
- **Dyslipidemia**: abnormal amount of cholesterol and fat in the blood
- **Functional dyspepsia**: chronic or recurrent upper abdominal pain or discomfort
- **Free radicals**: highly reactive molecules in the body. Free radicals from toxins damage membrane lipids, proteins and DNA
- **Gastric emptying**: the process of emptying food from the stomach
- **Gastric motor**: stomach contractions involved in digestion
- **Gingerol**: the active constituent of fresh ginger. Chemically, gingerol is a relative of capsaicin and is source of the hotness of ginger. [6]-gingerol is the most abundant
- **Helicobacter pylori**: a type of bacteria that causes infection in the stomach
- **Hyperglycaemia**: an excess of glucose in the bloodstream, often associated with diabetes mellitus
- **In vitro**: outside of the body – usually experiments conducted on human cells in a test tube
- **In vivo**: inside the body. In vivo may refer to the animal or human body
- **Meta-analysis**: methods that focus on contrasting and combining results from different studies to identifying patterns among study results, sources of disagreement among those results, or other interesting relationships that may come to light in the context of multiple studies. A meta-analysis aims to give a thorough summary of several studies that have been done on the same topic, and provides the reader with extensive information on whether an effect exists and the impact of that effect
- **Pharmacokinetics**: how drugs move within the body
- **Pharmacological**: understanding the properties of drugs and their actions
- **Prostaglandin**: hormones involved in inflammatory responses and maintaining stomach mucus integrity
- **Proton pump**: pumps protons out of the cells and into the stomach cavity, making the stomach very acidic
- **Shogaol**: the processed products of gingerols (i.e. powdered ginger). Shogaols have been shown to be more powerful than their corresponding gingerols. [6]-shogaol is the most abundant