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**Important Safety Information on
Green Tea Extract-Containing Natural Health Products –
Rare Risk of Serious Liver Injury**

2017/11/15

Audience

Healthcare professionals, including pharmacists, hospital nurses, naturopathic doctors, and physicians

Key messages

- **Green tea in any form, including as an extract, is considered generally safe for the majority of consumers.**
- **However, rare and unpredictable but potentially serious cases of liver injury associated with the use of green tea extract-containing natural health products, continue to be reported in Canada and internationally.**
- **As a result of a recent Health Canada safety review, the current cautionary risk statement in Health Canada's *Green Tea Extracts* monograph will be strengthened to the following:**
 - **"If you have a liver disorder, consult a health care practitioner prior to use. Stop use if you develop symptoms of liver trouble such as yellowing of the skin/ eyes (jaundice), stomach pain, dark urine, sweating, nausea, unusual tiredness and/ or loss of appetite and consult a health care practitioner"; and**
 - **"Rare, unpredictable cases of liver injury associated with green tea extract-containing products have been reported (in Canada and internationally)".**
- **The safety review also recommended that green tea extract-containing products be used by adults only. The *Green Tea Extracts* monograph was updated in August 2017 to include a subpopulation **"Adults (≥ 18 years)"**.**
- **As a precautionary measure, Health Canada is requesting product licence holders of natural health products containing green tea extract as a medicinal ingredient and are intended for children and adolescents, to either remove the green tea extract from the product, or revise the label to indicate that the product is for adults (over 18 years of age) only.**
- **Health Canada is working with manufacturers to strengthen the safety information on labels of these products, and continues to collect information on this issue.**

What is the issue?

Cases of serious liver injury associated with the use of green tea extract-containing

natural health products continue to be reported worldwide. However, they are rare and unpredictable (idiosyncratic) events.

Products affected

Numerous natural health products contain green tea extract (*Camellia sinensis* extract) as a medicinal ingredient. Green tea is a naturally occurring source of antioxidants, such as epigallocatechin gallate (EGCG) and other catechins, and all natural health products include recommended dosages on the labels.

According to Health Canada's Licensed Natural Health Products Database¹ there are currently over 2,500 products licensed in Canada containing green tea extract as a medicinal ingredient, of which over 550 are licensed with health claims referencing weight management (in combination with diet and exercise). Green tea extract-containing natural health products are also used in Canada as a source of antioxidants for the maintenance of good health.

Green tea in any form, including as an extract, is considered generally safe for the vast majority of consumers.

Background information

Green tea extract can be present in natural health products as a single ingredient or in combination with other medicinal ingredients for various uses, including to help in weight management and as a source of antioxidants for the maintenance of good health. These natural health products are available in Canada in various oral dosage forms such as capsules, tablets, powders and liquids. Health Canada's *Green Tea Extracts* monograph, which serves as a licensing standard for natural health products containing green tea extract as a medicinal ingredient, includes risk statements advising consumers to take these products with food and to consult a healthcare professional prior to use if they have a liver disorder or if they develop signs or symptoms of liver damage.

Because of ongoing reporting of serious cases of liver injury worldwide, Health Canada conducted an assessment to examine the current data on the potential risk of liver injury with green tea extract-containing natural health products, and to determine if the current mitigation measures are sufficient. Health Canada published a summary of a recent domestic case of serious liver injury in the Health Product InfoWatch² in October 2016, to increase awareness among healthcare professionals.

Between 2006 and 2016, 11 serious Canadian cases of liver injury associated with green tea extract-containing natural health products had been reported to Health Canada. Of these 11 cases, only 2 had enough information to be further assessed. In the most recent case published in a 2016 Health Product InfoWatch², it was determined that this case of hepatotoxicity (liver injury) had a "probable" causal association, while the second case, reported in 2006, had a "possible" relation to the use of green tea extract-containing natural health products. These cases were each reported with different green tea extract-containing natural health products. A search in the *World Health Organization Adverse Drug Reaction Database* found 89

global reports of liver injury associated with the use of green tea-containing products; however, due to limitations in the available information, no further causality assessment could be conducted by Health Canada.

Health Canada's review concluded that, as previously determined, there may be a link between consumption of green tea extract-containing natural health products and the risk of rare and unpredictable (idiosyncratic) cases of liver injury. As with other cases of idiosyncratic drug-induced liver injury, no dose-response relationship could be established, and this injury may be due to an interaction of factors, including genetic, host and environmental factors. The Health Canada *Green Tea Extracts* monograph, published in 2008, includes risk statements for consumers to:

- consult a healthcare practitioner prior to use of these products if they have a liver disorder or if they develop symptoms of liver trouble (such as abdominal pain, dark urine or jaundice), and
- take the product with food.

This safety information is also required to be included on the product label for green tea extract-containing natural health products. Although the safety information had already been required, Health Canada's review found that cases of liver injury continue to be reported in Canada and worldwide, and that Canadian labelling could be stronger. Therefore, Health Canada is requiring strengthening of the labelled safety information for impacted green tea extract-containing natural health products. The revised risk statements will advise consumers:

- to stop the use of green tea extract-containing natural health products if they develop symptoms of liver trouble (i.e., yellowing of the skin/eyes [jaundice], dark urine, sweating, nausea, stomach pain, unusual tiredness, and /or loss of appetite), and consult a healthcare practitioner; and
- that rare cases of unpredictable liver injury have been reported internationally and in Canada.

The safety review also recommended that green tea extract-containing products be used by adults only. While the 2008 *Green Tea Extracts* monograph did not specify the age limit, the monograph was updated in August 2017 to include a subpopulation "Adults (≥ 18 years)".

As a precautionary measure, Health Canada is requesting product licence holders of natural health products containing green tea extract as a medicinal ingredient and are intended for children and adolescents, to either remove the green tea extract from the product, or revise the label to indicate that the product is for adults (over 18 years of age) only.

Information for consumers

Green tea in any form, including as an extract, is considered generally safe for the vast majority of consumers. Green tea extract can be present in natural health products as a single ingredient or in combination with other medicinal ingredients

promoted for a range of uses, including to aid in weight management (along with diet and exercise) and as a source of antioxidants for the maintenance of good health. These products are sold in Canada in dosage forms such as capsules, tablets, powders and liquids. Green tea extract-containing natural health products should always be taken with food. They are recommended for use by adults only (18 years of age and older).

In rare cases, green tea extract-containing natural health products have been associated with serious liver injury, which can appear as symptoms including: yellowing of the skin/eyes, dark urine, sweating, nausea, stomach pain, unusual tiredness, and loss of appetite.

Consumers should stop taking the product immediately and inform a healthcare professional (e.g., doctor, pharmacist or nurse), if they are experiencing any of these symptoms, as they may be signs of liver injury. Liver injury requires diagnosis from a doctor. People with liver disorders should also avoid taking these products.

Information for healthcare professionals

Healthcare professionals are reminded that:

- green tea extract-containing natural health products are recommended for use in adults only (18 years of age and older), but are not recommended for individuals with liver disorders.
- these products should be taken with food.
- use of green tea extract-containing natural health products should immediately be stopped if any potential symptom of liver injury occurs.
- signs of liver injury include yellowing of the skin/eyes [jaundice], dark urine, sweating, nausea, stomach pain, unusual tiredness, and loss of appetite.

Action taken by Health Canada

Health Canada is currently working with manufacturers of green tea extract-containing natural health products to strengthen the labelled safety information of these products, and is continuing to collect information on this issue. Health Canada is also requesting product licence holders of natural health products containing green tea extract as a medicinal ingredient and which are intended for children and adolescents, to either remove the green tea extract from the product, or revise the label to indicate that the product is for adults (over 18 years of age) only.

Health Canada is also communicating this important safety information to Canadians in an Information Update via the Recalls and Safety Alerts Database on the Healthy Canadians Web Site, and will post a Summary of the Safety Review to Health Canada's Web site. This communication will be further distributed through the MedEffect™ e-Notice email notification system.

Report health or safety concerns

Managing marketed health product-related side effects depends on healthcare professionals and consumers reporting them. Any case of liver injury or other serious or unexpected side effects in patients receiving green tea extract-containing natural health products should be reported to Health Canada.

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on [Adverse Reaction Reporting](https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax.

For other health product inquiries related to this communication, contact Health Canada at:

Marketed Health Products Directorate

E-mail: mhpd_dpssc@hc-sc.gc.ca

Telephone: 613-964-6522

Fax: 613-952-7738

References

1. <https://www.canada.ca/en/health-canada/services/drugs-health-products/natural-non-prescription/applications-submissions/product-licensing/licensed-natural-health-products-database.html>
2. <https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/health-product-infowatch/health-product-infowatch-october-2016.html#a14>