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REVIEW ARTICLE

# In vivo, ex vivo and in vitro evidence for atropine-mediated attenuation of glucagon-like peptide-1 secretion: findings from a systematic review

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## Abstract

Glucagon-like peptide-1 (GLP-1) is involved in postprandial glucose homeostasis. Secretion of which involves a cholinergic pathway. Anticholinergic agent like atropine could act as a competitive antagonist of acetylcholine at muscarinic receptors. This review explores studies that assess the role of atropine in GLP-1 secretion. We selected published original articles from PubMed, Science Direct, The Cochrane Library, Trip, Google and the reference lists of the selected articles. Reporting was done according to the PRISMA statement. Relevant standard and previously published tools were used to assess the risk of bias of the selected articles. Twelve articles out of 185 search results fulfilled the review criteria. Eight were in vivo studies (six animal and two human studies), three were ex vivo studies and one was an in vitro study. Animal studies had rats, mice, pigs and monkeys as the subjects. Human studies involved healthy men and women. Majority of the studies reported an atropine-mediated attenuation of GLP-1 secretion and postprandial secretion of GLP-1 was mainly affected. However, atropine failed to significantly affect GLP-1 secretion when dipeptidyl peptidase-4 (DPP-4) enzyme was inhibited.

**Keywords** Atropine · Glucagon-like peptide-1 · Dipeptidyl peptidase-4 · Cholinergic pathway

## Background

An oral glucose load achieves a 40 to 60% increase in insulin secretion in comparison with iso-glycemic glucose infusion (Elrick et al. 1964; Perley and Kipnis 1967). The above is known as the incretin effect. Glucagon-like peptide-1 (GLP-1) is one of the two main incretin hormones (Prins 2008; Seino et al. 2010) which regulates glucose homeostasis mainly by increasing insulin release from pancreatic beta cells (UpToDate 2018a). Attenuation of GLP-1 secretion can result in hyperglycaemia. Thus, type 2 diabetes mellitus patients show a low GLP-1 response (3.113 pmol min $L^{-1}$) in comparison with controls (3.599 pmol min $L^{-1}$) (Vilsbøll et al. 2001). Therefore, dipeptidyl peptidase-4 enzyme (DPP-4) inhibitors are used in type 2 diabetes mellitus to enhance the incretin effect by inhibiting the DPP-4-mediated rapid inactivation of incretin hormones (Kuhre et al. 2015).

Secretion of GLP-1 at the distal ileum and colon occur in two phases (Prins 2008; Seino et al. 2010). Nutrients directly stimulate the late secretory phase (Anini et al. 2002). However, in the early secretory phase, glucose-dependent insulinotropic peptide (GIP) indirectly stimulates the secretion of GLP-1 via the vagus nerve. Acetylcholine action at muscarinic receptors is involved in the abovementioned indirect secretion (Herrmann-Rinke et al. 1996; Balks et al. 1997; Ahrén and Holst 2001; Anini et al. 2002). A recent hypothesis on a possible mechanism for organophosphate-related disruption of glucose homeostasis (Montgomery et al. 2008; Hectors

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