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1: [Blood](#). 2009 Feb 3. [Epub ahead of print]



Green tea polyphenols block the anticancer effects of bortezomib and other boronic acid-based proteasome inhibitors.

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The anticancer potency of green tea and its individual components is being intensely investigated, and some cancer patients already self-medicate with this 'miracle herb' in hopes of augmenting the anticancer outcome of their chemotherapy. Bortezomib (Velcade((R))) is a proteasome inhibitor in clinical use for multiple myeloma. Here, we investigated whether the combination of these compounds would yield increased antitumor efficacy in multiple myeloma and glioblastoma cell lines in vitro and in vivo. Unexpectedly, we discovered that various green tea constituents, in particular (-)-epigallocatechin gallate (EGCG) and other polyphenols with 1,2-benzenediol moieties, effectively prevented tumor cell death induced by bortezomib in vitro and in vivo. This pronounced antagonistic function of EGCG was only evident with boronic acid-based proteasome inhibitors (bortezomib, MG-262, PS-IX), but not with several non-boronic acid proteasome inhibitors (MG-132, PS-I, nelfinavir). EGCG directly reacted with bortezomib and blocked its proteasome inhibitory function; as a consequence, bortezomib could not trigger endoplasmic reticulum stress or caspase-7 activation, and did not induce tumor cell death. Taken together, our results indicate that green tea polyphenols may have the potential to negate the therapeutic efficacy of bortezomib and suggest that consumption of green tea products may be contraindicated during cancer therapy with bortezomib.

PMID: 19190249 [PubMed - as supplied by publisher]
