

THE EFFECTS OF ORAL MUCOLYTIC AGENTS AND MATING ON THE MICROFLORA OF GUINEA-PIG UTERI

J.S. Malhi, P.R. Gard, G.W. Hanlon, C. Marriott, Department of Pharmacy, Brighton Polytechnic, Moulsecoomb, Brighton BN2 4GJ

Under normal circumstances the uterus is sterile despite the fact that the vagina contains large numbers of microorganisms. This is due to a number of factors including the presence of a cervical mucus plug which is impenetrable to bacteria. In those women who are fitted with an intrauterine contraceptive device (IUCD) it has been suggested that microorganisms from the vagina may enter the uterus by adhesion to the marker tails; this has been demonstrated *in vitro* by Wilkins et al. (1985). Keith et al. (1984) have also suggested that bacteria may be able to attach to sperm and breach the cervical mucus barrier. If the ability of bacteria and sperm to progress through gels is dependant on gel viscoelasticity anything which brings about a thinning in the cervical mucus plug may predispose to entry of bacteria into the uterus. Although the effects of mucolytics in the lungs have been shown, there is no evidence for their side effects at other sites. This study assesses the effects of oral mucolytic therapy and mating on uterine microflora using guinea pigs as a mammalian model. Six groups of animals were used, two groups were treated with 0.1% w/w bromhexine hydrochloride (BHC), two with 1.0% w/w S-carboxymethyl-L-cysteine (SCMC) and two acted as vehicle controls. This represents a dose of approximately 25 mg/kg/day of BHC and approximately 300 mg/kg/day of SCMC. Drug was administered *ad libitum* in a cereal. After seven days of dosing one group from each of the two drug treatment groups were allowed to mate for a period of one oestrus cycle. Dosing was continued during this period and animals were then sacrificed. Uterine washes were taken from one horn using sterile saline and 0.2 ml aliquots inoculated onto blood agar which was incubated both aerobically and anaerobically. The other horn of the uterus was also incubated in nutrient broth. All media were incubated at 37°C for 24-48 hours. The number of uteri showing bacterial growth in control and drug treated groups is shown in the Table.

Table	Group	No. of uteri showing growth (n=8)	
		unmated	mated
	Control	0	5
	BHC	4	6
	SCMC	4	5

The results show that the uteri were sterile in the unmated control, but this was not so for drug treated animals. The differences in bacterial presence in the uteri of the unmated control group and the unmated BHC and SCMC groups were significant, as were the differences between the two control groups ($p < 0.05$ Fisher's Exact Test). The numbers of bacteria in the uteri were variable but in general anaerobic counts were higher than aerobic by up to five fold. Anaerobic but not aerobic counts were significantly greater ($p < 0.05$) for the BHC group than for the SCMC group in both mated and non-mated animals (Mann-Whitney U Test). These results suggest that sperm are important in the entry of bacteria into the uterus, and that mucolytics compromise the integrity of the cervical mucus plug, possibly by a reduction in the mucus viscoelasticity.

Wilkins, K.M. et al. (1985) *J. Pharm. Pharmac.* 37: 66P

Keith, L.G. et al. (1984) *Am. J. Obstet. Gynecol.* 149(2): 215-224