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Review

Chemopreventive effects of aspirin at a glance

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ABSTRACT

Experimental, epidemiological, and clinical data from the last two decades have each supported the hypothesis that aspirin possesses anticancer properties, and that its use may also reduce the lifetime probability of developing or dying from a number of cancers. Aspirin's ability to act on multiple key metabolic and signaling pathways via inhibition of the cyclooxygenase (COX) enzyme, as well as through COX-independent mechanisms, makes it particularly relevant in the fight against cancer. A growing body of evidence indicates that aspirin may not only reduce cancer risk, but also prevent metastasis and angiogenesis while slowing the rate of mutation-inducing DNA damage. These emerging benefits of aspirin are offset to some extent by the known risks of treatment, such as cardiovascular events and gastrointestinal bleeding. However, it has been shown that pre-treatment risk assessment of individual patients and the use of proton pump inhibitors or *Helicobacter pylori* eradication therapy concomitantly with aspirin treatment can reduce these potential risks. Thus, the significant benefits of aspirin treatment, coupled with recent data concerning its risks, may prove to tip the balance in favor of aspirin use in cancer prevention.

Contents

1. Background

Aspirin is a widely used, inexpensive drug that is easily available without any prescription. Its story began in the late 18th century with the use of willow bark extract containing salicylate as an analgesic and antipyretic agent. With few modifications, this ancient remedy was first given the name aspirin in 1897 by German Chemist Felix Hoffman [1]. Decades later, in 1971, Sir John Vane elucidated aspirin's active mechanism as an inhibitor of prostaglandin synthetase [2] through the irreversible acetylation of a serine residue at position 529 [3]. Today, the prevalence of aspirin use has significantly increased as it has also

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been shown to reduce the risk of myocardial infarction and stroke [4,5]. In recent years, emerging evidence showing the benefits of aspirin in cancer prevention has ignited a renewed interest in its research [6]. In this article, we review the recent literature concerning the role of aspirin in cancer prevention and highlight its influence on several key hallmarks of cancer as a disease. Furthermore, we consider the potential mechanism of aspirin in cancer prevention and its ability to target several signaling pathways. This review also presents some important insights into the benefits and risks of aspirin use as related to its dose and the duration of treatment, which may prove to be helpful in forming a future clinical standard of aspirin use for cancer prophylaxis.

2. Aspirin as a chemopreventive agent

In the last decade, multiple new lines of evidence from a rapidly growing body of research have strengthened the hypothesis that aspirin

Table 1
Effects of aspirin on overall and site-specific cancer incidence and mortality.

Study	Follow-up/exposure period	Definition of aspirin use	Case/control or subject	HR or RR, 95% CI	Reference
Cancer incidence					
Women Health Initiative Observational Study and Clinical Trial	Median follow-up period of 9.7 years	Any aspirin used for ≥5 years	496/3743	HR = 0.98, 95% CI (0.89 to 1.08)[a] overall cancer	Brasky et al. [23]
			82/5859	HR = 0.73, 95% CI (0.54 to 0.97)[b] gastrointestinal cancer	
			54/5887	HR = 0.69, 95% CI (0.48 to 0.99)[b] colorectal cancer	
			72/5869	HR = 0.89, 95% CI (0.65 to 1.22)[a] lung cancer	
			244/5697	HR = 1.05, 95% CI (0.89 to 1.23)[a] breast cancer	
			8/4824	HR = 0.37, 95% CI (0.16 to 0.84)[b] ovarian cancer	
			24/5917	HR = 0.69, 95% CI (0.40 to 1.20)[c] melanoma	
Cancer Prevention Study II Nutrition Cohort	Median follow-up period of 10 years	Daily use of adult-strength aspirin (≥325 mg/day) for ≥5 years	493/23,259	RR = 0.84, 95% CI (0.76 to 0.93)[b] male (overall cancer)	Jacobs et al. [7]
			146/12,427	RR = 0.86, 95% CI (0.73 to 1.03)[c] female (overall cancer)	
			225/24,033	RR = 0.81, 95% CI (0.70 to 0.94)[b] prostate cancer	
			55/12,721	RR = 0.83, 95% CI (0.63 to 1.10)[c] breast cancer	
			60/38,302	RR = 0.68, 95% CI (0.52 to 0.90)[b] colorectal cancer	
			85/38,400	RR = 0.98, 95% CI (0.76 to 1.25)[a] lung cancer	
Women Health Study	Average follow-up of 10.1 years	100 mg of aspirin administered every other day	2865/39,876	RR = 1.01, 95% CI (0.94 to 1.08)[a] overall cancer	Cook et al. [24]
			1230/39,876	RR = 0.98, 95% CI (0.87 to 1.09)[a] breast cancer	
			269/39,876	RR = 0.97, 95% CI (0.77 to 1.24)[a] colorectal cancer	
			205/39,876	RR = 0.78, 95% CI (0.59 to 1.03)[c] lung cancer	
			205/39,876	RR = 0.95, 95% CI (0.68 to 1.35)[a] ovarian cancer	
Cancer mortality					
Long Term Effect of Aspirin on Cancer Mortality	20 years follow up	Daily use of aspirin for ≥5 years	1378/10,502	HR = 0.78, 95% CI (0.70 to 0.87)[b] overall cancer	Rothwell et al. [8]
			126/NS	HR = 1.09, 95% CI (0.76 to 1.56)[a] hematological cancers	
			179/NS	HR = 0.60, 95% CI (0.45 to 0.81)[b] colorectal cancer	
			210/NS	HR = 0.81, 95% CI (0.61 to 1.06)[a] prostate cancer	
			326/NS	HR = 0.71, 95% CI (0.58 to 0.89)[b] lung cancer	
			62/NS	HR = 0.42, 95% CI (0.25 to 0.71)[b] esophageal cancer	
Women Health Study	Average follow-up of 10.1 years	100 mg of aspirin administered every other day for ≥5 years	583/39,876	RR = 0.98, 95% CI (0.89 to 1.09)[a] overall cancer	Cook et al. [24]
			65/39,876	RR = 0.96, 95% CI (0.78 to 1.18)[a] colorectal cancer	
			140/39,876	RR = 0.68, 95% CI (0.45 to 1.05)[c] lung cancer	
			63/39,876	RR = 0.96, 95% CI (0.83 to 1.12)[a] breast cancer	

Abbreviations: NS, not specified; CI, confidence interval; HR, hazards ratios; RR, relative risk.
[a] No reduction.
[b] Statistically significant reduction.
[c] Statistically non-significant reduction.