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POTENTIATION OF LOCAL ANAESTHETIC ACTIVITY OF *ARTOCARPUS HETEROPHYLLUS* LATEX WITH ADRENALINE AND PH BY INFILTRATION METHOD

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ABSTRACT
The present work describes the potentiation of local anaesthetic activity exhibited by milky latex obtained from *Artocarpus heterophyllus* ,with adrenaline and pH. The milky latex at a dilution of 1:05, exhibited significant local anaesthetic activity. Both adrenaline (5µg/ml) and pH of 7.2 prolonged the duration of local anaesthetic activity. The method used is infiltration anaesthesia in Guinea pig. In conclusion, the duration of the effect produced by combination of*Artocarpus heterophyllus* latex and adrenaline was longer than the combination of latex and pH as well as latex alone.

KEYWORDS: *Artocarpus heterophyllus*, Milky latex, Adrenaline, pH and Infiltration anaesthesia.

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INTRODUCTION

Artocarpus heterophyllus (Moraceae family) is one of the most significant trees in tropical home gardens and perhaps the most widespread and useful tree in the important genus *Artocarpus*. The tree is reportedly native to the rainforests of Malaysia, the Western Ghats of India and also found in central and eastern Africa, south-eastern Asia, the Caribbean, Florida, Brazil, Australia, Puerto Rico and many Pacific Islands. All parts of the tree exude a sticky, white, milky latex when injured[1]. The whole tree has valued place in research due to its medicinal and nutritive properties. All parts of the tree are said to have medicinal properties. The young fruits are acrid, astringent, and carminative. The ripe fruits are sweet, cooling, laxative, aphrodisiac and also used as a brain tonic. The seeds are, diuretic, and constipating. The wood is nervine, antidiabetic, sedative and is useful in convulsions [2]. The latex is useful in dysopia, ophthalmic disorders and pharyngitis and also used as antibacterial agent [3]. Mixed with vinegar, the latex promotes healing of abscesses, snakebite and glandular swellings[4]. Hot water extract of mature jack leaves is recommended by Ayurvedic and traditional medical practitioners as a treatment for diabetes mellitus[5]. Phytochemical screening has revealed that the hot water extract contains flavonoids, leucoanthocyanins, anthocyanins and tannins as components. It is an important source of compounds like morin, dihydromorin, cynomacurin, artocarpin, isoartocarpin, cyloartocarpin, artocarpesin, oxydihydroartocarpesin, artocarpetin, norartocarpetin, jacalin, ellagic acid, cycloheterophyllin, sapogenins, carotenoids,cycloartinone, betulinic acid, artocarpanone and heterophylol[6].

Recently we reported the evaluation and potentiation of local anaesthetic activity of latex of *Tabernaemontana coronaria*[7,8], *Calotropis gigantea*[9,10], *Calotropis procera*[11] and *Artocarpus heterophyllus*[12].

Local anaesthetics are the agents which prevent or relieve pain by interrupting nerve conduction. They effectively block and relieve pain,but with a relatively short duration of action, limiting their analgesic effectiveness. Therefore, a long acting local anaesthetic would improve the management of pain, but no such agent is yet available for clinical use[13]. As early as 1903, Braun discovered that the addition of adrenaline to solutions of local anaesthetics increased and prolonged their action. Therefore, the present work was undertaken to evaluate the potentiation of the local anaesthetic activity of milky latex, obtained from *Artocarpus heterophyllus*, with adrenaline and pH by infiltration method in Guinea pig.

MATERIALS AND METHODS

Chemicals and Equipments

Milky latex of *Artocarpus heterophyllus*, centrifuge (REMI), Distilled water, Xylocaine (0.25w/v), Adrenaline (Vasocon 1mg/ml), Sodium hydroxide solution (0.2M), Normal saline solution (0.65%Nacl), Hair depleting agent and sharp pins.

Animals

Guinea pig (Male)

Method

Infiltration anaesthesia method

Collection of Milky Latex

The milky latex was collected usually between 8 am and 10 am by cutting the leaves of *Artocarpus heterophyllus*. Then 1 ml of latex was centrifuged at 5,000 r.p.m after being diluted 5 times its volume with distilled water. The gummy pellet was discarded and the supernatant liquid was used for evaluation of local anaesthetic activity.

Dilution of Adrenaline

Vasocon injection (Adrenaline1mg /1ml) was purchased from the local market and diluted with distilled water to get a solution containing 10µg/1ml. 0.5 ml of diluted solution was used in the present study.

Preparation of 0.2m Sodium Hydroxide Solution

0.2 M of sodium hydroxide solution was prepared by dissolving 8.0 gm of sodium hydroxide in 1000 ml of distilled water. 34.7 ml of 0.2M sodium hydroxide solution was used in the present study[14].

Preparation of Standard Solution and Test Solution

Xylocaine solution (0.25w/v) was purchased from the local market. 0.5 ml of this solution was mixed with 0.5 ml of diluted adrenaline solution (Standard solution-I). Similarly, 0.5 ml of latex (1:05) was mixed with 0.5 ml of diluted adrenaline solution (Test solution-I). Xylocaine solution was mixed with 34.7 ml of 0.2M sodium hydroxide solution (Standard solution-II) and 50 ml of latex (1:05) was mixed with 34.7 ml of 0.2M sodium hydroxide solution(Test solution-II).

Infiltration Anaesthesia Method

Six healthy adult Guinea pigs (CPSCEA regd no 1016-a-06-CPSCEA-0112009) were taken and fur on their back was removed by using depleting agents. The depleted area was washed with normal saline and allowed to dry. Then 1 ml each of xylocaine solution, latex (1:05) Standard-I, II and Test-I, II were injected intradermally to six different guinea pigs separately. Squeak or twitch response of animal upon touching the injection site with sharp pin was marked as (+) and (-) if the animal does not show any response to pin prick[15].

RESULTS AND DISCUSSION

In the Infiltration method, before administration of the standard and test there was a sharp reponse for pin prick.After administration of the standard (Xylocaine alone) there was response for pin prick up to 1 minute. Then the response reproduced at 50^{th} minute. Test(latex1:05 alone) , Standard – I(Xylocaine+Adrenaline), Test-I (Latex1:05 + Adrenaline), Standard-II (Xylocaine + 0.2M Sodium hydroxide), Test-II(Latex1:05+0.2M Sodium hydroxide) reproduced response at 45^{th} minute,65^{th} minute,55^{th} minute,60^{th} minute and 43^{rd} minute respectively. The results are shown in **Table 1**.

The duration of infiltration anaesthesia can be prolonged by the addition of adrenaline (5µg/ml) to the injection solution. Adrenaline also decreases peak concentrations of local anaesthetics in blood.

Local anaesthetics tend to be only slightly soluble as unprotonated amines. Therefore, they are generally marketed as water soluble salts, usually hydrochlorides. Many local anaesthetics are weaker bases with typical pK_a values ranging from 8 to 9, but their hydrochloride salts are mildly acidic. This property increases the stability of the local anaesthetic esters and any accompanying vasoconstrictor substance.

Although the unprotonated species of the local anaesthetics is necessary for diffusion across cellular membranes, it is the cationic species that interacts preferentially with sodium channels. This conclusion has been supported by the results of experiments on anaesthetized mammalian non myelinated fibers.In these experiments,conduction could be blocked or unblocked merely by adjusting the pH of the bathing medium to7.2 or 9.6,respectively, without altering the amount of anaesthetic present.

CONCLUSION

The duration of the effect produced by combination of latex and adrenaline was longer than the combination of latex and pH as well as by latex alone.From the above observation, we conclude that,adrenaline and pH 7.2 potentiate the local anaesthetic effect of *A.heterophyllus* latex in Guinea pig when co-injected intradermally. The present results may probably support the development of a long acting local anaesthetic.

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Table 1: Infiltration Anaesthesia Method

Group	Time in minutes	Squeak Response
Before administration of the drug	0	+
Standard	1	+
(Xylocaine alone)	5	-
	10	-
	15	-
	20	-
	25	-
	30	-
	35	-
	40	-
	45	-
	50	- +
Test		
(Latex 1:05 alone)		
	1	+
	5	-
	10	-
	15	-
	20	-
	25	-
	30	-
	35	-
	40	-+
Standard-I		
(Xylocaine+ Adrenaline)	1	+
	5	-
	10	-
	15	-
	20	-
	25	-
	30	-
	35	-
	40	-
	45	-
	50	-
	55	-
	60	-
	65	-+
Test-I		
(Latex1:05+Adrenaline)	1	+
	5	-
	10	-
	15	-
	20	-
	25	-
	30	-
	35	-

	40	-
	45	-
	50	-
	55	+
Standard-II (Xylocaine+0.2M Sodium hydroxide)	1	+
	5	-
	10	-
	15	-
	20	-
	25	-
	30	-
	35	-
	40	-
	45	-
	50	-
	55	-
	60	+
Test-II (Latex1:05+0.2M Sodium hydroxide)	1	+
	5	-
	10	-
	15	-
	20	-
	25	-
	30	-
	35	-
	40	-
	43	+

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