Green tea catechins decrease the systemic exposure of the anti-cancer drug pazopanib

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Background and rationale.

Green tea is a widely consumed beverage and dietary supplement. *In vitro* evidence has shown that catechins, the abundant polyphenolic compounds in green tea, modulate the activity of key drug pharmacokinetic determinants, including the activity of certain drug-metabolising enzymes (e.g., Cytochrome P450 3A4) and drug-transporters (e.g., P-glycoprotein (P-gp)) (Kyriacou et al, 2025). Consequently, concomitant consumption of green tea catechins has been reported to significantly alter the systemic exposure (by 18-99%) of eleven orally-administered medications *in vivo* (e.g., rosuvastatin, digoxin, nadolol) (Kyriacou et al, 2025). Despite the prevalence of green tea consumption among patients living with cancer, the influence of green tea catechins on the systemic exposure of anti-cancer therapies remains understudied. Pazopanib is an anti-angiogenic tyrosine kinase inhibitor that has been used clinically for over a decade for the treatment of advanced renal cell carcinoma and advanced soft tissue sarcoma. Evidence from *in vitro* studies indicates that green tea catechins could influence important determinants of pazopanib pharmacokinetics *in vivo*, potentially leading to clinically significant changes in pazopanib systemic exposure when concomitantly administered with green tea catechins.

Hypothesis/Aims.

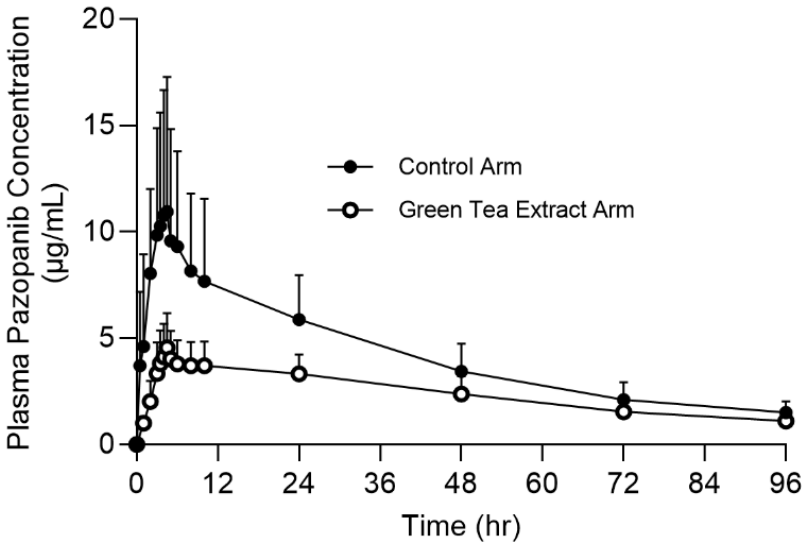
The clinical study aimed to investigate the influence of green tea catechin consumption on the pharmacokinetics of pazopanib in healthy participants. It was hypothesised that concomitant administration of a green tea extract (GTE) would influence pazopanib systemic exposure by altering pazopanib absorption from the gastrointestinal tract and/or by changing the clearance and elimination of pazopanib.

Methodology.

An open-label, single-dose, fixed-sequence pharmacokinetic study in 15 healthy participants (ACTRN12625000814471) was conducted. Participants were administered a 200 mg oral pazopanib tablet (VOTRIENT®) on two occasions: Day 1 (Control Arm) and Day 15 co-administered with an 833 mg GTE tablet (Caruso's GREEN TEA 25,000; GTE Arm). In the GTE Arm, participants were also administered an 833 mg GTE tablet once daily for 5 days prior to Day 15 (Days 10-14 inclusive) and for 3 days thereafter (Days 16-18 inclusive). Plasma samples were collected for 96 hours post-pazopanib dose and pazopanib plasma concentrations were quantified using a validated UHPLC-MS/MS assay. Pazopanib pharmacokinetic parameters were determined using noncompartmental analyses and appropriate statistical analyses were performed.

Results.

Fourteen healthy participants completed the study. Concomitant GTE administration significantly reduced ($P < 0.05$, paired *t*-test) pazopanib systemic exposure (see Figure below). The geometric mean ratios (GTE Arm/Control Arm) for pazopanib C_{max}, $AUC_{0\text{-}t}$, $AUC_{0\text{-}\infty}$ and $t_{1/2}$ were 0.44 (90% CI: 0.30 – 0.64, n = 14), 0.53 (90% CI: 0.41 – 0.68, n = 13), 0.57 (90% CI: 0.44 – 0.74, n = 13) and 1.12 (90% CI: 1.05 – 1.20, n = 13), respectively. Median pazopanib T_{max} was slightly shorter in the Control Arm (4.0 hr) than the GTE Arm (4.5 hr, $P = 0.0039$, n = 14, Wilcoxon signed-rank test).



Conclusions.
Green tea catechins decreased oral pazopanib systemic exposure. Potential mechanisms for this interaction include a catechin-mediated decrease in gastrointestinal solubility and/or availability (via physicochemical interactions) and/or an increase in the activity of intestinal P-gp. Pazopanib exhibits exposure-dependent anti-tumour activity, where systemic exposure below the therapeutic threshold has been associated with poorer treatment outcomes (Kyriacou et al, 2026). Consequently, the observed decrease in pazopanib systemic exposure with concomitant green tea catechin administration raises concerns for the potential effect of green tea consumption on therapeutic efficacy, especially for patients at risk of subtherapeutic exposure and who are regularly consuming green tea.

Statement of the scientific innovation and significance of the study.
This clinical study represents the first clinical investigation of a pharmacokinetic interaction between pazopanib and green tea catechins, and is among the first to demonstrate a significant effect of green tea catechin consumption on the systemic exposure of an anti-cancer drug. This clinical study was built upon the mechanistic insights gained from a review of green tea-drug interaction studies (Kyriacou et al, 2025) and a review of pazopanib pharmacokinetics (Kyriacou et al, 2026). Previous clinical green tea-drug studies primarily focused on the effects of green tea catechins on drug absorption, whereas in this clinical study GTE administration was initiated during a pretreatment phase, co-administered with pazopanib and continued throughout the drug elimination phase to enable an assessment of the potential effects of catechins on both absorption and elimination pathways, including time-dependent pharmacokinetic processes.

Given the widespread and regular consumption of green tea, together with the marked reduction in pazopanib systemic exposure observed, these findings highlight the importance of increasing awareness among medical professionals of the potential for green tea catechins to influence pazopanib anti-cancer response. These findings also have broader implications for other tyrosine kinase inhibitors and anti-cancer drugs with the same determinants driving pharmacokinetics and where drug response may also be impacted by changes in drug concentration with green tea catechin consumption.

Statement on the nominating student's specific role in the study.
Nicki Kyriacou led the conceptualisation and design of the clinical study and the development of the clinical study protocol. She worked closely with the clinical facility to support implementation and oversee the conduct of the study at the clinical trials unit. Nicki performed the UHPLC-MS/MS quantification of pazopanib in collected plasma samples as well as the pharmacokinetic and statistical analyses. She also contributed to the interpretation of the findings.

Declaration.
We declare that this document was prepared primarily by the nominating student and has undergone minimal corrections by the supervisor or any other author on the accompanying abstract.

Student's name: Nicki Kyriacou

Student's signature: 
Date: 8th May 2026

Supervisor's name: Professor Andrew McLachlan

Supervisor's signature: 
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References.
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