



Introduction

It would not be an over statement to define Green tea as one of the world's first "functional foods". Historians claim its use dates back over 40 centuries to ancient China. The myth of the Emperor Shen-Nung discovering the brew accidentally in 2737 BC when tea leaves fell into a pot of water he was boiling remains a part of the folklore of that nation. In any event, the earliest mention of green tea is punctuated not by its soothing flavour but rather by its healing powers, which have survived every type of scrutiny from antiquity to the present day. The modern citizens of Japan boast one of the longest average lifespan in the world, and there is a plethora of research to suggest that green tea plays a significant role in that claim.



Pharmacokinetic Mechanism of Action

The active ingredients in the extract of green tea are called catechins. Catechins are polyphenolic compounds present in high concentrations in green tea and display a number of antioxidant, anticarcinogenic, antiinflammatory, antiatherogenic, antimicrobial and thermogenic activities.

There are four main types of catechins occurring naturally in green tea extract; epicatechin (EC), epigallocatechin (EGC), epicatechin gallate (ECG) and epigallocatechin gallate (EGCG). EGCG is the largest and most potent of the catechins and comprises approximately 10%-50% of the total catechin content in most green tea extracts.

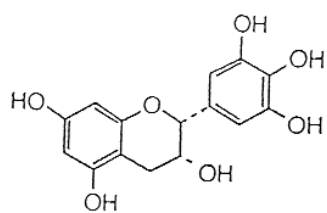
The antioxidant activity of green tea extract includes the scavenging of such reactive oxygen species as superoxide, hydroxyl and peroxy radicals.¹ It also inhibits lipid peroxidation, oxidation of low-density lipoproteins, and 2'-deoxyguanosine oxidation in DNA to 8-hydroxy-2'-deoxyguanosine.² The anticarcinogenic activity of green tea catechins may be attributable to a number of different mechanisms. The green tea catechins containing the gallate group in their structure (EGCG, EGC and ECG) have all been found to induce apoptosis in numerous tumor cell lines.³ EGCG has also been shown to inhibit angiogenesis.⁴ EGCG and ECG have been demonstrated to restrict tyrosine phosphorylation of the receptor tyrosine kinase PDGFR-beta (platelet-derived growth factor receptor-beta) and its downstream signaling pathway, consequently inhibiting the transformation of human glioblastoma cells.⁵ There is also evidence demonstrating that green tea catechins promote the synthesis of hepatic phase II enzymes that are involved in the detoxification of certain xenobiotics.

The Research

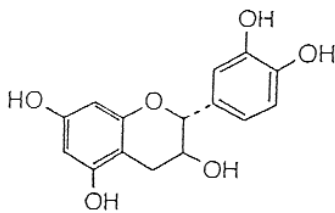
Scientists have examined the medicinal properties of green tea catechins in their most elemental form - as ordinary, commonly available green tea beverages. In fact, one study that observed 8,552 Japanese green tea drinkers aged 40 and over from 1986 to 1996 concluded that there was a significant inverse relationship between green tea consumption and incidence of cancer.⁶ The greatest degree of protection was among females consuming 10 or more cups of green tea daily with each cup containing 150mg of EGCG.⁷ The researchers attributed the difference between their degree of protection and that among males drinking an equal amount to the fact that a significantly higher percentage of the males were smokers.⁸ Green tea has also been reported to increase the tolerability of chemotherapy drugs, with one study indicating that green tea consumption can lower the cardiotoxicity of doxorubicin (Caelyx(r), Myocet(r)) without inhibiting its anti-tumor effects.⁹

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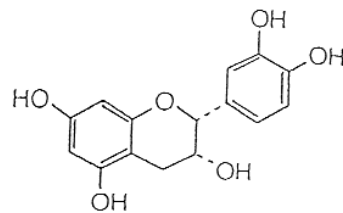
Structure of catechin derivatives



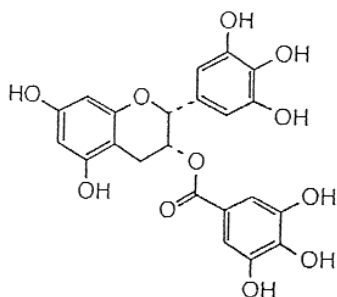
(-)-Epigallocatechin ((-)-EGC),



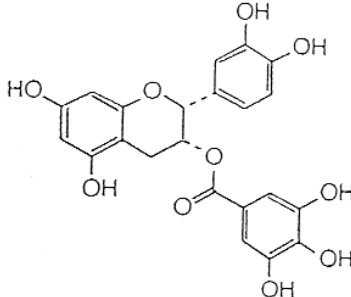
(+)-Catechin ((+)-C),



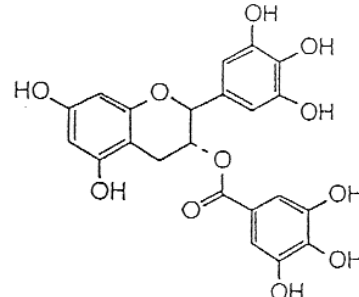
(-)-Epicatechin ((-)-EC),



(-)-Epigallocatechin gallate ((-)-EGCG),



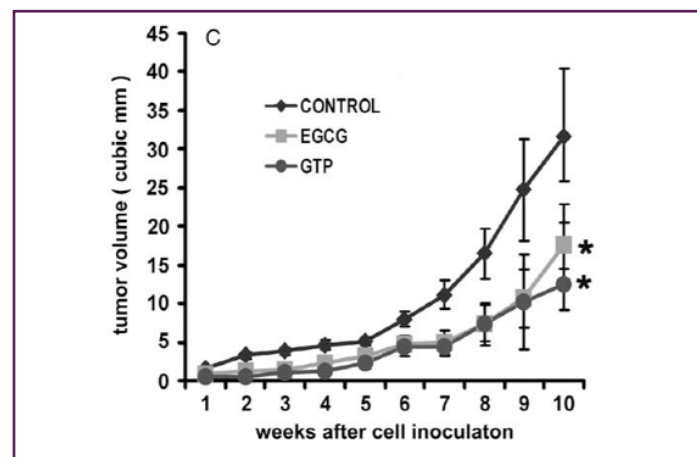
(-)-Epicatechin gallate ((-)-ECg),



(-)-Gallocatechin gallate ((-)-GCG),

The catechin constituents of green tea have also been individually examined for their effects on various types of carcinomas in animal and in-vitro studies. A very recent study demonstrated the ability of EGCG to induce apoptosis in human breast cancer cells in-vivo and in-vitro.¹⁰ The latter was assessed using a tetrazolium dye-based (MTT) assay to study the growth of a human breast cancer cell line. Both green tea polyphenols (GTP) and EGCG treatment had the ability to arrest the cell cycle in its early phase as assessed by flow cytometry.¹¹ There was also more than a 50% reduction in the expression of Cyclin E, Cyclin D and CDK 4 as well as a moderate reduction in other Cyclins and CDKs in both the GTP and EGCG groups as opposed to the controls.¹² A CDK, or Cyclin-dependent-kinase, is a special enzyme that is involved in the regulation of the cell cycle, itself a critical pathway for angiogenesis. CDK's are activated by forming a complex with cyclins.

In the in-vivo segment of the study, human breast cancer cells were injected in laboratory mice and were orally administered GTP and EGCG solutions. At the end of 10 weeks, 10% and 20% of the mice in the EGCG and GTP groups respectively, did not develop tumors whereas all the animals in the untreated control group did develop tumors.¹³ At the end of 10 weeks, the tumor volume was also reduced by 45% and 61% in the EGCG and GTP-treated groups respectively, as compared to the untreated controls, which was found to be statistically significant ($P < 0.05$).¹⁴



EGCG and the other green tea catechins have an established scientific record of contending with other forms of carcinoma as well. In fact, one particularly comprehensive in-vitro study examines the inhibitory effects of six green tea catechins and caffeine on the growth of four selected human tumor cell lines. These lines were: breast carcinoma, colon carcinoma, lung carcinoma and melanoma.¹⁵ The three most potent green tea components against all four tumor cell lines were EGCG, GC (gallocatechin) and EGC. EGCG was the most potent of the seven green tea components against three out of the four cell lines (i.e. breast cancer, colon cancer and melanoma).¹⁶ A follow-up study confirmed that these inhibitory effects were cancer-specific in the sense that they induced apoptosis in the tumor cells while leaving non-tumor cells unaffected.¹⁷

Another study examined EGCG's specific effect on human colon carcinoma cells. This EGCG study bore many of the same characteristics as the previous breast cancer study. It too, involved an in-vitro and an in-vivo phase, the latter being conducted once again with laboratory mice being injected with human cancer cells, this time of the human colon cancer cell variation.¹⁸ The in-vivo segment of the study revealed that EGCG - in a dose-dependent fashion - decreased the expression of VEGF (Vascular Endothelial Growth Factor), a critical factor in the process of angiogenesis.¹⁹ Treatment with EGCG inhibited tumor growth by 58%, microvessel density by 30%, and tumor cell proliferation by 27% - while nearly doubling tumor cell apoptosis and tripling endothelial cell apoptosis.²⁰

Conclusion

The study of the anticarcinogenic activity of green tea catechins in general and EGCG in particular is still ongoing. While EGCG and other green tea catechins are first and foremost antioxidants, it is clear that EGCG does considerably more than simply scavenge free radicals. It is true that there can be a great deal of overlap between antioxidant and antiinflammatory, antiatherogenic and even anticarcinogenic mechanisms of action. However, EGCG has always provided evidence of its uniquely diffuse capabilities. These include its antimicrobial and antiviral actions, themselves supported by in-vitro evidence. One such example of that evidence is a study that found that various green tea catechins (including EGCG) inhibited the extracellular release of verotoxin from enterohemorrhagic *Escherichia coli*.²¹ The ability to induce thermogenesis is another feature that helps to distinguish EGCG from other antioxidants. One human study concluded that green tea extracts increased energy expenditure and fat utilization in a manner that goes beyond their caffeine content and is in fact synergistic with that content. Compared with the placebo, 90 mg of EGCG and 50 mg of caffeine produced a significant 4% increase in 24-hour energy expenditure and a significant decrease in 24-hour respiratory quotient in healthy men.²² Supplementation with 50 mg of caffeine alone did not produce significant thermogenic effects.²³ (A respiratory quotient is the ratio of the volume of carbon dioxide expired to the volume of oxygen consumed).

This is testimony to the relative diversity of EGCG's biological actions, diversity that has led researchers to combine EGCG with other natural substances in the hope of producing a synergistic combination - particularly with respect to EGCG's anti-carcinogenic potential. One of these attempts has involved the ayurvedic herb curcumin, with some initially promising in-vitro results due to the

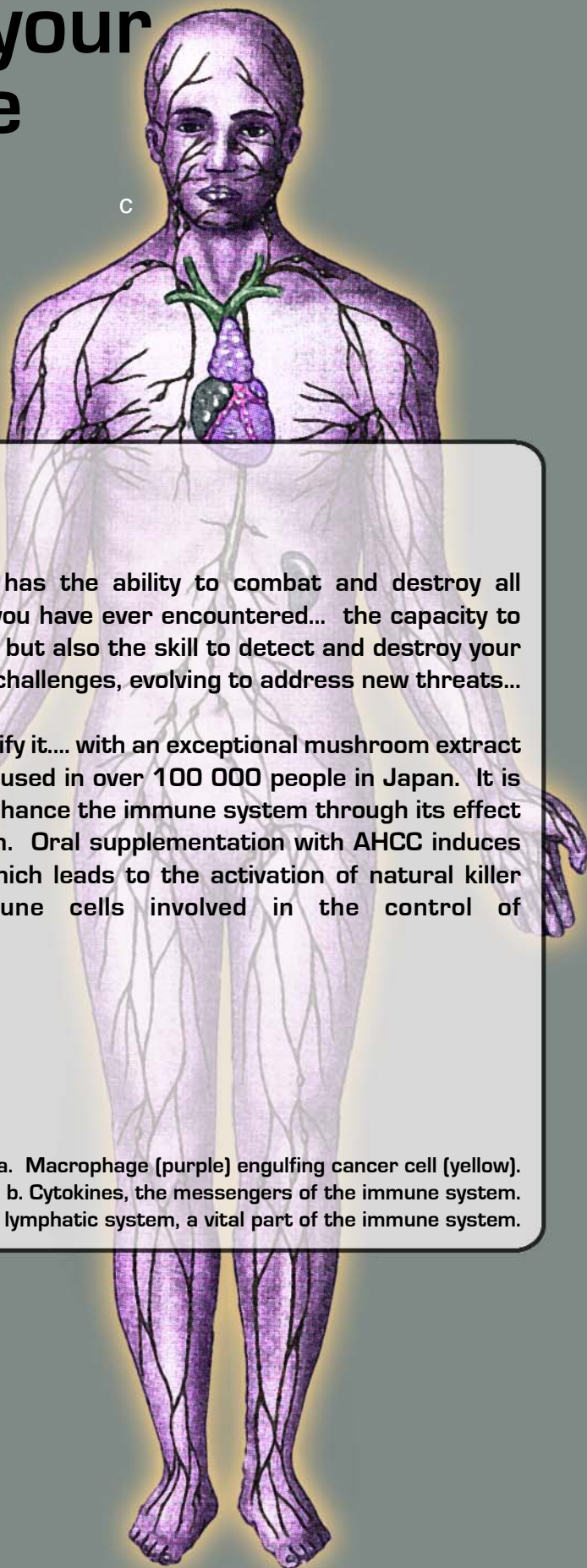
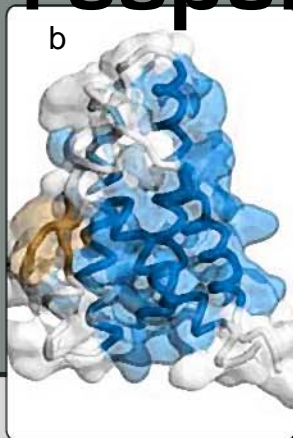
distinct mechanisms of action of each substance.²⁴ However, more research is needed with this and other substances (including advanced lipid-based delivery systems) to fully maximize the already-impressive potential of EGCG and other green tea catechins.



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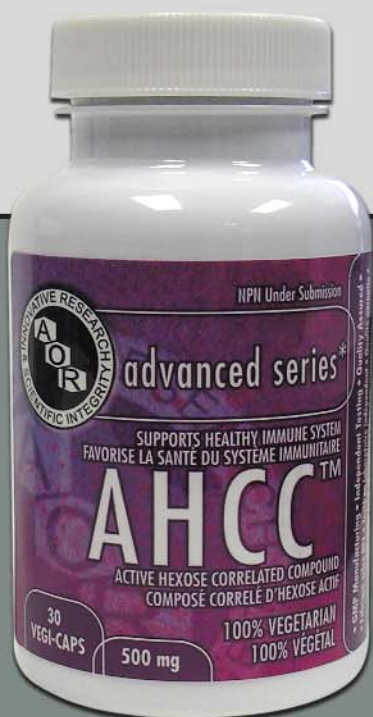
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An approach that focuses on health, not disease...



- a. Macrophage (purple) engulfing cancer cell (yellow).
- b. Cytokines, the messengers of the immune system.
- c. The lymphatic system, a vital part of the immune system.

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