TABLE II. Thymus Gland Weights of Adrenalectomized or Hypophysectomized Female Rats Fed Control Diet or Diet Containing 3,4-Dihydroxyphenylacetic Acid.

	Control diet			Diet containing 3,4-dihydroxyphenylacetic		
	No. of rats	Mean final body wt, g	Thymus, % of body wt	No. of rats	Mean final body wt, g	Thymus, % of body wt
Adrenalectomized	10	64.9	.460 ± .030	12	59.8	.474 ± .026
Hypophysectomized	9	49.6	.354 ± .014	8	51.1	.348 ± .009

the other hand, are m-hydroxyphenylpropionic and m-coumaric acids but no catecholic acids. m - Hydroxyphenylpropionic acid (which readily forms m-coumaric acid in the body) did not accelerate involution (Table I). Thus, it may be inferred that this action of flavonoids is due in part at least to the intact molecule and, in certain instances, may also be due to the metabolites they yield.

The flavonoids hesperetin, naringenin, and morin, which have no catecholic groups do not cause thymus involution(2) and produce phenolic metabolites(5,6,9), which also fail to cause thymus involution (Table I).

Certain non-catecholic phenolic acids such as salicylic, gentisic and γ-resorcylic markedly affect level of circulating corticosteroids(12, 13). Whether flavonoids possessing radicals of these acids (constituting the prime ring of flavonoid) also stimulate adrenal function merits consideration.

Summary. (1) Several phenolic acid metabolites of flavonoids and compounds related to these metabolites were tested for thymolytic action by feeding in the diet to young normal rats. (2) Catecholic acids 3,4-dihydroxyphenylacetic, protocatechuic and caffeic, accelerated thymus involution. Several other phenolic acids did not. (3) 3,4-Dihydroxyphenylacetic acid did not accelerate thymus involution in either hypophysectomized or adrenalectomized rats. (4) Whether the action of flavonoids on thymus involution is due to intact flavonoids or their metabolites is discussed.

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Serum Lactic Dehydrogenase Activity in Experimental Endotoxic Shock.* (25852)

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Elevations of plasma lactic dehydrogenase (LDH) activity in experimental hemorrhagic shock have been described(1). This paper demonstrates elevations of serum LDH activity after endotoxin administration.

Materials and methods. One MLD_{100} of

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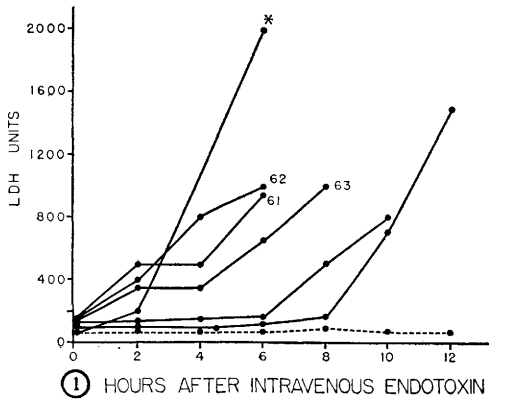

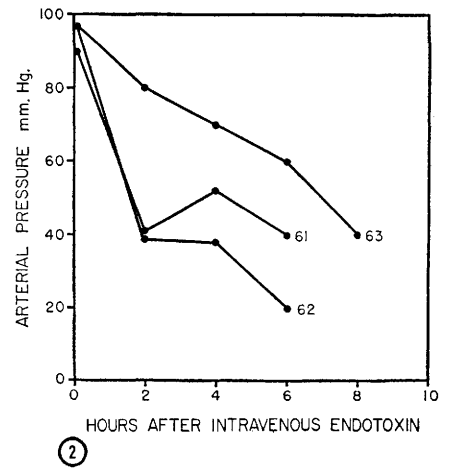

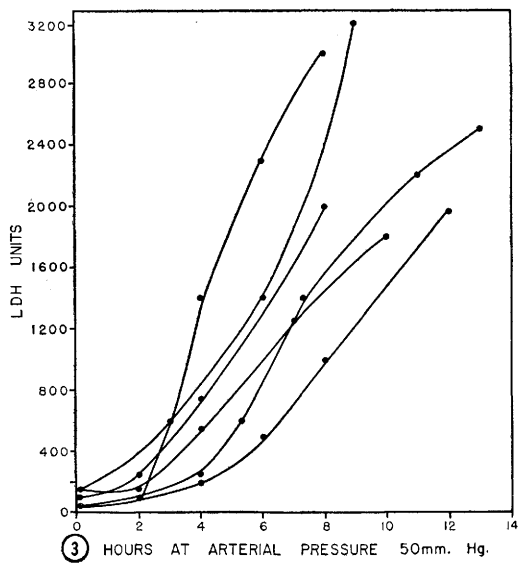

FIG. 1. Solid lines show serum LDH activity in 6 rabbits given one MLD_{100} of *Escherichia coli* endotoxin at time 0. Curve marked with asterisk reached 4000 units at 8 hr. Dotted line represents LDH activity in control rabbit given saline.

FIG. 2. Arterial pressures of rabbits 61, 62 and 63 following toxin administration.

FIG. 3. Plasma LDH activity of 6 rabbits during sustained hemorrhagic hypotension.

Escherichia coli endotoxin (Difco) was administered intravenously to adult albino rabbits (average weight 2 kg). Femoral artery pressure was obtained at intervals thereafter. In another group of similar rabbits hemorrhagic hypotension was produced by the technic described elsewhere(2). Arterial blood samples† were drawn before endotoxin administration or hemorrhagic hypotension and at intervals thereafter and the serum was collected at once, kept at 4°C for less than 24 hours, and then assayed spectrophotometrically for LDH activity(3).

Results. The serum LDH activity of 6 rabbits after endotoxin administration showed elevations to 800 to 4000 units, 6 to 50 times the initial value (Fig. 1). In 3 of these rabbits initial arterial pressures were 95, 95, and 90 mm Hg respectively before endotoxin administration. They began to fall 2 hours later and were 40, 40 and 20 mm Hg before death (Fig. 2). Death occurred between 6 and 18 hours after endotoxin was injected. Rabbits given saline intravenously showed no rise in serum LDH activity (Fig. 1).

Six rabbits subjected to hemorrhagic hypotension revealed plasma LDH elevations reaching 1800 to 3200 units (Fig. 3). Death occurred between 8 and 12 hours after bleeding was initiated.

Discussion. These experiments reveal progressive elevations of serum LDH activity in rabbits after endotoxin administration. Curves of the LDH activities of the 6 rabbits given endotoxin (Fig. 1) resemble the curves of the 6 rabbits in hemorrhagic hypotension (Fig. 3). This is in accord with other observations from this laboratory showing similarities between endotoxic and hemorrhagic shock(4). The mechanism of serum LDH alterations in disease states has not been fully established (5). Recent data suggest that elevations are due to release of enzyme from damaged tissues(1,6).

† No hemolysis was present.

Summary. 1. Marked elevations of serum LDH activity are described in rabbits given *Escherichia coli* endotoxin intravenously. Elevations reached 6 to 50 times the initial values. 2. Alterations in LDH activity of rabbits in endotoxic shock resemble those seen in hemorrhagic shock.

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6-Aminopenicillanic Acid in Urine after Oral Administration of Penicillins. (25853)

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Sakaguchi and Murao(1) postulated existence of a hydrolytic enzyme capable of cleaving the acyl side-chain from the penicillin molecule. Batchelor *et al.*(2) isolated the actual penicillin moiety, 6-aminopenicillanic acid (6-APA) that results from such cleavage, as a fermentation product of *Penicillium chrysogenum.* Studies to determine whether or not 6-APA could be detected in urine of animal species after oral administration of Penicillin G and several other known penicillins are reported here.

Results. Penicillin G was administered orally at 500 mg/kg to mice housed in metabolism cages. Urine samples (feces free) were collected, pooled, and presence or absence of 6-APA determined by chromatographic procedure described by Batchelor *et al.*(2). The fact that 6-APA *per se* could be absorbed orally and appear in urine was shown by administration of this compound at 50 mg/kg to mice, and its subsequent detection in urine at 2, 6 and 24 hours.

The hydrolytic cleavage of acyl side-chain of Penicillin G *in vivo* was readily indicated by detection of 6-APA in urine of animals after oral administration of the intact antibiotic. 6-APA was detected within ½ hour and at 2, 6, and 24 hours in urine of mouse after oral or intravenous administration of Penicillin G (Table I). Similar results were found after oral administration of Penicillin G to rats, cats, rabbits, dogs,

TABLE I. Appearance of 6-Aminopenicillanic Acid in Urine of Animals after Administration of Various Penicillins.

Penicillins and dosage in mg/kg	Species	Route of admin.	Presence of 6-aminopenicillanic acid in urine*
6-Aminopenicillanic acid—50	Mouse	PO	Positive
Penicillin			
G—50, 500	Mouse	PO	Positive
V—500	"	"	"
V— "	"	IV	" †
G— "	Rat	PO	"
Dihydro F penicillin—1000	"	"	"
Penicillin			
K—1000	"	"	"
X— "	"	"	"
G— "	Dog	"	"
V— "	"	"	"
G— "	Cat	"	" ‡
G— "	Rabbit	"	"
V— "	"	"	"
G—200,000 units	Man	"	" §
G—500, 1000	Guinea pig	"	Negative
V— "	"	"	"

* Control urines from representative species were always negative. Sample times were at 2, 6, and 24 hr.

† Sample times at ½, 2½, and 3 hr.

‡ " " " 4 hr.

§ 24 hr samples.