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Cocoa polyphenols in oxidative stress: Potential health implications

María Angeles Martín, Sonia Ramos *

Department of Metabolism and Nutrition, Institute of Food Science and Technology and Nutrition (ICTAN), Consejo Superior de Investigaciones Científicas (CSIC), José Antonio Novais 10, Ciudad Universitaria, 28040 Madrid, Spain

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A B S T R A C T

Oxidative stress has been related to the pathogenesis of chronic diseases. Therefore, prevention of these pathologies by avoiding the damaging effects of free radicals and oxidants has become an important potential chemopreventive and therapeutic approach. In this line, epidemiologic studies have demonstrated that dietary antioxidants seem to play a main role in the prevention of chronic diseases caused by oxidative stress, such as cancer, cardiovascular disease and diabetes. Indeed, cocoa and its flavanols can interfere in the initiation and progression of the mentioned diseases through different mechanisms. This review summarises recent progress on the health benefits of cocoa and its flavanols associated to the antioxidant effects, and discusses their potential molecular mechanism of action in the prevention and/or treatment of relevant chronic diseases.

Contents

* *Corresponding author.* Department of Metabolism and Nutrition, Institute of Food Science and Technology and Nutrition (ICTAN), Consejo Superior de Investigaciones Científicas (CSIC), José Antonio Novais 10, Ciudad Universitaria, 28040 Madrid, Spain. Fax: +34 91 549 36 27.
E-mail address: s.ramos@ictan.csic.es (S. Ramos).

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1. Introduction

Oxidative stress is recognised as a main responsible for the pathogenesis of chronic diseases such as cancer, cardiovascular diseases (CVD) and diabetes (Ramos, 2008; Valko et al., 2007). These pathologies constitute a global health problem and cause death and disability to millions of people (World Health Organization, 2014). Accumulating evidence suggest that a high consumption of fruits and vegetables, which are rich in phenolic compounds, is inversely correlated with the risk and/or incidence of cancer, CVD and diabetes (Arranz et al., 2013; Ramos, 2008; Ríos, Francini, & Schinella, 2015; Shahidi & Ambigaipalan, 2015).

Cocoa is a rich source of phenolic compounds and has the highest flavanol (a polyphenol class) content of all foods on a per-weight basis (Vinson, Proch, & Zubik, 1999). Cocoa mainly contains high quantities of flavanols such as (–)-epicatechin (EC), (+)-catechin and their dimers procyanidins B2 (PB2) and B1 (Fig. 1), although other polyphenols such as quercetin, isoquercitrin (quercetin 3-O-glucoside), hyperoside (quercetin 3-O-galactoside), quercetin 3-O-arabinose, apigenin, luteolin and naringenin, have also been identified at minor amounts (Table 1) (Belscak, Komes, Horzic, Ganic, & Karlovic, 2009; Gu, House, Wu, Ou, & Prior, 2006; Kim et al., 2014; Miller et al., 2009; Sánchez-Rabaneda et al., 2003). However, it should be considered that phenolic compound content can enormously vary between cocoa beans and cocoa-derived products depending on the processing conditions and the origin of the beans (Andrés-Lacueva et al., 2008; Gu et al., 2006; Kim et al., 2014; Miller et al., 2009; Vinson et al., 1999). Indeed, the alkalinisation treatment that takes place during cocoa processing, results in 60% loss of the mean total flavonoid content (Andrés-Lacueva et al., 2008). (–)-Epicatechin shows a larger loss (67%, as a mean percentage difference) than (+)-catechin (38%), probably because of its epimerisation into (–)-catechin. Similarly, a reduction is also observed for di-, tri-, and tetrameric procyanidins (69% for dimer B2, 67% for trimer C, and 31% for tetramer D); for flavonols, quercetin seems to present the highest loss (86%, being under the limit of quantification), whereas quercetin-3-arabinoside, and isoquercitrin showed a similar reduction (62 and 61%, respectively) (Andrés-Lacueva et al., 2008). Moreover, it is essential to distinguish between the natural product cocoa and the processed product chocolate, which is a combination of cocoa, sugar, fat and other components (Gu et al., 2006; Miller et al., 2009).

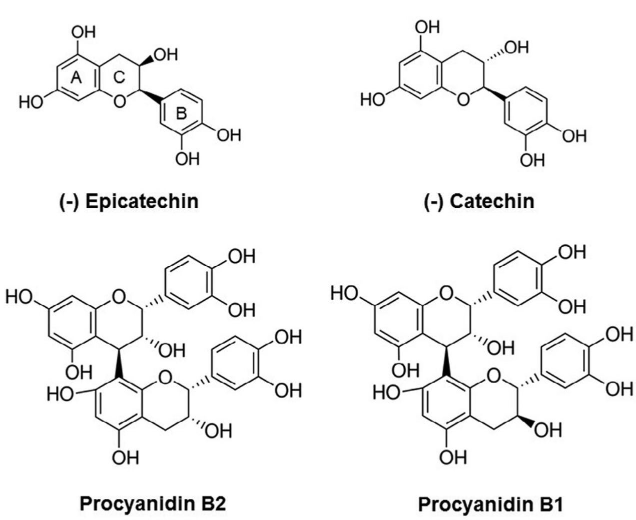

Fig. 1 – Chemical structures of main flavanols present in cocoa.

Cocoa and cocoa-derived products are highly consumed in many countries in Europe and United States (Vinson et al., 1999) and because of its high content in polyphenols have recently attracted a great interest. Cocoa flavanols seem to act as highly effective chemopreventive agents against chronic diseases including cancer, heart disease, diabetes, neurodegenerative disease, and ageing (reviewed in Kerimi & Williamson, 2015; Martín, Goya, & Ramos, 2013, 2016; Ramos, 2008). Numerous mechanisms have been proposed to account for the preventive effects of cocoa and its flavanols in cultured cells and animal models.

These mechanisms include the stimulation of tumour suppressor genes, induction of nitric oxide (NO) signalling, and activation of the insulin pathway, among many others (revised in Kerimi & Williamson, 2015; Martín et al., 2013, 2016; Ramos, 2007, 2008). The antioxidant activity of cocoa polyphenols has also been suggested as potential mechanisms for cancer, CVD and diabetes prevention (Andujar, Recio, Giner, & Rıos, 2012; Martín et al., 2016; Ramos, 2008; Shahidi & Ambigaipalan, 2015). Interestingly, the direct antioxidant effects of cocoa and its flavonoids seem to be partly based on their structural characteristics, including the hydroxylation of the basic flavan-ring system, especially 3',4'-dihydroxylation of the B-ring (catechol structure), the oligomer chain length, and the stereochemical features of the molecule (Andujar et al., 2012; Shahidi & Ambigaipalan, 2015). The chemical structure of flavanols is responsible for their hydrogen donating (radical-scavenging) properties and their metal-chelating antioxidant properties (Lambert & Elias, 2010; Nakagawa, Hasumi, Woo, Nagai, & Wachi, 2004; Shahidi & Ambigaipalan, 2015). It is worth mentioning that due to the relatively low bioavailability of catechins and extensive metabolism it is supposed that hydrogen donation reaction seems not to play a major role *in vivo*, but despite the levels of transition metals being tightly regulated