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EFFECTS OF SPE-CONTAINED FATTY ACIDS ON BLADDER MUSCARINIC RECEPTORS AND VOIDING FUNCTION IN RATS

Hypothesis / aims of study

Saw palmetto extract (SPE), an extract from the ripe berried of the American dwarf palm, has been widely used as a therapeutic remedy for urinary dysfunction due to benign prostatic hyperplasia (BPH). We reported that SPE significantly increased bladder capacity and subsequently prolonged the micturition interval and SPE bound to autonomic receptors in the lower urinary tract [1]. SPE contained saturated and unsaturated free fatty acid (more than 90%). So we examined the effects of SPE and free fatty acid containing SPE on the rat micturition and on muscarinic receptor related to micturition.

Study design, materials and methods

Binding activities of SPE and free fatty acids (lauric acid, oleic acid and myristic acid) for muscarinic receptors were measured by inhibitory effect on specific binding of selective radioligand, [^{3}H]*N*-methylscopolamine (NMS) in rat brain. In order to test the effect of SPE on lower urinary functions, we recorded voiding behaviors and bladder pressure using telemetry methods in Goto-Kakizai rats (GK rats, 10-18 weeks old) after administration of SPE (3, 20, 60, 180 mg/kg). Maximum bladder pressure, micturition frequency, voiding speed and voiding volume were calculated from the recorded data. SPE (60 mg/kg) or fatty acid (24 mg/kg) were orally administered to GK rats for two month to test the effect of repeated administration of SPE or fatty acids (mixture of oleic acid and lauric acid) on the voiding behaviors. The time of micturition and micturition volume was measured after the administration of pure water (30 mL/kg). Micturition frequency, voiding speed, voiding volume and micturition interval were calculated from the recorded data.

Results

SPE and oleic acid inhibited specific [^{3}H]NMS binding in rat brain in a concentration-dependent manner with IC_{50} values of 131.2 and 176.5 µg/mL, respectively (Fig. 1). Lauric acid and myristic acid did not inhibit specific [^{3}H]NMS binding. However, lauric acid and myristic acid potentiated inhibition by oleic acid of specific [^{3}H]NMS binding. Single oral administration of SPE increased voided volume and decreased number of micturition without changes in bladder pressure. Repeated (2-month) oral administration of SPE and mixture of oleic acid and lauric acid, which are main components of SPE, increased significantly the voided volume in the GK rats (Table1).

Interpretation of results

The present results revealed that oleic acid could bind to muscarinic receptor and that lauric acid and myristic acid potentiated muscarinic receptor binding. Repeated administration of SPE and mixture of oleic acid and lauric acid increased significantly the bladder capacity.

Concluding message

The fatty acids including oleic acid, lauric acid and myristic acid may contribute largely to the pharmacological activities of SPE on the urinary dysfunction.

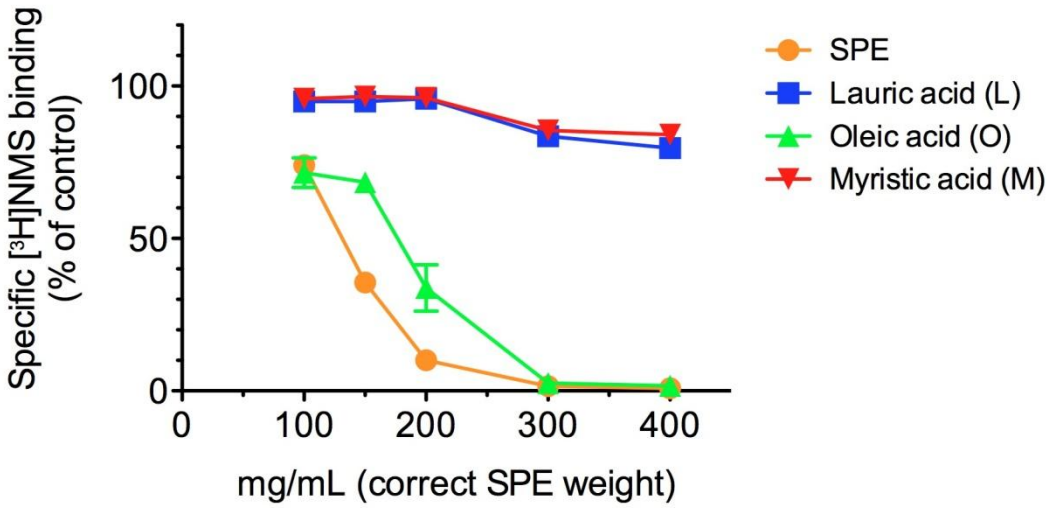

Fig. 1. In vitro competitive inhibition by saw palmetto extract (SPE) and fatty acids of specific [^{3}H]NMS binding in rat brain.

Table 1. Effect of repeated oral administration of saw palmetto extract (SPE) and a mixture of fatty acids (FA: oleic acid and lauric acid) on urodynamic parameters in conscious and un-restrained rats.

	Vehicle			SPE			FA		
Number, N/hr	4.67	±	1.22	3.67	±	0.86	3.83	±	0.84
VV per hr, g/hr・kg B.W.	10.7	±	2.22	11.9	±	3.81	13.2	±	2.81
VV, g/kg B.W.	2.35	±	0.38	3.21	±	0.52*	3.52	±	0.72*
Micturition speed, ml/s	0.20	±	0.02	0.24	±	0.04	0.27	±	0.04*

Each value represents mean ± S.D. of 4 experiments. Asterisks show significant differences from vehicle value, *P<0.05. VV: voided volume

References
1. J Urol, 173: 1395-1399 (2005)

Disclosures
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