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The role of polyphenols in the development of colorectal cancer: a systematic review and meta-analysis of case-controlled studies

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Polyphenols may inhibit carcinogenesis through their antioxidant and anti-inflammatory properties.[(1)] While their efficacy has been explored *in vitro*, clinical evidence of their impact on human health is lacking. This study aims to systematically review case-controlled studies examining dietary intake of polyphenols and the development colorectal cancer (CRC).

MEDLINE, EMBASE, Web of Science, CABI, BIOSIS, CINAHL, DARE, TRIP & CDSR were searched using a predefined search strategy including 52 polyphenolic compounds. The primary outcome was diagnosis of CRC. Case-control studies measuring polyphenol intake in humans published in English between 1990–2012 were included. Study quality was assessed by the Newcastle-Ottawa Scale (NOS). Meta-analysis of adjusted odds ratios (OR) was performed with RevMan5.2. Heterogeneity was assessed using I^2 statistics.

6411 articles were identified and 7 studies met inclusion criteria (Table 1). These studies had a combined total of 18,071 patients, consisting of 6965 cases and 11106 controls. All studies were of moderate to good quality (NOS range 5–8/9). Based on self reported food-frequency questionnaires (FFQs), a total of 20 polyphenol measurements were assessed.

Based on single reports, consumption of anthocyanidins, catechin, epicatechin, enterolignans and enterolactone were associated with a reduced CRC risk. Pooled analysis showed intake of flavonols and procyanidins was associated with a reduced risk (OR:0.70 95% CI:0.61–0.80 and OR:0.78 95% CI:0.65–0.94 respectively). Non-significant trends were demonstrated with intake of phytoeostrogens (pooled OR:0.87 95% CI:0.65–1.18), quercetin (pooled OR:0.82 95% CI:0.60–1.12) and total isoflavones consumption (pooled OR:0.84 95% CI:0.66–1.06) however statistical heterogeneity was high ($I^2 > 70\%$) with one study* skewing results significantly. No other polyphenols showed significant associations.

Table 1. Case-controlled studies investigating polyphenol intake and development of colorectal cancer

Study	Population	Polyphenols Investigated
Budhathoki 2011	Japanese	Total Isoflavones
Cotterchio 2006	Canadian	Lignans, Total Isoflavones & Total Phytoeostrogens
Djuric 2012	American	Quercetin
Kyle 2010	Scottish	Quercetin, Total Flavonols, Procyanidins, Total Flavon-3-ols, Flavanones, Kampferol & Myricetin
Rossi 2006	Italian	Total Isoflavones, Total Flavonols, Total Flavon-3-ols, Flavanones, Flavones, Anthocyanidins & Total Flavanoids
Theodoratou 2007	Scottish	Total Phytoeostrogens, Quercetin, Total Flavonols, Procyanidins, Total Flavon-3-ols, Flavanones, Flavones, Catechin & Epicatechin
*Ward 2010	English	Lignans, Total Isoflavones, Total Phytoeostrogens, Daidzen, Genistein, Enterolignans & Enterolactone

In conclusion, results from case-controlled studies suggest that dietary consumption of some polyphenol sub-groups are associated with a reduced risk of developing CRC. However these associations are not as strong as *in vitro* studies would suggest. Differences in quantification of polyphenol consumption within the reported literature may hide the true role that other polyphenols play in CRC prevention. Different FFQs were used between studies and most were not validated to assess polyphenol consumption. Future epidemiological studies may consider utilising objective biomarkers as proxy measures of polyphenol intake to negate uncertainty in polyphenol intake measurements based on patient reported FFQs.

1. Lambert *et al.* (2006) *Am J Clin Nutr* **81**, 284S–291S.