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### Experimental errors resulting from uptake of lipophilic drugs by soft plastic materials

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FORREST *et al.*<sup>1</sup> reported a few years ago that soft plastic containers adsorb measurable quantities of chlorpromazine and suggested the use of the plastic material, nalgene. Although more observations of this kind have become known, too little is known about the extent of uptake by plastic materials and the pitfalls of experimental work with highly lipophilic drugs.

A study on the metabolism of imipramine in the isolated perfused rat liver was initiated with a perfusion apparatus previously used in our laboratory.<sup>2</sup> In preliminary experiments the livers were perfused with 10-<sup>14</sup>C-imipramine. The label in this position is known not to be eliminated as <sup>14</sup>CO<sub>2</sub>.<sup>3</sup> After perfusion the recovery of <sup>14</sup>C-activity in the total of the three compartments (perfusion medium, liver, bile) amounted to 5 to 10 per cent only. Experiments, summarized in Table 1, showed that the

TABLE 1. UPTAKE OF LIPOPHILIC DRUGS BY PLASTIC MATERIALS

			% <sup>14</sup> C-IP†		% <sup>3</sup> H-CTP‡	
			(15 min)	(60 min)	(30 min)	(120 min)
Silicone rubber (tube)	250 · 2.5 mm	A*	98	99	96	98
PVC (tube)	250 · 2.0 mm	A	98	99	97	99
Rubber (tube)	250 · 2.5 mm	A			93	96
Silicone rubber (tube)	200 · 5.0 mm	B		30		
Teflon (tube)	200 · 5.0 mm	B		3		
Teflon (tube)	300 · 2.0 mm	B		0		
Nylon (filter)	1 cm <sup>2</sup>	C		2		

\* A: ring-shaped tube in roller pump, 4 ml.

B: ring-shaped tube on rotating disc, 3-5 ml.

C: agitated in 5 ml.

† imipramine

‡ clothiapine, 2-chloro-11(4-methyl-1-piperazinyl)-dibenzo [b,f][1,4] thiazepine.

The two silicone rubber tubes are from different manufacturers.

remaining imipramine could have been rapidly taken up by the silicone rubber tubing used in the perfusion apparatus. The uptake was increased to near-total if the silicone rubber was treated with a roller pump as in the perfusion apparatus. Similar results were obtained with the lipophilic drug, clothiapine, and with the soft plastic, polyvinylchloride, or rubber, but not with the hard plastic, teflon. Based on these results the perfusion apparatus was modified in the following way: The roller

pump was substituted by a piston pump connected to the circulation of the perfusion medium by an air cushion and a system of glass valves, and all silicone rubber tubes were replaced by glass tubes and teflon connections. In addition, a nylon filter was used. The radioactivity recoveries obtained with this apparatus then averaged 91 per cent.<sup>4</sup>

In order to check for errors made in previous studies with lipophilic drugs, the uptake of imipramine by polyethylene centrifuge tubes and scintillation vials was measured but found to be negligible.

The reported experience demonstrates that uptake of lipophilic drugs by soft plastic materials can be extreme and can constitute a serious source of error or misinterpretation. E.g. during the slow passage of bile through a soft plastic canula lipophilic molecular species present may be taken up and only polar metabolites appear in the recipient. It is therefore strongly recommended that uptake be controlled in all plastic containers, tubing or canula when working with lipophilic substances.

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