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The role of α- and β-adrenoceptor subtypes in mediating the effects of catecholamines on fasting glucose and insulin concentrations in the rat

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1 The role of α- and β-adrenoceptor subtypes in the regulation of plasma glucose and immunoreactive insulin (IRI) levels has been investigated in normal conscious fasted rats by employing selective agonists and antagonists.

2 Adrenaline ($0.2\,mg\,kg^{-1}$)-induced hyperglycaemia was abolished by the selective α_2-adrenoceptor antagonist idazoxan ($1.0\,mg\,kg^{-1}$), unaltered by non-selective β-adrenoceptor blockade (propranolol, $1.0\,mg\,kg^{-1}$) and potentiated by the selective α_1-adrenoceptor antagonist prazosin ($0.3\,mg\,kg^{-1}$). Adrenaline increased plasma IRI levels in the presence of idazoxan but not in the presence of either prazosin or propranolol.

3 The selective α_2-adrenoceptor agonists UK 14304 (0.1 and $0.3\,mg\,kg^{-1}$) and BHT-920 (0.2 and $0.5\,mg\,kg^{-1}$) elicited dose-dependent hyperglycaemic responses, but did not alter plasma IRI levels. UK 14304 ($0.1\,mg\,kg^{-1}$)-evoked hyperglycaemia was blocked by idazoxan but not by prazosin.

4 The selective α_1-adrenoceptor agonists methoxamine ($0.3\,mg\,kg^{-1}$) and phenylephrine ($0.3\,mg\,kg^{-1}$) failed to modify either plasma glucose or IRI levels.

5 Isoprenaline ($0.2\,mg\,kg^{-1}$) elicited hyperglycaemic and insulinotropic responses which were attenuated by propranolol ($1.0\,mg\,kg^{-1}$) and the selective β_2-adrenoceptor antagonist ICI 118551 ($1.0\,mg\,kg^{-1}$), but not by the β_1-selective antagonists atenolol ($1.0\,mg\,kg^{-1}$) and betaxolol ($1.0\,mg\,kg^{-1}$).

6 None of the antagonists *per se* affected basal plasma glucose or IRI concentrations, except prazosin ($1.0\,mg\,kg^{-1}$).

7 The results indicate that adrenoceptors do not appear to be involved in regulating basal plasma glucose and IRI concentrations in the fasted rat. However, the effects of catecholamines on these parameters are mediated by α_2- and β_2-adrenoceptors, whereas α_1- or β_1-adrenoceptors do not appear to be involved.

Introduction

The sympatho-adrenal system plays an important role in regulating blood glucose levels and insulin secretion under both basal and glucose-stimulated conditions. This is mediated by the activation of α- and β-adrenoceptors (Gerich & Lorenzi, 1978; Lundquist & Ericson, 1978).

α-Adrenoceptor agonists inhibit basal and glucose-induced insulin release *in vivo* as well as *in vitro* (Coore & Randle, 1964; Porte, 1967a). In contrast, β-adrenoceptor agonists stimulate insulin secretion (Porte, 1967b; Loubatières *et al.*, 1971).

The physiological effect of catecholamines on insulin secretion appears to depend on a balance between stimulation mediated by β-adrenoceptors and an inhibitory influence through α-adrenoceptor activation (Lundquist & Ericson, 1978).

Kato and co-workers demonstrated that the inhibitory α-adrenoceptors modulating insulin secretion both *in vitro* and *in vivo* were of the α_2-subtype (Nakaki *et al.*, 1980; Nakadate *et al.*, 1980a). This has subsequently been confirmed by others (Ismail *et al.*, 1983; Langer *et al.*, 1983). However, Ahren *et al.* (1984) have since demonstrated a possible involvement of inhibitory α_1-adrenoceptors in addition to α_2-adrenoceptors in the regulation of basal insulin secretion in the rat.

Loubatières *et al.* (1971) proposed that insulin secretion was stimulated by β_2-adrenoceptors, and this has since received support from other investigators (Kaneto *et al.*, 1975). However, there have been some reports of β_1-adrenoceptor mediated insulin secretion (Furman & Tayo, 1975; Harms *et al.*, 1978).

The β-adrenoceptor subtype which mediates catecholamine-induced hyperglycaemia has been proposed to be of the β_2-subtype (Kuo *et al.*, 1977), although there have been reports of β_1-adrenoceptor-mediated hyper- or hypoglycaemia (Furman & Tayo, 1975).

α_2-Adrenoceptors also appear to be involved in regulating plasma glucose levels (Nakadate *et al.*, 1980b). Clonidine, a preferential α_2-adrenoceptor agonist (Hoffman *et al.*, 1979), appears to mediate hyperglycaemia by both central (Bock & Van Zwieten, 1971) and peripheral α_2-adrenoceptor-mediated mechanisms (Ditullio *et al.*, 1984; Smythe *et al.*, 1985).

The role of α- and β-adrenoceptor subtypes in the modulation of basal insulin secretion and glucose metabolism in normal, conscious rats, was studied with newer, more selective α_1-, α_2-, β_1- and β_2-adrenoceptor agonists and antagonists. Since isoprenaline is hyperglycaemic in fasted but not in fed rats (Fleming & Kenny, 1964), fasted rats were used throughout these studies.

Some of these results have been presented to the British Pharmacological Society (Doxey *et al.*, 1986).

Methods

Experimental procedure

Normal male albino Sprague-Dawley rats (250–420 g, Olac Ltd, U.K.) that had been implanted with permanent thoracic

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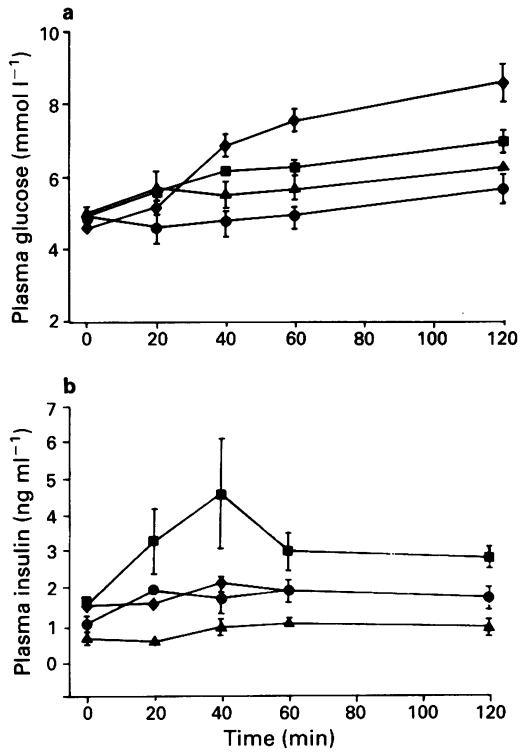

Figure 1 Changes in plasma glucose (a) and immunoreactive insulin (IRI) (b) levels elicited by adrenaline (0.2 mg kg^{-1}, ◆, $n = 4$), idazoxan (1.0 mg kg^{-1}, ●, $n = 6$), idazoxan (1.0 mg kg^{-1}) and adrenaline (0.2 mg kg^{-1}) in combination (■, $n = 5$), or saline vehicle (▲, $n = 4$). Each point shows the mean and vertical lines indicate s.e.mean. Plasma glucose responses: idazoxan vs. saline = NS; adrenaline vs. adrenaline plus idazoxan, or saline $P < 0.01$, respectively. Plasma IRI responses: idazoxan or adrenaline vs. saline = NS, respectively; idazoxan plus adrenaline vs. adrenaline $P < 0.05$.

aortic cannulae by a modification of the method of Popovic & Popovic (1960), at least 48 h previously, were fasted overnight (18 to 24 h) whilst being allowed free access to water.

At the beginning of an experiment, animals were placed in cages under minimal restraint. Control blood samples were taken once the animals had settled down.

Drugs were dissolved immediately before use in sterile saline (0.9%) except prazosin which was dissolved in distilled water. Other drugs used in the eprazosin experiments were also dissolved in distilled water to avoid any differential effects of vehicle. Drugs or saline (0.9%), or distilled water, were injected subcutaneously in volumes of 10 ml kg^{-1}, and second injections were administered in a dorsal area contralateral to the first injection.

Antagonists (or vehicle) were injected 15 min before agonists (or vehicle), which were administered at 0 min. Arterial blood samples (0.6 ml) were then taken via the aortic cannula at 20, 40, 60 and 120 min after agonist delivery for the measurement of plasma glucose and immunoreactive insulin (IRI) levels. Following each blood sample withdrawal, cannulae were flushed with sterile saline (0.9%, 0.6 ml) containing heparin (100 u ml^{-1}).

Blood samples were kept on ice throughout each experiment which was conducted in a tranquil environment.

Analytical methods

Plasma glucose was determined by a glucose oxidase method (Analox GM6 analyser) at the end of each experiment. Plasma samples were then frozen (−20°C) until IRI levels could be measured by radioimmunoassay (Novo Rat Insulin kit), the detection limit of which was 0.1 ng ml^{-1}.

Statistical methods

The areas under the curves (AUC) of the responses were initially compared for homogeneity of variance by a Bartlett's test. Data groups of homogeneous variance were then compared by the Newman-Keuls parametric test for statistically significant differences. NS indicates not significant.

Drugs

The following drugs were purchased commercially or were gifts: isoprenaline sulphate and methoxamine hydrochloride (Burroughs Wellcome, U.K.); atenolol hydrochloride, ICI 118551 (erythro-DL-1 (7-methylindan-4-yloxy)-3-isopropylaminobutan-2-ol) and propranolol hydrochloride (Imperial Chemical Industries Ltd, U.K.); BHT-920 (2-amino-6 - allyl - 5,6,7,8 - tetrahydro - 4H - thiazolo[4,5 - d]azepine dihydrochloride) (Dr. Karl Thomae GmbH), (−)-phenylephrine hydrochloride (Koch Light Ltd, U.K.); prazosin hydrochloride and UK 14304 (5-bromo-N-(4,5-dihydro-1H-imidazol-2-yl)-6-quinoxalinamine) (Pfizer, U.K.); idazoxan (Reckitt and Colman plc, U.K.); (−)-adrenaline bitartrate (Sigma, U.K.); and betaxolol (Synthelabo, France).

Results

Effects of agonists

The mixed α- and β-adrenoceptor agonist adrenaline (0.2 and 0.5 mg kg^{-1}) caused a pronounced dose-dependent hyperglycaemia. Mean basal plasma glucose levels increased progressively from 5.3 ± 0.1 and 5.5 ± 0.1 mmol l^{-1} to mean peak levels of 11.5 ± 0.9 ($n = 5$) and 16.4 ± 0.8 mmol l^{-1} ($n = 5$) respectively 120 min after its administration (both $P < 0.01$), whereas no significant changes occurred in the mean plasma IRI levels.

The mixed β_1- and β_2-adrenoceptor agonist isoprenaline (0.2 and 0.5 mg kg^{-1}, Daly & Levy, 1979) elicited dose-dependent hyperglycaemic responses. The lower and higher doses of isoprenaline respectively elevated mean basal plasma glucose levels from 5.4 ± 0.1 and 6.1 ± 0.3 mmol l^{-1} to mean maximal levels of 8.2 ± 0.2 ($n = 6$) and 9.8 ± 0.4 mmol l^{-1} ($n = 4$) 60 min after its administration (both $P < 0.01$). Both doses caused similar marked insulinotropic responses. Mean plasma IRI levels were raised from 0.6 ± 0.1 and 0.5 ± 0.1 ng ml^{-1} to mean peak levels of 3.2 ± 0.6 and 4.0 ± 0.9 ng ml^{-1} respectively, 20 min after its administration (both $P < 0.01$ compared to saline, but NS for lower vs. higher dose of isoprenaline).

The selective α_1-adrenoceptor agonists phenylephrine (0.3 mg kg^{-1}) and methoxamine (0.3 mg kg^{-1}, Van Meel *et al.*, 1981) caused no significant alterations of either plasma glucose or IRI levels.

In contrast, the selective α_2-adrenoceptor agonists BHT-920 (0.2 and 0.5 mg kg^{-1}) and UK 14304 (0.1 and 0.3 mg kg^{-1}, Van Meel *et al.*, 1981) evoked comparable, mild dose-dependent hyperglycaemic responses. Mean basal plasma glucose levels were raised from 4.3 ± 0.1 and 4.6 ± 0.2 mmol l^{-1} to mean peak levels of 7.3 ± 0.3 ($n = 6$) and 9.1 ± 0.5 mmol l^{-1} ($n = 6$) (BHT-920) and from 4.6 ± 0.3 and 4.7 ± 0.1 mmol l^{-1} to 7.6 ± 0.6 ($n = 4$) and 9.6 ± 0.7 mmol l^{-1} ($n = 4$) (UK 14304) ($P < 0.01$ in each case), results similar to those observed with adrenaline. Like adrenaline, plasma IRI levels were unchanged by either BHT-920 or UK 14304.

Effects of selective α_1- and α_2-adrenoceptor antagonists

The selective α_2-adrenoceptor antagonist, idazoxan (0.3 or 1.0 mg kg^{-1}, Doxey *et al.*, 1983) caused no significant changes in basal plasma glucose or IRI levels. In contrast, although the selective α_1-adrenoceptor antagonist prazosin (0.3 or

1.0 mg kg^{-1}, Cavero & Roach, 1980) did not affect basal plasma IRI levels, a significant mean maximal increase in basal plasma glucose levels of 2.5 mmol l^{-1} occurred at the higher prazosin dose ($P < 0.01$ compared to vehicle or 0.3 mg kg^{-1} prazosin). For this reason, prazosin was employed in all other experiments at 0.3 mg kg^{-1}.

Effects of selective α_1 or α_2-adrenoceptor blockade on adrenaline-induced hyperglycaemia

In order to determine which α-adrenoceptor subtype(s) was involved in mediating adrenaline hyperglycaemia, rats were pretreated with either idazoxan or prazosin before adrenaline administration.

Idazoxan (1.0 mg kg^{-1}) pretreatment resulted in a dual effect upon adrenaline (0.2 mg kg^{-1}) hyperglycaemia (Figure 1). Firstly, adrenaline failed to elevate plasma glucose levels in the presence of idazoxan. Secondly, adrenaline elicited a significant increase in plasma IRI levels following idazoxan administration.

Pretreatment with prazosin (0.3 mg kg^{-1}) appeared to exert an opposite effect to that evoked by idazoxan upon adrenaline hyperglycaemia (Figure 2). Prazosin dramatically augmented the adrenaline hyperglycaemia, with a mean maximal increase in plasma glucose of 10.2 mmol l^{-1} being observed. However, prazosin (0.3 mg kg^{-1}) did not modify the effects of adrenaline on plasma IRI levels, even though increases were observed in some animals after 120 min.

Effects of non-selective β-adrenoceptor blockade upon adrenaline-induced hyperglycaemia

The relative contribution of β-adrenoceptor stimulation by adrenaline in mediating the hyperglycaemic response was examined by pretreatment with propranolol (1.0 mg kg^{-1}), a mixed β-adrenoceptor antagonist (Shanks, 1984). This drug produced small ($\simeq$1 mmol l^{-1} at 60 and 120 min) reductions in adrenaline (0.2 mg kg^{-1})-induced hyperglycaemia, but these were not statistically significant. Plasma IRI levels remained unaffected in each treatment group.

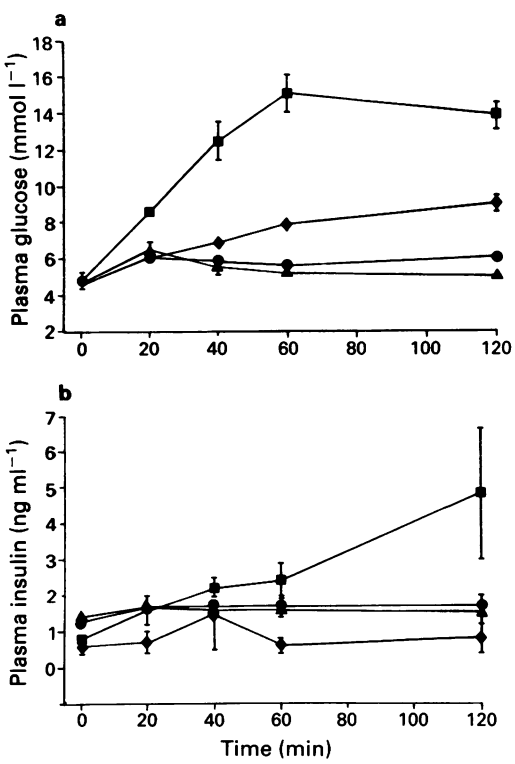

Figure 2 Changes in plasma glucose (a) and immunoreactive insulin (IRI) (b) levels induced by adrenaline (0.2 mg kg^{-1}, ◆, $n = 4$), prazosin (0.3 mg kg^{-1}, ●, $n = 4$), prazosin (0.3 mg kg^{-1}) and adrenaline (0.2 mg kg^{-1}) in combination (■, $n = 4$), or distilled water vehicle (▲, $n = 4$). Each point shows the mean and vertical lines indicate s.e.mean. Plasma glucose responses: prazosin vs. water = NS; adrenaline vs. adrenaline plus prazosin, or water $P < 0.01$, respectively. Plasma IRI responses = NS for each comparison.

Effects of selective α_1- or α_2-adrenoceptor blockade upon UK 14304-induced hyperglycaemia

The hyperglycaemia induced by UK 14304 was examined further by employing the selective α_2- and α_1-adrenoceptor antagonists idazoxan and prazosin.

Pretreatment with idazoxan (1.0 mg kg^{-1}) completely obtunded the hyperglycaemic response to UK 14304 (0.1 mg kg^{-1}) (Figure 3a). However, neither idazoxan (1.0 mg kg^{-1}) nor UK 14304 (0.1 mg kg^{-1}) alone, nor idazoxan and UK 14304 in combination altered plasma IRI levels.

Prazosin (0.3 mg kg^{-1}) pretreatment slightly but significantly augmented UK 14304 (0.1 mg kg^{-1})-induced hyperglycaemia (Figure 3b). The mean maximal increase in plasma glucose elicited by UK 14304 of 3.0 mmol l^{-1} was increased to 4.1 mmol l^{-1} in the presence of prazosin ($P < 0.01$). However, no change in plasma IRI levels occurred in any of the latter treatment groups.

Effects of selective β_2-adrenoceptor blockade upon the hyperglycaemic and insulinotropic effects of isoprenaline

The β-adrenoceptor subtype involvement in the glucose and insulin responses to isoprenaline was examined by using the

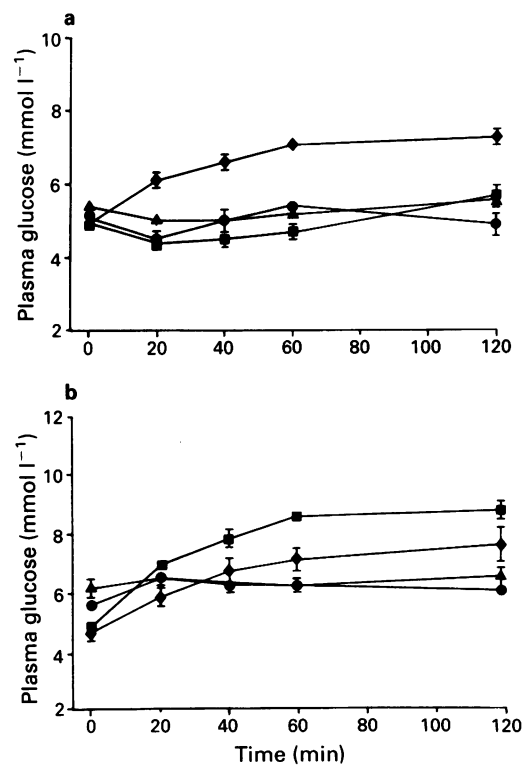

Figure 3 (a) Changes in plasma glucose levels produced by UK 14304 (0.1 mg kg^{-1}, ◆, $n = 5$), idazoxan (1.0 mg kg^{-1}, ●, $n = 4$), UK 14304 (0.1 mg kg^{-1}) and idazoxan (1.0 mg kg^{-1}) in combination (■, $n = 5$), or saline vehicle (▲, $n = 4$). Idazoxan vs. saline = NS; UK 14304 vs. UK 14304 plus idazoxan, or saline $P < 0.01$, respectively. (b) Changes in plasma glucose levels produced by UK 14304 (0.1 mg kg^{-1}, ◆, $n = 4$), prazosin (0.3 mg kg^{-1}, ●, $n = 4$), UK 14304 (0.1 mg kg^{-1}) and prazosin (0.3 mg kg^{-1}) in combination (■, $n = 4$), or distilled water vehicle (▲, $n = 4$). Prazosin vs. water = NS; UK 14304 vs. UK 14304 plus prazosin, or water $P < 0.01$, respectively, In (a) and (b), each point represents the mean and vertical lines show s.e.mean.

selective β_2-adrenoceptor antagonist ICI 118551 (Bilski et al., 1983). Pretreatment with ICI 118551 ($1.0\,mg\,kg^{-1}$) totally abolished the hyperglycaemia induced by isoprenaline ($0.2\,mg\,kg^{-1}$) (Figure 4). In fact the two drugs in combination resulted in a slight but significant hypoglycaemia ($P < 0.01$ compared to ICI 118551 alone, saline vehicle, or isoprenaline). ICI 118551 ($1.0\,mg\,kg^{-1}$) also effectively antagonized isoprenaline ($0.2\,mg\,kg^{-1}$)-evoked increases in plasma IRI levels ($P < 0.01$). ICI 118551 ($1.0\,mg\,kg^{-1}$) alone did not alter either basal plasma glucose or IRI levels.

Effects of selective β_1-adrenoceptor blockade upon the hyperglycaemic and insulinotropic effects of isoprenaline

The β-adrenoceptor involvement in the actions of isoprenaline was further investigated with the selective β_1-adrenoceptor antagonists atenolol (Conway et al., 1976) and betaxolol (Boudot et al., 1979). Neither atenolol ($1.0\,mg\,kg^{-1}$) nor betaxolol ($1.0\,mg\,kg^{-1}$, $n = 6$) significantly altered the hyperglycaemic and insulinotropic responses to isoprenaline ($0.2\,mg\,kg^{-1}$, NS in each case).

At these doses neither drug caused any significant changes in basal plasma glucose or IRI levels ($n = 6$, NS in each case; data not shown).

Effects of isoprenaline during non-selective β-adrenoceptor blockade

In order to assess any possible effects of isoprenaline which were not β-adrenoceptor-mediated, propranolol pretreatment was used. Similar to effects seen with ICI 118551, propranolol ($1.0\,mg\,kg^{-1}$) effectively antagonized isoprenaline-evoked elevations in both plasma glucose and IRI levels (both $P < 0.01$). Propranolol ($1.0\,mg\,kg^{-1}$) alone produced no effect (data not shown).

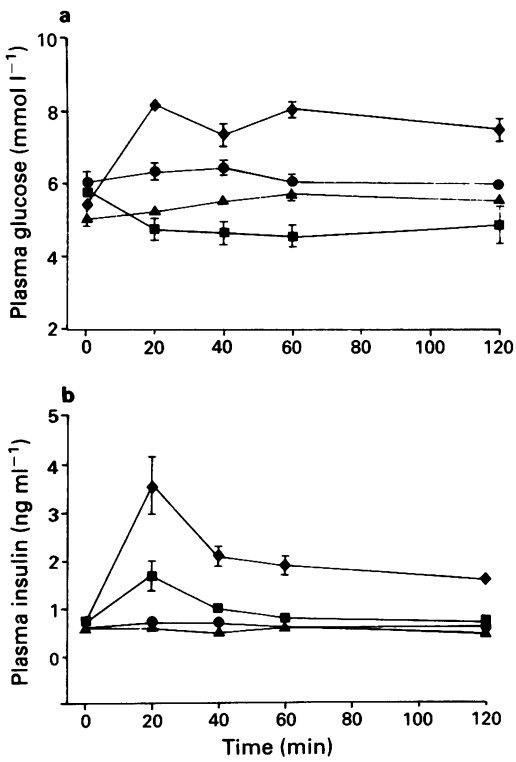

Figure 4 Changes in plasma glucose (a) and immunoreactive insulin (IRI) (b) levels induced by isoprenaline ($0.2\,mg\,kg^{-1}$, ◆, $n = 4$), ICI 118551 ($1.0\,mg\,kg^{-1}$, ●, $n = 4$), isoprenaline ($0.2\,mg\,kg^{-1}$) and ICI 118551 ($1.0\,mg\,kg^{-1}$) in combination (■, $n = 5$), or saline vehicle (▲, $n = 4$). Each point represents the mean and vertical lines show s.e.mean. Plasma glucose responses: ICI 118551 vs. saline = NS; isoprenaline vs. isoprenaline plus ICI 118551, or saline $P < 0.01$, respectively; isoprenaline plus ICI 118551 vs. saline $P < 0.01$. Plasma IRI responses: ICI 118551 vs. saline = NS; isoprenaline vs. isoprenaline plus ICI 118551, or saline $P < 0.01$, respectively.

Discussion

The observed adrenaline and isoprenaline-induced hyperglycaemic responses correlate well with the findings of Fleming & Kenny (1964) and Potter & Ellis (1975), in that adrenaline elicited a significantly larger rise in plasma glucose levels than that evoked by the same dose of isoprenaline. In contrast to isoprenaline, adrenaline exerted no significant effects on plasma IRI levels.

The hyperglycaemic responses to the selective α_2-adrenoceptor agonists UK 14304 and BHT 920 agree with the findings of Nakadate et al. (1980b) and Ditullio et al. (1984). However, neither compound produced the expected reduction in plasma IRI levels.

The absence of hyperglycaemic response to the selective α_1-adrenoceptor agonists methoxamine and phenylephrine do not lend support for an important role of α_1-adrenoceptors in regulating blood glucose levels.

None of the α_1-, α_2-, β_1- or β_2-adrenoceptor antagonists alone affected basal plasma IRI levels. This finding is at variance with those of Ahren et al. (1984) and Torella et al. (1976) who demonstrated increases in plasma IRI levels in response to infusions of α_1- and α_2-adrenoceptor antagonists (phentolamine, yohimbine and prazosin), and a reduction in plasma IRI levels in response to an infusion of propranolol. However, Ahren and co-workers employed fed, anaesthetized rats, and although Torella et al. used 16 h fasted rats, they demonstrated increases in basal plasma IRI levels only after phentolamine infusion. In addition, recent studies have demonstrated that phentolamine can induce insulin secretion by an action which is independent of its α-adrenoceptor antagonist properties (Schulz & Hasselblatt, 1988).

Basal plasma glucose levels were also unaffected by any of the antagonists employed, with the exception of prazosin, which evoked mild hyperglycaemic responses at $1.0\,mg\,kg^{-1}$, but not at $0.3\,mg\,kg^{-1}$. This is not easily explainable, although Ahren et al. (1984) proposed that prazosin hyperglycaemia could be a result of diminished peripheral glucose uptake. This latter proposal is in agreement with several findings which have demonstrated an increase in glucose uptake and its subsequent metabolism following peripheral α-adrenoceptor activation (Kneer et al., 1974; Clark et al., 1983). This finding suggests that adrenoceptors are not involved in the regulation of basal plasma glucose and insulin levels under fasting conditions.

Adrenaline hyperglycaemia was abolished by idazoxan, unaffected by propranolol and markedly potentiated by prazosin. This finding indicates that adrenaline hyperglycaemia is mediated predominantly by α_2-adrenoceptors in fasted rats. This contrasts with previous studies which have demonstrated a complete abolition of adrenaline hyperglycaemia only in the presence of dual α- and β-adrenoceptor blockade (Nash & Smith, 1972; Shikama & Ui, 1975). The enhanced hyperglycaemic response to adrenaline in the presence of prazosin may be explained by the hypotensive effects of the drug combination. The blood pressure drop may have been sufficient to elicit a sympatho-adrenal reflex response, in which catecholamines released from the adrenal medulla and an inhibition of insulin secretion mediated by the sympathetic nerves supplying the pancreas result in a profound hyperglycaemia (Jarhult & Holst, 1978). Another possible explanation which is not mutually exclusive is that peripheral glucose uptake was inhibited by the synergistic combination of adrenaline activation of peripheral β-adrenoceptors which inhibit glucose uptake (Clark et al., 1983); and prazosin blockade of peripheral α_1-adrenoceptors, which are thought to facilitate glucose uptake (Clark et al., 1983; Clark & Patten, 1984).

Adrenaline caused an elevation of plasma IRI levels in the presence of the selective α_2-adrenoceptor antagonist idazoxan, which is in agreement with the work of Nakadate *et al.* (1980a), who showed that adrenaline can inhibit insulin secretion *in vivo* by activation of pancreatic postjunctional α_2-adrenoceptors. It is probable that the observed increases in plasma IRI levels observed in the presence of idazoxan were due to stimulation of pancreatic β-adrenoceptors by adrenaline.

Adrenaline elicited no apparent changes in plasma IRI levels after prazosin pretreatment, indicating that either pancreatic α_1-adrenoceptors are absent or they play only a minor role in controlling the release of insulin under fasting conditions in the rat.

UK 14304-induced hyperglycaemia was abolished by idazoxan but not by prazosin pretreatment, indicating that UK 140304 probably elevated plasma glucose by an α_2-adrenoceptor mediated mechanism.

Isoprenaline-induced increases in plasma glucose and IRI levels were effectively attenuated by propranolol and similarly by ICI 118551, but not by atenolol and betaxolol. These observations imply that β_2-adrenoceptors mediated the hyperglycaemic and insulinotropic responses to isoprenaline. These findings do not support a major role for β_1-adrenoceptors modulating plasma insulin or glucose levels in the fasted rat, which agrees with the results of Loubatières *et al.* (1971) and Kuo *et al.* (1977).

In conclusion, our results demonstrate that adrenoceptors are seemingly not involved in the regulation of basal plasma glucose and insulin concentrations in the fasted rat. However, the effects of the catecholamines, adrenaline and isoprenaline, upon these latter parameters are mediated by α_2- and β_2-adrenoceptors, but not by α_1- or β_1-adrenoceptors. Our findings differ from studies in man in which idazoxan reversed the adrenaline-induced inhibition of insulin secretion, but not adrenaline hyperglycaemia (Struthers *et al.*, 1985). It therefore appears that α_2-adrenoceptors do not have identical physiological roles in rat and man.

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