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doi:10.1016/j.jnutbio.2008.07.011

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**Research article**

**Green and black tea extracts inhibit HMG-CoA reductase and activate AMP kinase to decrease cholesterol synthesis in hepatoma cells**☆

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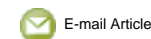
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Received 15 May 2008; revised 24 July 2008; accepted 29 July 2008. Available online 15 October 2008.

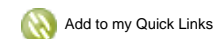
**Abstract**

Recent studies have demonstrated that green and black tea consumption can lower serum cholesterol in animals and in man, and suppression of hepatic cholesterol synthesis is suggested to contribute to this effect. To evaluate this hypothesis, we measured cholesterol synthesis in cultured rat hepatoma cells in the presence of green and black tea extracts and selected components. Green and black tea decreased cholesterol synthesis by up to 55% and 78%, respectively, as measured by a 3-h incorporation of radiolabeled acetate. Inhibition was much less evident when radiolabeled mevalonate was used, suggesting that the inhibition was mediated largely at or above the level of HMG-CoA reductase. Both extracts directly inhibited HMG-CoA reductase when added to microsomal preparations, although the extent of inhibition was considerably less than the decrease in cholesterol synthesis observed in whole cells. As HMG-CoA reductase activity also can be decreased by enzyme phosphorylation by AMP kinase, the phosphorylation state of

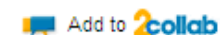
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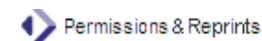
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HMG-CoA reductase and AMP kinase, which is activated by phosphorylation, was determined in lysates from cells treated with tea extracts. Both extracts increased AMP-kinase phosphorylation and HMG-CoA reductase phosphorylation by 2.5- to 4-fold, but with different time courses: maximal phosphorylation with green tea was evident within 30 min of treatment, whereas with black tea phosphorylation was slower to develop, with maximal phosphorylation occurring  $\geq 3$  hours after treatment. These results suggest that both green and black tea decrease cholesterol synthesis in whole cells by directly inhibiting HMG-CoA reductase and by promoting its inactivation by AMP kinase.

**Keywords:** Cholesterol; AMP kinase; HMG-CoA reductase; Hepatoma cells; Tea


## Article Outline

1. [Introduction](#)
2. [Methods and materials](#)
  - 2.1. [Materials](#)
  - 2.2. [Cytotoxicity assays](#)
  - 2.3. [Determination of cholesterol synthesis](#)
  - 2.4. [Determination of  \$^{14}\text{C}\$ -acetate uptake](#)
  - 2.5. [Determination of squalene and lanosterol synthesis](#)
  - 2.6. [Determination of HMG-CoA reductase activity in microsomes](#)
  - 2.7. [Immunoquantitation of AMP kinase and HMG-CoA reductase](#)

3. [Results](#)
4. [Discussion](#)

[References](#)

★ Supported in part by grant AT-003488 from the National Institutes of Health.

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