

See discussions, stats, and author profiles for this publication at: <http://www.researchgate.net/publication/14265137>

The pharmacological basis for the use of dried sheep placenta in traditional obstetric practice in Nigeria

ARTICLE *in* JOURNAL OF ETHNOPHARMACOLOGY · NOVEMBER 1996

Impact Factor: 3 · DOI: 10.1016/0378-8741(96)01445-6 · Source: PubMed

CITATIONS

8

READS

110

2 AUTHORS, INCLUDING:



Samuel Ghasi

University of Nigeria

35 PUBLICATIONS 232 CITATIONS

SEE PROFILE

The pharmacological basis for the use of dried sheep placenta in traditional obstetric practice in Nigeria

G. Onuaguluchi*, S. Ghasi

Department of Pharmacology and Therapeutics, College of Medicine, University of Nigeria, Enugu, Nigeria

Received 6 February 1995; revised 30 April 1996; accepted 24 May 1996

Abstract

Dried sheep placenta is sometimes used in traditional medicine to facilitate labour. The effects of an extract of powdered dried sheep placenta with normal saline on guinea-pig uterus, ileum, spontaneously beating atrium and Langendorff heart, rat uterus and hindquarters, and cat blood pressure were therefore examined. It was found that 1 g of dried sheep placenta had, on the guinea-pig uterus, an oxytocic activity equipotent with 0.075–0.32 i.u. of oxytocin. The oxytocic activity was unaffected at pHs between 4 and 10 or by boiling for 30 min or autoclaving for 15 min. Neither atropine nor promethazine inhibited the oxytocic action, but promethazine inhibited, to the same degree, contractions induced in the ileum by equipotent doses of the infusion and histamine. Atropine, however, had no effect on infusion-induced contractions in the ileum. The vasoconstriction induced in the rat hindquarters was antagonized by promethazine and phentolamine. Cat blood pressure was reduced, but it had positive inotropic and chronotropic effects on the spontaneously beating guinea-pig atrium and on the guinea-pig Langendorff heart. It was concluded that the dried placenta contains a chorionic oxytocic substance the action of which is independent of stimulation of H_1 receptors or of muscarinic receptors.

Keywords: Dried sheep placenta; Oxytocic effect; Mammalian smooth muscle; Langendorff heart

1. Introduction

The placenta, which produces many hormones, is not known to produce oxytocin. This hormone is produced in the posterior pituitary and primarily responsible for uterine contraction

during labour. Although oxytocin receptors are present in the endometrium and, on activation, cause the decidua to produce prostaglandins, especially PGF_2 (Ganong, 1985; Wathes et al., 1993), it is doubtful if the chorion from which the foetal part of the placenta arises, synthesizes any prostaglandins (La Barbera, 1993). It was therefore of great interest when a female traditional medicine practitioner, during a discussion,

* Corresponding author.

claimed that she uses powdered dried sheep placenta, administered orally, to facilitate delivery in patients with uterine inertia.

Sisson et al. (1961) have shown that dialysates from homogenates of rabbit placenta contain a hypotensive-inducing, smooth muscle contracting principle, which was later shown by Sisson (1963) to be a polypeptide which was not oxytocin or bradykinin. The substance, however, did not contract the gravid rabbit uterus.

Even if the sheep placenta produced an oxytocic peptide, it would seem unreasonable to assume that the dried placenta could contain an active oxytocic peptide. Nonetheless, it was decided to investigate the possible oxytocic effects of infusions of fresh placenta in normal saline. To our great surprise, it was found that the infusion had a strong oxytocic action on pregnant and non-pregnant adult guinea-pig uteri, and that from 1 g of the sheep placenta, an oxytocic effect equipotent with 2.5–60 IU of oxytocin could be obtained. Pregnant and non-pregnant rat uteri were also stimulated. The oxytocic activity was not affected by boiling or by autoclaving the infusion for 15 min at 121°C at a pressure of 1.05 kg/cm². It was therefore decided to examine the oxytocic effects of normal saline extract of the pulverized dried placenta on pregnant and non-pregnant mature guinea-pig uterus, and on pregnant rat uterus. The effects of heat, changes in pH of the extract, and enzyme hydrolysis with trypsin and pepsin on the oxytocic activity were then investigated. The effect of the saline extract on the intestine (guinea-pig ileum) and on the cardiovascular system using four animal models were also examined.

2. Methods and materials

2.1. Preparation of saline extract from dried placenta

Fresh placenta from recently delivered sheep was cleaned with normal saline and all blood clots were removed. The placenta was then weighed, cut into small pieces and dried in a hot air oven at 40–50°C until a constant weight was obtained.

The dried placenta was then pulverized in a ceramic mortar and the powder was stored in a desiccator. Ten g aliquots of the powder were extracted at room temperature with 25 ml of normal saline for 3 h, after which it was centrifuged at 4800 rev./min for 10 min. The supernatant was collected and stored in a refrigerator at 4°C. Any volume of the extract, therefore, was easily related to the weight of the powdered placenta and thus to the weight of the fresh placenta. The weight of the extract was expressed as weight of dry placenta which produced that quantity of extract.

2.2. Preparation of saline infusion from fresh placenta

Fresh sheep placenta cleaned as already described was weighed and put into a beaker containing normal saline such that 1 g of placenta was in 1 ml of saline. After 3 h, the saline infusion was filtered through gauze and then through Whatman paper. The filtrate was stored in a refrigerator at 4°C. The weight of the extract was expressed as weight of fresh placenta yielding that quantity of extract.

2.3. Guinea-pig uterus preparation

Pregnant and non-pregnant mature guinea-pigs weighing between 250 g and 400 g were used. The uterine horn was dissected out and was mounted vertically in a 50 ml organ bath according to standard procedures. The bath contained De Jalon solution with the following composition (g/l): NaCl, 9.0; KCl, 0.42; NaHCO₃, 0.5; CaCl₂, 0.3; glucose, 0.5. The bath was aerated with a mixture of 95% oxygen and 5% CO₂ and was maintained at 33°C ± 0.5°C. The tension of the tissue was about 1 g and the contractions were recorded with a frontal writing lever on smoked paper mounted on a rotating kymograph drum.

Increasing concentrations of oxytocin (0.2–4 ng/ml) were administered to the tissue until maximal contraction was obtained. The effects of increasing concentrations of histamine (0.02–0.4 mg/ml) and the extract (1–8 mg/ml) were also recorded on the same uterine horn. The drug-

tissue contact time was 30 s and the time cycle was 5 min. The tissue was washed twice between additions of drugs.

The height of contractions expressed as % of height of the maximum contraction induced by oxytocin was plotted against log-dose of oxytocin, histamine or placental extract. From the log-dose response curves, ED₅₀ was calculated. The effects of pretreatment for 2 min with promethazine (4 ng/ml) or mepyramine (2–4 ng/ml) on contractions induced by the equipotent doses of histamine and extract were investigated. Also, the effects of pretreatment for 2 min with atropine (4 ng/ml) on contractions induced by equipotent doses of acetylcholine (ACh) and the extract were determined.

The effects of boiling the extract for 30 min or autoclaving at a pressure of 1.05 kg/cm² at 121°C for 15 min on the oxytocic activity were then examined by comparing, on the same uterine preparation, the oxytocic activity of the same volume of untreated and treated samples. For the pH studies, 5 N HCl was added drop by drop to bring down the pH of the extract from its original value of pH 6.1–6.6 to new levels of pH 4, pH 2, pH 1. Also, using 5 N NaOH solution, the pH was raised to pH 8 or pH 10. The oxytocic activity of the same volume of untreated and treated samples after 30 min incubation (arbitrarily chosen) was examined on the same uterine horn. The bath fluid was changed every 5 min during the 30 min incubation period. The % change in height of contraction from the value obtained from the untreated sample was calculated. The pH of the bathing-fluid was measured after addition of the treated sample to determine whether there was any significant change in pH of the fluid.

In order to determine the effects of pepsin or trypsin hydrolysis on the oxytocic activity of the extract, 10 ml of the extract was incubated at 37°C for 30 min with 0.1 g of pepsin powder (1 Anson unit/g, BDH Chemicals) at pH 4 or with 0.1 g of trypsin powder (1 Anson unit/g, BDH Chemicals) at pH 8 using barbital buffer. The reactions were terminated by immersion of the beaker in ice cold water. To show that the pepsin powder was active, one drop of the treated extract

was dropped on a piece of X-ray film and allowed to act for 3 min before washing the film with distilled water to see if the gelatin was digested, as would be shown by an area of transparency. The oxytocic activities of the untreated extract and the enzyme treated extract were then compared on the same uterine horn.

In another series of experiments, a portion of fresh placenta was weighed after cleaning with normal saline and then put into a beaker containing normal saline for 3 h. The infusion was filtered through guaze and Whatman paper. The remaining portion of the placenta was washed, dried, pulverized and extracted as already described. Dose-response to concentrations of oxytocin, histamine, the extract and the infusion were obtained. The log-dose response curves were constructed as already described and the ED₅₀ determined.

2.4. Rat uterus preparation

Pregnant albino Wister rats weighing between 200 and 260 g were used. The preparation was set up as described for the guinea-pig uterus. The effects of varying concentrations of the extract and oxytocin were recorded. Log-dose response curves were constructed as already described and the ED₅₀ was determined.

2.5. Guinea-pig ileum preparation

The preparation was set up according to standard procedures in a 50 ml bath containing Tyrode solution with the following composition in g/l. NaCl, 8.0; KCl, 0.2; MgCl₂, 0.2; KH₂PO₄, 0.5; NaHCO₃, 1.0; glucose 1.0. The bath was gassed with a mixture of 95% oxygen and 5% CO₂ and the temperature was maintained at 37 ± 0.5°C. The tension on the tissue was 1 g and the contractions were recorded with a frontal writing lever on smoked kymograph paper.

Responses to various concentrations of the extract, histamine and acetylcholine (ACh) were obtained. The log-dose response curves were constructed as already described and ED₅₀ was determined. The effects of pretreatment for 2 min with a constant dose of promethazine or mepyra-

mine on the contraction induced by equipotent doses of the extract and histamine were examined. Likewise, the effects of pretreatment for 2 min with a constant dose of atropine on contractions induced by equipotent doses of the extract and Ach were examined.

2.6. Rat hindquarters preparation

Rats of either sex weighing between 180 and 225 g were used. The preparation was set up according to standard procedures and was connected to two reservoirs through a Y tube which was also connected to the cannula inserted into the abdominal aorta. Each reservoir was filled with Ringer-Locke solution with the following composition (g/l): NaCl, 9; KCl, 0.42; NaHCO₃, 0.5; CaCl₂, 0.24; glucose, 1.0, and was aerated with oxygen and its temperature maintained at $37 \pm 0.5^\circ\text{C}$. The perfusion pressure was kept constant at 550 mmH₂O. One reservoir contained only Ringer-Locke solution while the other contained the extract (expressed as weight of dried placenta/ml) 0.4 mg/ml or 0.8 mg/ml. The equilibration time was at least 30 min when the flow had become steady over 3 readings, the reservoir containing only Ringer-Locke solution was turned off and the other reservoir containing the extract was turned on and measurements made for another 40 min. In some experiments, at peak activity of the extract, the effects of washing with normal Ringer-Locke solution or of bolus injections of promethazine or phentolamine (0.5 mg in 0.5 ml) were examined. Five control experiments were performed in which the extract was not added and the preparation was perfused with only Ringer-Locke solution for at least 40 min after equilibration. At least four preparations were used to study the effects of each dose of the extract or drug.

2.7. Isolated spontaneously beating guinea-pig atria preparation

Guinea-pigs of either sex weighing between 200 and 400 g were used. The preparation was set up according to standard procedures. The bathing fluid was Ringer-Locke solution and was

aerated with a mixture of 95% oxygen and 5% CO₂ and maintained at 30–31°C. The tension on the tissue was 1 g and the contractions were recorded with a frontal writing lever on smoked kymograph paper. The equilibration time was 30 min. The effects of the extract (0.8–1.8 mg/ml) on the rate and height of contraction were examined. The % changes from values before the addition of extract were calculated. The effects of pretreatment for 2 min with promethazine (50–200 µg/ml), cimetidine, (100–200 µg/ml) and propranolol, (0.01 µg/ml) on contractions induced by the extract were also examined. Five control experiments were performed in which the extract was not added into the bathing fluid and the records were taken for 10 min after equilibration.

2.8. Isolated guinea-pig Langendorff heart preparation

Guinea-pigs weighing between 200 and 400 g were used and the preparation was set up according to standard procedure. The perfusion fluid was Ringer-Locke solution in two reservoirs, one of which contained only the perfusing fluid while the other contained a suitable concentration of the extract. The fluid was equilibrated with 95% oxygen and 5% CO₂ and was maintained at $37 \pm 0.5^\circ\text{C}$. The perfusion pressure was kept constant at 600 mmH₂O. The perfusate was collected through a funnel into a measuring cylinder and measured every 5 min. Ventricular contractions were recorded on smoked kymograph paper. The heart rate was calculated from strips of the tracing at fast drum speed. A period of at least 30 min was required for equilibration. When equilibration had been attained, i.e., when the values of the rate, height of contraction and coronary flow had been steady for 3 readings, the reservoir containing only Ringer-Locke solution was turned off and the other reservoir containing the extract was turned on and measurements made for another 30 min. Five control experiments were also performed in which the preparation was perfused with only Ringer-Locke solution for 30 min after equilibration. At least four hearts were used for each concentration of the extract.

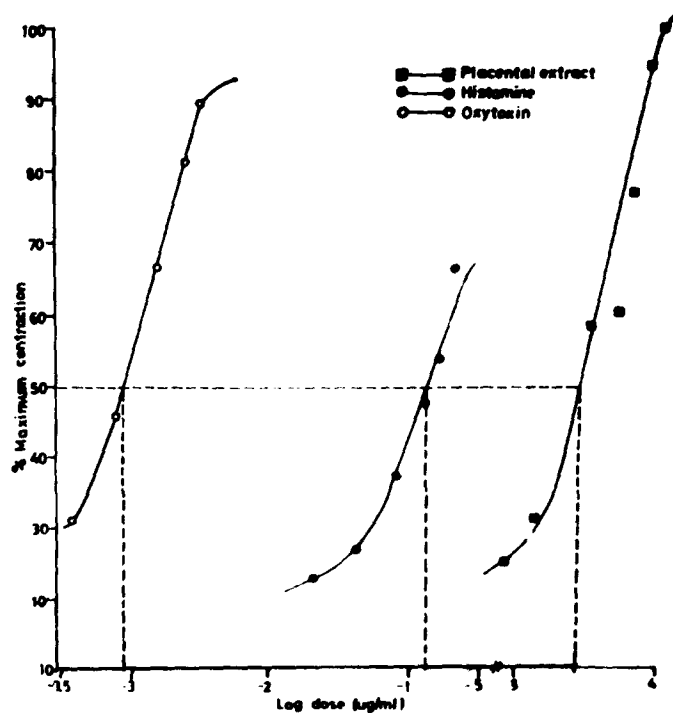


Fig. 1. Isolated guinea-pig uterus: Dose-response curves and the determination of ED_{50} of oxytocin, histamine and the extract. The weight of the extract is expressed as weight of dried placenta that produced that quantity of extract.

2.9. Blood pressure of the anaesthetized cat

Cats weighing between 1.5 and 2.0 kg were anaesthetized with thiopentone sodium (40 mg/kg) i.p. and prepared according to standard procedure for blood pressure recording from a carotid artery using a mercury manometer. Earlier, the trachea was cannulated and connected to a tambour with a recording device, a femoral vein was cannulated and connected to a three way stop cock to allow for injection of drugs or solution of extract. Records of blood pressure and respiration were obtained on smoked kymograph paper. The effects of various doses of adrenaline, histamine and the extract were investigated. Then, the effects of pretreatment with promethazine (1–8 µg/kg) on the hypotensive action of histamine and the extract were examined. About 3 ml of normal saline was used to completely flush out the femoral vein after each dose of drug or extract.

In all these experiments, the weight of the ex-

tract is expressed as the weight of the dried placenta that produced that quantity of extract. Statistical analysis utilizing the unpaired *t*-test was performed with a *P*-value of < 0.05 taken as indicating significance. Results were expressed as arithmetic means \pm SEM.

3. Results

3.1. Isolated guinea-pig uterus

There was no material difference between the sensitivity of the gravid and non-gravid uterus. At ED_{50} , oxytocin was between 1.6 and 6.7×10^6 times more potent, but histamine was about 10^4 times more potent (Fig. 1). Promethazine and mepyramine, in addition to atropine, at concentrations which respectively caused more than 50% inhibition of histamine and Ach-induced contractions, had no effect on contractions induced by equipotent doses of the extract.

One g of the placenta was obtained from approximately 7.6 g of fresh placenta. It was found that when the weight of the dried placenta was equated with the weight of the fresh placenta that produced it, the fresh placenta was 3–6 times more potent. Boiling for 30 min had no effect on the oxytocic activity, nor did autoclaving at 121°C, 1.05 kg/cm². Addition of the treated sample to the 50 ml bathing fluid had little or no effect on the pH. Even the addition of 0.2 ml of treated sample at pH 1 only changed the pH of the fluid in the 50 ml bath from pH 7.6 to pH 7.3 (0.2 ml was the maximum quantity of the sample fluid added to the bath). The oxytocic activity was stable at alkaline pH (pH 8–10) but was diminished as the pH was reduced from pH 6.4 to pH 1. There was low activity at pH 2; often there was less than 10% activity. Fig. 2 shows the effect of changes in pH on the oxytocic activity of the extract. Pepsin hydrolysis at pH 4 had no effect. Likewise, trypsin at pH 8 had no effect on the oxytocic activity.

3.2. Rat uterus preparation

The extract induced concentration-dependent contractions. At ED₅₀, oxytocin was about 10³ times more potent.

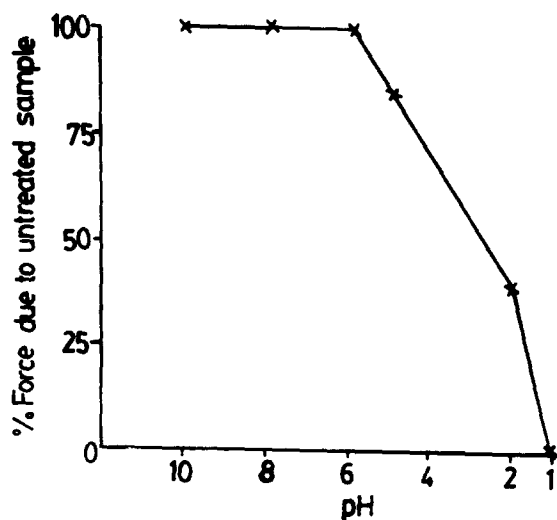


Fig. 2. Effect of change in pH of the extract on its oxytocic activity.

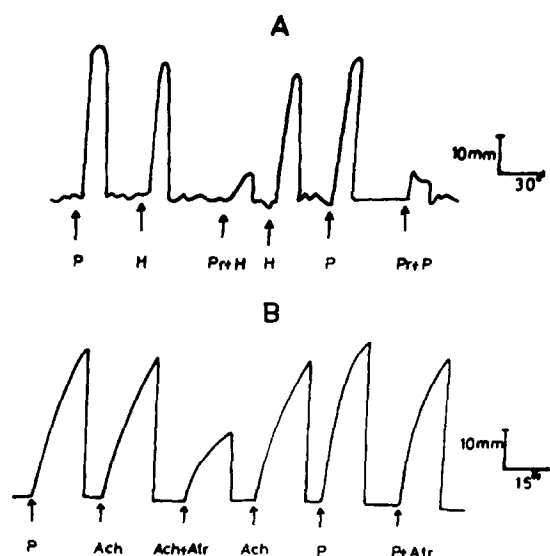


Fig. 3. The guinea-pig ileum preparation: Panel A shows the effects of pretreatment for 2 min with promethazine 4×10^{-11} g/ml (Pr) on contractions induced by equipotent doses of histamine (H) and the placental extract (P). Panel B shows the effects of pretreatment for 2 min with atropine 4×10^{-9} g/ml (Atr) on contractions induced by equipotent doses of acetylcholine (Ach) and the extract (P). All the agonists acted for 15 s.

3.3. Guinea-pig ileum preparation

The extract induced concentration-dependent contractions, which showed that histamine at ED₅₀ was $1.8\text{--}8.2 \times 10^5$ times more potent than the reference drugs. Promethazine and mepyramine antagonized, to about the same degree, contraction induced by equipotent doses of histamine and the extract. Atropine, at a dose which gave approximately 50% inhibition of Ach-induced contractions, had no effect on contractions induced by equipotent doses of the extract (Fig. 3).

3.4. Rat hindquarters preparation

The flow rate at equilibration for various preparations was: for control experiments, 9–12 ml/5 min; for the extract (0.4 mg/ml), 8.90–12.5 ml/5 min and 9.70–12.6 ml/5 min (for 0.8 mg/ml). Peak activity was at 35–40 min after adding the extract. At 0.4 mg/ml, the extract reduced the flow rate by $18.6 \pm 5.1\%$ from values at equilibration.

At 0.8 mg/ml, there was $60.6 \pm 8.25\%$ reduction. For control experiments, the reduction 40 min after equilibration was $6.0 \pm 3.2\%$. Compared with controls, these reductions were statically significant ($P < 0.05$ for 0.4 mg/ml and $P < 0.001$ for 0.8 mg/ml). The vasoconstrictive action was easily washed out by perfusing with normal Ringer-Locke solution. The reductions in flow rate were also antagonized by phentolamine and promethazine.

3.5. Isolated spontaneously beating guinea-pig atrial preparation

At equilibration, the atrial rates were between 108 and 168 beats/min and the heights of contraction between 3 and 10 mm. The extract induced concentration-dependent increases in rate. The % increases from values at equilibration to peak activity (which occurred within 2 min) were for 0.8 mg/ml, 26.6 ± 1.1 ($P < 0.001$); for 1.6 mg/ml, 32.85 ± 4.2 ($P < 0.001$); for 1.8 mg/ml, 36.8 ± 8.4 ($P < 0.01$) when compared with controls where the reduction was negligible ($2.1 \pm 0.3\%$). For force of contraction, there were marked concentration-dependent increases from values at equilibration. At 0.8, 1.6 and 1.8 mg/ml, the increases were respectively $84.7 \pm 3.2\%$, $181.9 \pm 14.4\%$, and $239.6 \pm 40.4\%$ compared with little or no reduction ($1.5 \pm 0.4\%$) in the control experiments. These increases were very highly statistically significant ($P < 0.001$). Fig. 4 is a histogram showing the effects of various concentrations of the placental extract. Fig. 5 shows the positive inotropic and chronotropic effects of the extract (1.6 mg/ml) and the marked antagonism shown by propranolol (0.2 mg/ml) and promethazine (50 $\mu\text{g/ml}$).

3.6. Isolated guinea-pig Langendorff heart preparation

At equilibration, the heights of contraction were between 2 and 4 mm, the rates between 84 and 120 beats/min, while the coronary flow rates were between 4.8 and 20.8 ml/min. For control hearts, 30 min after equilibration, there were reductions in the values of the height of contraction, heart rate and coronary flow: $8.4 \pm 5.1\%$, $3.0 \pm$

1.2% , $9.2 \pm 4.1\%$ respectively when compared with values at equilibration.

At 7.5 $\mu\text{g/ml}$, the extract had no effect on height and rate of contraction. However, the coronary flow rate was decreased by $26.1 \pm 8.0\%$ when compared with values at equilibration. This was not statistically significant ($P > 0.05$) when compared with the control value. At 80 and 120 $\mu\text{g/ml}$, the reductions in coronary flow rate were respectively $42.1 \pm 12.5\%$ and $46.7 \pm 14.2\%$. These reductions were statistically significant ($P < 0.05$). For height of contraction, there were concentration-dependent statistically significant increases: $75.0 \pm 20.2\%$ and $150.0 \pm 40.3\%$, respectively ($P < 0.01$). For heart rate, there were concentration-dependent statistically significant increases: $16.7 \pm 7.3\%$ and $30.0 \pm 10.6\%$, respectively ($P < 0.05$).

At 800 $\mu\text{g/ml}$, although an increase in height of contraction of 275% was obtained in one preparation, there was ventricular asystole in 4 others, although the atria of these hearts continued to beat. In 2 of the 4 hearts, however, reperfusion

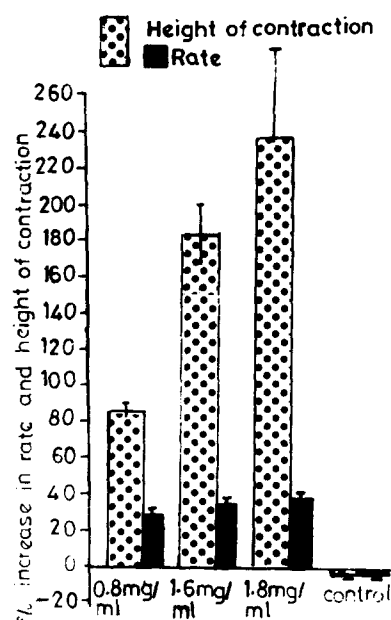


Fig. 4. Spontaneously beating guinea-pig atrial preparation: Histogram showing the effect of various concentrations of the placental extract on the atrial rate and force of contraction. At least 4 preparations were used for each dose of drug.

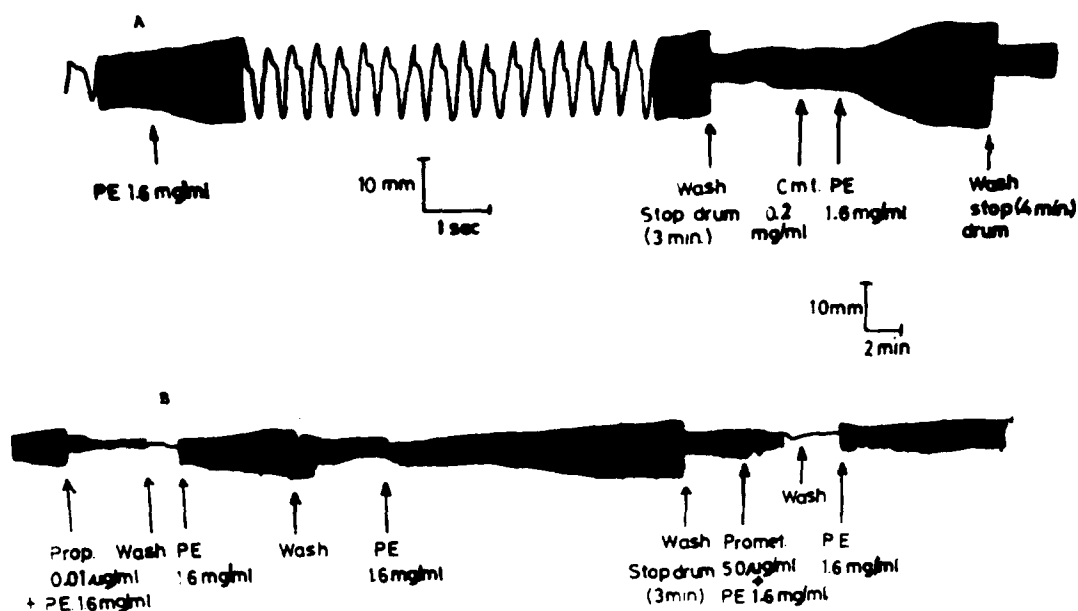


Fig. 5. Spontaneously beating guinea-pig atrial preparation: Shows the positive inotropic and chronotropic effects of the extract (PE), the ineffectiveness of cimetidine 0.2 mg/ml (Cmt) to antagonize the effect of the extract (PE), and the marked antagonism exhibited by propranolol (Prop) and promethazine (Promet).

with drug free Ringer-Locke solution restored the normal activity of the heart.

3.7. Blood pressure of the anaesthetized cat

The extract induced dose-dependent transient falls in blood pressure, returning to the original level within 2 min. Thus, at 12.5 mg/kg, there was a fall of between 20 and 30 mmHg, while the fall at 25 mg/kg was between 45 and 60 mmHg. Pretreatment with promethazine (1.2 μ g/kg) antagonised more the hypotensive action of histamine than that due to an equipotent dose of the extract (Fig. 6).

4. Discussion and conclusions

There is no doubt that the normal saline extract of dried sheep placenta contains some oxytocic factor which is unaffected by the enzymatic activity of pepsin or trypsin.

The oxytocic activity is not antagonized by H_1 receptor antagonists or by antimuscarinic receptor

agents, thus indicating that H_1 and muscarinic receptors are not involved in the stimulant action on the uterus. However, the extract-induced contractions in guinea-pig ileum are antagonised by H_1 receptor antagonists but not by atropine. It would appear, therefore, that the contractions induced in the gut may be due to histamine released by the extract from the gut wall or that the extract directly stimulates H_1 receptors in the guinea-pig ileum.

The fact that the strong vasoconstriction induced in the rat hindquarters was antagonized by promethazine would indicate that the extract liberated histamine or directly stimulated H_1 receptors. The finding that its positive inotropic effect in the spontaneously beating guinea-pig atrium was not antagonized by cimetidine, an H_2 receptor antagonist, but was antagonized by promethazine, a H_1 receptor antagonist, would suggest that the extract directly stimulated H_1 receptors. The hypotensive action in the anaesthetized cat is probably due to histamine release because promethazine was less effective in preventing the hypotensive effect when the fall in

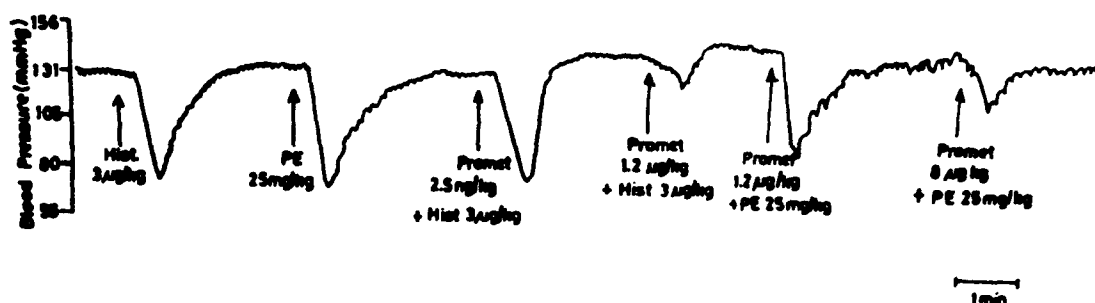


Fig. 6. Blood pressure of the anaesthetized cat: Effect of promethazine (Promet) on hypotension induced by equipotent doses of histamine (Hist) and the placental extract (PE).

blood pressure was due to the extract than when a comparable hypotensive effect was due to histamine. The hypotensive effect of the extract is certainly not due to any cardiac depressant activity. On the contrary, the extract very markedly increased the force of contraction in the spontaneously beating guinea-pig atrium, as well as in the isolated guinea-pig Langendorff heart.

When the weight of the dried placenta is expressed as the weight of the fresh placenta that produced it, the oxytocic activity of the fresh placenta is about 3–6 times greater than that of the dry placenta, thus indicating some loss of oxytocic activity during drying of the placenta. The oxytocic activity from 1 g of powdered placenta was found to be equipotent with 0.075–0.32 IU of oxytocin. In the human, induction of labour is often achieved by less than 2 IU of oxytocin given via an i.v. drip (Clayton and Newton, 1983; Russell, 1982). 1–2 IU of oxytocin activity can be obtained from 4–30g of dried placenta if there is no loss of potency as a result of activities of gastrointestinal enzymes. However, as there is complete loss of oxytocic activity at very low pH, it would appear that the dried powder should be given with antacids to minimize the loss of potency from the high acidity of gastric juice. These results show that there is some scientific rationale in using orally administered powdered dried sheep placenta to facilitate labour in traditional obstetric practice in parts of Nigeria.

It is noteworthy that, in the guinea-pig, histamine is about 10^5 – 10^6 times more potent than the extract in stimulating the ileum, but only 10^4

times more potent in stimulating the uterus. It would seem, therefore, that a dose of the extract that would stimulate the uterus may not be sufficient to cause much increase in peristalsis. Indeed, severe abdominal colic was not complained of by women who had taken the extract to facilitate labour.

Acknowledgements

We are much indebted to Hajiya Onyejura-karakaya for information regarding the use of dried sheep placenta in her traditional obstetric practice. Our thanks go to Mrs. Eunice Emeruwa for typing the manuscripts and to the Medical Illustration Unit for producing the photographs.

References

- Clayton, S.G. and Newton, J.R. (1983) *A Pocket Obstetrics*, Churchill Livingstone, Edinburgh, London, New York, p.144.
- Ganong, W.F. (1985) *Review of Medical Physiology*, Lange Medical Publications, Los Altos, California, p. 373.
- La Barbera, A.R. (1993) Fertilization, pregnancy and lactation. In: Sperelakis, N. and Banks, R.O. (Eds.), *Physiology*, Little, Brown and Company, Boston, Toronto, London.
- Russell, K.P. (1982) The course and conduct of normal labour and delivery. In: Benson, R.C. (Ed.), *Current Obstetric and Gynecologic Diagnosis and Treatment*, Lange Medical Publications, Los Altos, California, p. 680.
- Sisson, J.A. (1963) Smooth muscle contracting peptide from the rabbit placenta and its comparison to bradykinin. *Archives Internationales de Pharmacodynamie et de Therapie* 144, 112–119.

Sisson, J.A. Smith, D. Davis, J. and Burton, R.M. (1961) A hypotensive smooth muscle-contracting principle from fetal placenta of the rabbit. *Journal of Pharmacology and Experimental Therapeutics* 132, 117–125.

Wathes, D.C., Gilbert, C.L. and Ayad, V.J. (1993) Interactions between the ovaries and the reproductive tract in the regulation of fertility in the ewe. *Annals of the New York Academy of Sciences* 689, 396–410.