

## **A chlorogenic acid-induced increase in GLP-1 production may mediate the impact of heavy coffee consumption on diabetes risk**

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### Summary:

Recent prospective epidemiology links heavy coffee consumption to a substantial reduction in risk for type 2 diabetes. Yet there is no evidence that coffee improves insulin sensitivity and, at least in acute studies, caffeine has a negative impact in this regard. Thus, it is reasonable to suspect that coffee influences the risk for beta cell “failure” that precipitates diabetes in subjects who are already insulin resistant. Indeed, there is recent evidence that coffee increases production of the incretin hormone glucagon-like peptide-1 (GLP-1), possibly owing to an inhibitory effect of chlorogenic acid (CGA – the chief polyphenol in coffee) on glucose absorption. GLP-1 acts on beta cells, via cAMP-dependent mechanisms, to promote the synthesis and activity of the transcription factor IDX-1, crucial for maintaining the responsiveness of beta cells to an increase in plasma glucose. Conversely, the “glucolipotoxicity” thought to initiate and sustain beta cell dysfunction in diabetics can suppress expression of this transcription factor. The increased production of GLP-1 associated with frequent coffee consumption could thus be expected to counteract the adverse impact of chronic free fatty acid overexposure on beta cell function in overweight insulin resistant subjects. CGA’s putative impact on glucose absorption may reflect the ability of this compound to inhibit glucose-6-phosphate translocase 1, now known to play a role in intestinal glucose transport. Delayed glucose absorption may itself protect beta cells by limiting postprandial hyperglycemia – though, owing to countervailing effects of caffeine on plasma glucose, and a paucity of relevant research studies, it is still unclear whether coffee ingestion blunts the postprandial rise in plasma glucose. More generally, diets high in “lente carbohydrate”, or administration of nutraceuticals/pharmaceuticals which slow the absorption of dietary carbohydrate, should help preserve efficient beta cell function by boosting GLP-1 production, as well as by blunting the glucotoxic impact of postprandial hyperglycemia on beta cell function.

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