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FULL-TEXT ARTICLE**Direct inhibition of the ubiquitin-proteasome pathway by ester bond-containing green tea polyphenols is associated with increased expression of sterol regulatory element-binding protein 2 and LDL receptor.**[Kuhn DJ](#), [Burns AC](#), [Kazi A](#), [Dou OP](#).

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Green tea has been shown to lower plasma cholesterol, associated with up-regulation of the low-density lipoprotein receptor (LDLR) although the responsible molecular mechanism is unknown. Previously, we reported that ester bond-containing green tea polyphenols (GTPs), such as (-)-epigallocatechin-3-gallate [(-)-EGCG], potently inhibit the tumor cellular proteasome activity, which may contribute to the cancer-preventative effect of green tea. In the current study, we hypothesize that the proteasome is a heart disease-associated molecular target of GTPs. We have shown that ester bond-containing GTPs, including (-)-EGCG, potently inhibit the proteasomal activity in intact hepatocellular carcinoma HepG2 and cervical carcinoma HeLa cells, as evident by accumulation of ubiquitinated proteins and three natural proteasome targets (p27, IkappaB-alpha and Bax). (-)-EGCG selectively inhibits the chymotrypsin-like, but not trypsin-like, activity of the proteasome. Associated with proteasome inhibition by ester bond-containing GTPs, there was a significant, time- and concentration-dependent increase in levels of the cleaved, activated, but not the precursor, form of sterol regulatory element-binding protein 2 (SREBP-2), an essential factor for LDLR transcription. Subsequently, LDL receptor expression was increased dramatically in HepG2 and HeLa cells treated with (-)-EGCG. Our results suggest that ester bond-containing GTPs inhibit ubiquitin/proteasome-mediated degradation of the active SREBP-2, resulting in up-regulation of LDLR. This identified molecular mechanism may be related to the previously reported cholesterol-lowering and heart disease-preventative effects of green tea.

PMID: 15158750 [PubMed - indexed for MEDLINE]

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