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Review

The cardiovascular benefits of dark chocolate

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ABSTRACT

Dark chocolate contains many biologically active components, such as catechins, procyanidins and theobromine from cocoa, together with added sucrose and lipids. All of these can directly or indirectly affect the cardiovascular system by multiple mechanisms. Intervention studies on healthy and metabolically-dysfunctional volunteers have suggested that cocoa improves blood pressure, platelet aggregation and endothelial function. The effect of chocolate is more convoluted since the sucrose and lipid may transiently and negatively impact on endothelial function, partly through insulin signalling and nitric oxide bioavailability. However, few studies have attempted to dissect out the role of the individual components and have not explored their possible interactions. For intervention studies, the situation is complex since suitable placebos are often not available, and some benefits may only be observed in individuals showing mild metabolic dysfunction. For chocolate, the effects of some of the components, such as sugar and epicatechin on FMD, may oppose each other, or alternatively in some cases may act together, such as theobromine and epicatechin. Although clearly cocoa provides some cardiovascular benefits according to many human intervention studies, the exact components, their interactions and molecular mechanisms are still under debate.

Contents

1. Relevant components of chocolate and their bioavailability

After consumption of dark chocolate, the various components are digested and absorbed by distinct pathways (Fig. 1). The main ingredients of interest are theobromine, catechins, procyanidins, sucrose and lipid, and each of these can exert complementary or opposing effects on endothelial function and cardiovascular biomarkers.

Theobromine is a xanthine alkaloid and is also one of the compounds derived from caffeine metabolism. It is resistant to cocoa processing, found at high levels in dark chocolate, and has been used as a marker to indicate the cocoa content of chocolates [9]. Bioavailability studies on pure theobromine show efficient absorption into the blood with a half-life of 7.2 h [27]. A 40 g portion of dark chocolate contains a mean of 240 mg theobromine [9] which is absorbed in the small intestine to give a predicted C_{max} of 20–25 μM [27].

Catechins are flavan-3-ols found at high levels in dark chocolate. A 40 g portion of dark chocolate provides a mean of 31 mg (−)-epicatechin and 9 mg of (+)-catechin [9]. A detailed recent pharmacokinetic study on pure (−)-epicatechin indicated a half-life of 1.5 h, a T_{max} of 2 h, and no plateauing of the maximum plasma concentration up to a dose of 200 mg [2]. A 40 g portion of procyanidin-rich chocolate would achieve a plasma C_{max} of 0.2 μM [40], but most of the epicatechin in plasma is conjugated as sulfate, glucuronide and methyl derivatives [1]. Procyanidins are oligomeric flavonoids consisting of covalently-linked epicatechin and catechin moieties, and procyanidins containing 2 to 10 epicatechin "units" can be readily measured in cocoa and dark chocolate using a multi-lab validated method [36]. The

Abbreviations: BP, blood pressure; COX, cyclooxygenase; ET-1, endothelin-1; FMD, flow-mediated dilation; PDE, phosphodiesterase.

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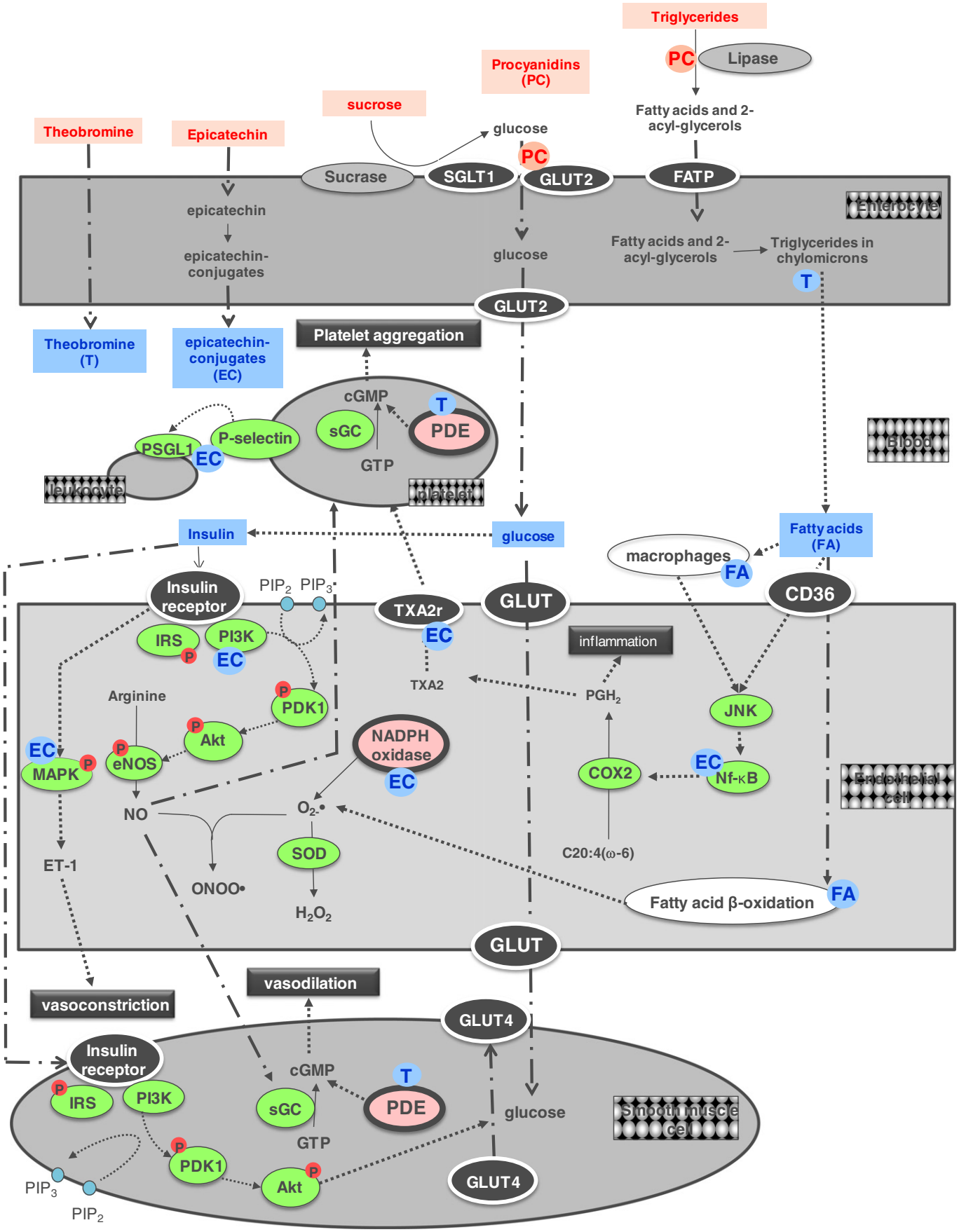
Triglycerides
PC
Lipase
Procyanidins (PC)
sucrose
Fatty acids and 2-acyl-glycerols
Theobromine
Epicatechin
glucose
PC
Sucrase
SGLT1
GLUT2
FATP
Enterocyte
epicatechin
epicatechin-conjugates
glucose
Fatty acids and 2-acyl-glycerols
Triglycerides in chylomicrons
T
GLUT2
Theobromine (T)
epicatechin-conjugates (EC)
Platelet aggregation
cGMP
T
sGC
PDE
GTP
PSGL1
P-selectin
EC
leukocyte
platelet
Blood
Insulin
glucose
Fatty acids (FA)
macrophages
FA
CD36
Insulin receptor
PIP2
PIP3
TXA2r
GLUT
EC
IRS
P
PI3K
EC
inflammation
TXA2
PGH2
Arginine
P
PDK1
JNK
P
Akt
NADPH oxidase
EC
EC
MAPK
P
P
eNOS
COX2
EC
Nf-κB
Endothelial cell
NO
O2-•
EC
SOD
ET-1
ONOO•
H2O2
C20:4(ω-6)
Fatty acid β-oxidation
FA
GLUT
vasodilation
vasoconstriction
GLUT4
Insulin receptor
cGMP
T
P
IRS
PI3K
sGC
PDE
glucose
Smooth muscle cell
GTP
P
PDK1
Akt
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GLUT4
PIP3
PIP2