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## The role of cocoa in human health

**Zeynep Ozlem Cinar <sup>1</sup>, Maria Atanassova <sup>2</sup>, Tugba Boyunegmez Tumer <sup>3</sup>, Gianluca Caruso <sup>4</sup>, Gizem Antika <sup>1</sup>, Somesh Sharma <sup>5</sup>, Javad Sharif-Rad <sup>6</sup>, Raffaele Pezzani <sup>7,8,\*</sup>**

1 Graduate Program of Molecular Biology and Genetics, School of Graduate Studies, Canakkale Onsekiz Mart University, Canakkale, 17020, Turkey

2 Scientific Consulting, Chemical Engineering, UCTM, Sofia, Bulgaria

3 Department of Molecular Biology and Genetics, Faculty of Arts and Science, Canakkale Onsekiz Mart University, Canakkale, 17020, Turkey

4 Department of Agricultural Sciences, University of Naples Federico II, via Università 100, 80055, Portici (Napoli), Italy

5 Department of Food Technology, School of Bio Engineering and Food Technology, Shoolini University, Solan, HP, India

6 Phytochemistry Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

7 Phytotherapy Lab, Endocrinology Unit, Dept Medicine (DIMED), University of Padova, Italy

8 AIROB, Ass. Ita. Ric. Onc. Base

\* Corresponding author: [raffaele.pezzani@unipd.it](mailto:raffaele.pezzani@unipd.it)



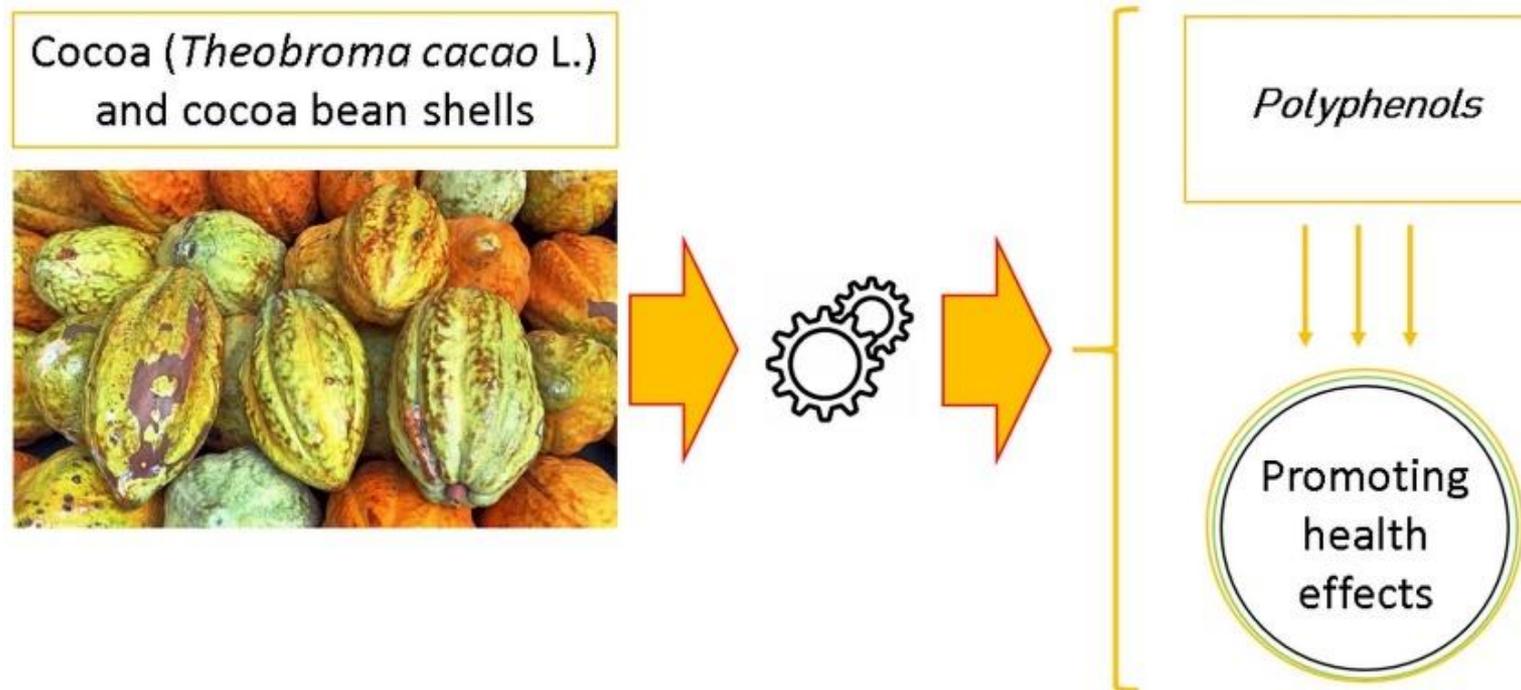
Phytotherapy lab



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# The role of cocoa in human health

## Graphical Abstract



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## **Abstract**

Cocoa is derived from the seeds of *Theobroma cacao* L., an evergreen tree typical of tropical regions. It contains numerous phytochemicals, with polyphenols representing the largest groups of compounds inside the seed, and has been implicated in numerous biological properties, such as antioxidant, antiproliferative, antiapoptotic, anti-inflammatory, anti-cancer. Moreover, cocoa has been investigated in different health conditions, including heart diseases, dyspepsia, nervous system diseases, circulation problems, and many others. Given its high consumption in many countries all over the world, it is important to know and understand its effects on human health. In addition, the cocoa bean shell, a by-product of the process of cocoa preparation, has been gaining remarkable interest due to its high content of phytochemicals. This presentation focuses on the health benefits of cocoa investigating its possible therapeutic roles in human diseases.

**Keywords:** cocoa; food; chocolate; health properties



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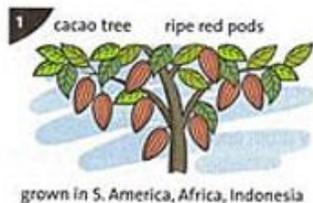
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# Introduction

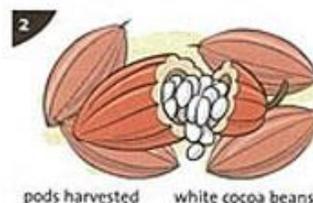
Cocoa is derived from the seeds of *Theobroma cacao* L. (a dried and thoroughly fermented product of cocoa beans)



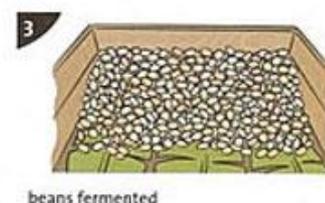
It is the peculiar ingredient of chocolate



grown in S. America, Africa, Indonesia



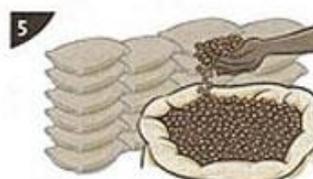
white cocoa beans



beans fermented



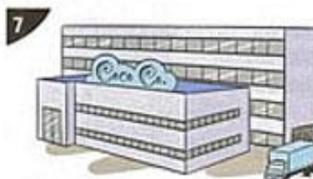
spread in sun to dry



put in large sacks



transported by train or lorry



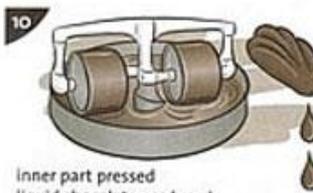
taken to factory



beans roasted



beans crushed outer shell removed



inner part pressed  
liquid chocolate produced



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# Composition

## Cocoa bean powder

Macronutrients	Fiber Content
(Caprioli et al., 2016)	(Lecumberri et al., 2007)
24.4 %–43.4 % Carbohydrates	≈60 % of the dry Cocoa sample
11.7 %–13.4 % Proteins	
24.6 %–43.1 % fats; Stearic acid (C18:0) Oleic acid (C18:1, n-9) Palmitic acid (C16:0)	

Cocoa powder

proanthocyanidins 58%,  
catechins 37%,  
anthocyanidins 4%

(Total polyphenols ≈5% w/w)

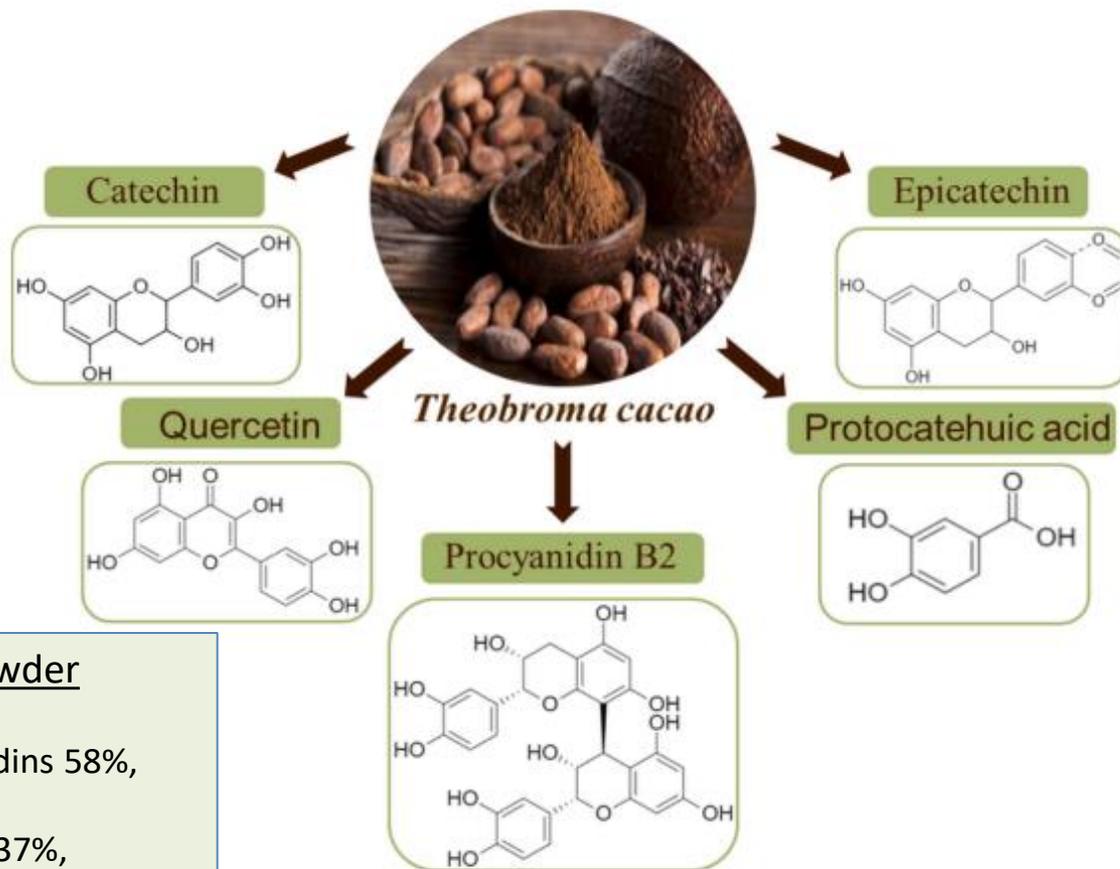


Fig. 1. Major polyphenols found in cocoa.



# Composition

## Cocoa bean powder

### Phytochemicals

(Aranaz et al., 2019; Ávila-Gálvez et al., 2019; Caprioli et al., 2016)

#### Flavanols

(-)-Epicatechin  $\approx 16,868$  mg/kg extract

Epicatechin glucoside  $\approx 951$  mg/kg extract

Catechin glucoside  $\approx 1623$  mg/kg extract

(+)-Catechin  $\approx 5782$  mg/kg extract

#### Procyanidins;

Dimer fraction of procyanidin B2  $\approx 10,116 \pm 1191$  mg/kg extract

#### Flavonols

Quercetin  $\approx 139$  mg/kg extract

Quercetin-3-arabinoside  $\approx 826$  mg/kg extract

Quercetin 3-O-glucuronide  $\approx 801$  mg/kg extract

#### Methylxanthines

Caffeic acid  $\approx 2.1$  mg/g dried extract

Theobromine  $\approx 4.7$ – $11.6$  mg/g dried extract

#### Theophylline

(Total polyphenols  $\approx 5\%$  w/w)

Fermentation, roasting and other processes can change cocoa polyphenols composition:

- reduced caffeic acid and theobromine
- reduced antioxidant capacity
- reduced polyphenols (especially epicatechin)
- etc.

Sample	Unroasted	Roasted
Ghana	$1.423 \pm 0.080^a$	$0.644 \pm 0.019^c$
Arriba	$1.716 \pm 0.014^b$	$1.156 \pm 0.179^{c,d}$
Ivory coast	$1.500 \pm 0.001^a$	$0.927 \pm 0.016^d$
Hulls	$0.023 \pm 0.002$	

Means  $\pm$  SD followed by the same letter are not significantly different ( $p > 0.05$ ). Statistical analysis was performed among samples from differ-

Table 1 Total phenolic content expressed as g catechin equivalents/100 g powder, dw (mean  $\pm$  SD, n = 3)

*Other factors can affect cocoa phytochemicals, i.e. cocoa variety, tree cultivation conditions, climatic conditions, bean maturity, harvest time, and storage after harvest*



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# Aim

Given high consumption of cocoa in many countries all over the world, it is important to know and understand its effects on human health



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# Results and discussion

According to the statistical report of the ICCO (The International Cocoa Organization), the worldwide cocoa bean production was recorded as 3.9 million tons for 2016 and 5.5 million tons for 2019

COCOA products: chocolates, sweets, pastries, beverages, confectionery, dairy products, pharmaceuticals, cosmetics



## Chocolate consumption per capita in 2017 in Kg

Switzerland	8.8
Austria	8.1
Germany	7.9
Ireland	7.9
Great Britain	7.6
Sweden	6.6
Estonia	6.5
Norway	5.8
Poland	5.7
Belgium	5.6
Finland	5.4
Slovakia	5.2
The Netherlands	5.1
New Zealand	5
Denmark	4.9
Australia	4.9
Czech Republic	4.9
Russia	4.8
United States	4.4
France	4.3



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# Cocoa health-promoting effects

1. Oxidative stress and inflammation
2. Insulin resistance and obesity
3. Cardiovascular diseases
4. Antimicrobial and antiviral
5. Antiproliferative and chemopreventive effects



Cocoa possess higher antioxidant activity compared to black tea, green tea, and red wine, by limiting ROS generation *in vitro* experiments



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# Cocoa health-promoting effects

## 1. Oxidative stress and inflammation

Protective effects of cocoa flavanols against oxidative stress in human endothelial cell line

Cells submitted to an oxidative challenge with realistic concentrations (2.5, 5, 10, and 20 µg/mL) of a cocoa phenolic extract and epicatechin



Both products **reduced** stress-induced **reactive oxygen species** and biomarkers of oxidative stress recovered depleted glutathione, antioxidant defences and cell viability (Martins et al 2020 Plant Foods Hum Nutr . 2020 Jun;75(2):161-168)

Double-blind, randomized, placebo-controlled, and crossover clinical trial, evaluation of high-polyphenols cocoa consumption

The supplementation was given as a single dose (2 h before blood sampling) in the form of high-polyphenol cocoa powder



Various genes related to inflammatory cytokines and redox balance showed a moderate differential expression in PBMCs, reduced production of reactive oxygen species, leukocyte activation as well as calcium mobilization (Barrera-Reyes et al. 2019 Eur. J. Nutr. 58 (5), 1887–1898)



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# Cocoa health-promoting effects

## 2. Insulin resistance and obesity

Low doses of a cocoa extract induced metabolic benefits in a diet-induced obesity.

Rat models fed with high fat/high sucrose diet for 70 days, treatment with cocoa extract (14 or 140 mg/kg, each day for 70 days)



**Reduced triglyceride** content and **insulin levels**, and visceral and subcutaneous fat accumulation accompanied by a significant reduction in the adipocyte size (Aranaz et al. 2019 Food Funct. 1;10(8):4811-4822)

Metanalysis with 84 studies (36 prospective observational studies and 48 interventional) in humans taking chocolate



Chocolate consumption was associated with reduced risk of cardiovascular disease death, acute myocardial infarction, stroke and diabetes. Chocolate consumption positively associated with flow-mediated dilatation at 90-150 min and at 2-18 weeks and insulin resistance markers (Veronese et al. 2019 Clin Nutr Jun;38(3):1101-1108).

**weak**  
**evidence**  
**of**  
**credibility**



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# Cocoa health-promoting effects

## 3. Cardiovascular diseases

Chocolate as a powerful in vivo antioxidant, studied in animal model of atherosclerosis

Cocoa powder (1 g (0.1 %) or 10 g (1%)) per day to Syrian Golden hamsters



Increased HDL (12 %, 23 %) and decreased LDL (62 %, 66 %) levels; reduced atherosclerosis (40 % and 36 %) if compared to untreated animals (Vinson et al. 2006 J. Agric. Food Chem. 54 (21), 8071–8076)

A double-blind, randomized, placebo-controlled trial with flavanol-rich chocolate or cocoa-free control chocolate

20 subjects with congestive heart failure followed for 4 weeks



Flavanol-rich chocolate improves vascular function in congestive heart failure patients by preventing platelet function. Blood pressure and heart rate did not change in either groups (Flammer et al. 2012 Eur. Heart J. 33 (17), 2172–2180)



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# Cocoa health-promoting effects

## 4. Antimicrobial and antiviral (numerous works available, reported the most important)

Antibacterial activity of cocoa ethanolic extract (CEE) tested in vitro and in vivo

MIC for *Staphylococcus aureus* and *Staphylococcus epidermidis* and topical applications for infected wound models



MIC of CEE towards *S. aureus* and *S. epidermidis* were at 341.9 mg/mL and 359.7 mg/mL, respectively. CEE cream 8% improved wound recovery to 72.7% and 86.1% from original rates of 23.5% and 34.7% (base cream application) for *S. aureus* and *S. epidermidis* respectively (Ariza et al. 2016 Pelita Perkebunan 32(1) 2016, 34—42)

Antibacterial activity of cocoa ethanolic extract against *Escherichia coli*.

Resulted as bacteriostatic (Ariza et al. 2014)

Fermented and unfermented dry cocoa beans against *S. aureus* and *S. typhimurium*

Resulted as bacteriostatic (Prayoga et al. 2013)

Cocoa powder in milk (1%, 2.5 % and 5% (w/v)) tested against *Cronobacter sakazakii*

Resulted as bacteriostatic (Pina-Perez et al. 2011)



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# Cocoa health-promoting effects

## 5. Antiproliferative /chemopreventive (numerous works available, reported the most important)

Study investigated the protective effect of cocoa on mice colitis-associated cancer (CAC) model

Mice fed with 5% and 10 % cocoa diet (containing AIN-93G) for 62 days



Significant reduction in disease activity index by 2–3 folds and Ki-67, iNOS and COX-2 in mouse colon tissues, with antioxidant and anti-inflammatory effects via activation of the Nrf2/Keap1 pathway (Pandurangan et al. 2015 Biofactors Jan-Feb 2015;41(1):1-14)

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Study investigating protective effect of cocoa on photocarcinogenesis and photoaging in vivo models

SKH-1 mice treated by 228 mg of cocoa extract/kg body weight daily for two weeks before UV radiation exposure



Cocoa suppressed the development of invasive squamous carcinoma, remodeling matrix metalloproteinase-9 and tissue inhibitor of metalloproteinases-1 were improved in the cocoa group (Gomez-García et al. 2020PLoS One 15 (4), e0232009)



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## Conclusions

- Highly rich in polyphenols (epicatechin, oligomers of flavan-3,4-diol, etc.)
- Any process lowers the amount of polyphenols (polyphenol content might decrease from 100% to 10%)
- Health properties:
  1. Oxidative stress and inflammation
  2. Antimicrobial and antiviral
  3. Cardiovascular diseases
  4. Insulin resistance and obesity
  5. Antiproliferative and chemopreventive effects



Dark side of cocoa products: added sugar!

Data not so consolidated (if any) in humans



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