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The Growth-Promoting Properties of Quinic Acid

Malcom Gordon

Francis A. Haskins
University of Nebraska - Lincoln, fhaskins@neb.rr.com

Herschel Mitchell
The Kerckhoff Laboratories of Biology, California Institute of Technology, Pasadena

*THE GROWTH-PROMOTING PROPERTIES OF QUINIC ACID**

BY MALCOLM GORDON,† FRANCIS A. HASKINS‡ AND HERSCHEL K. MITCHELL

THE KERCKHOFF LABORATORIES OF BIOLOGY,
CALIFORNIA INSTITUTE OF TECHNOLOGY, PASADENA

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Evidence is accumulating that there is a common metabolic precursor to many of the benzene ring derivatives found in living organisms[1–4]. Recent work by Davis[3] and Tatum[4] indicates that one such precursor is the naturally occurring shikimic acid (Fig. 1) since this compound serves as a growth factor for certain mutants of *Escherichia coli*[3] and Neurospora[4] which otherwise require a combination of tyrosine, phenylalanine, tryptophan and *p*-aminobenzoic acid for growth. These mutants cannot utilize the closely related, naturally occurring quinic acid (Fig. 1) as a substitute for any of their requirements.[3, 4]

In an earlier investigation of quinic acid and shikimic acid, Fischer and Dangschat[5, 6] showed that quinic acid is chemically convertible to shikimic

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acid and that the latter is convertible to glucodesonic acid. They pointed to the possibility that these compounds are formed directly from glucose.

For these reasons the growth-promoting properties of quinic acid and shikimic acid were reinvestigated with a Neurospora mutant, C-86, which is capable of utilizing a variety of aromatic compounds for growth[2, 7, 8]. Table 1 gives a list of compounds utilized by C-86 together with those utilized by several other mutants used in this investigation[2, 7–9].

Experimental.—Methods: The growth responses of the several strains of Neurospora tested were measured as dry weight of mycelium after 120 hours at 25° in 20 ml. of the standard Fries medium, adjusted to pH 4.6. Inoculations were made with drops of suspensions of conidia in sterile water. The shikimic acid[10] and the quinic acid[11] were filter sterilized and added sterilely to the autoclaved medium after cooling.

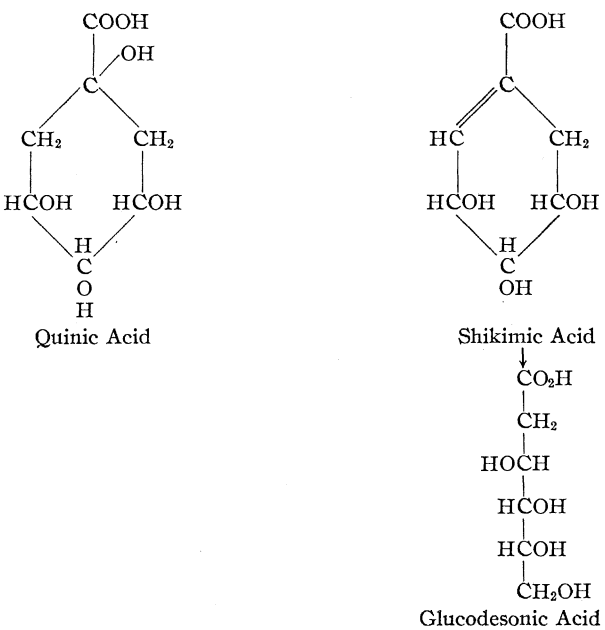

FIGURE 1

Analytical: The quinic acid used was recrystallized from water, melted at 162–163° and had a molecular rotation of −42.8° at 25°. Calculated, C, 43.75, H, 6.29; found, C, 43.49, H, 6.18.

Responses of Mutant Strains: The following compounds were tested for their ability to promote the growth of Neurospora, strain C-86: shikimic acid, quinic acid, dopa, protocatechuic acid, *p*-aminobenzoic acid and gentisic acid. Except for a very small response to gentisic acid, quinic acid

is the only one of these which supports the growth of C-86. Table 2 compares this effect with the growth-promoting effect of tryptophan.

While the activity of quinic acid is about the same as that reported for tyrosine and *trans*-cinnamic acid at low levels,[2] the inhibitory effect noted at higher concentration with *trans*-cinnamic acid is not observed with quinic acid.[12]

To eliminate the possibility that the growth response of C-86 to quinic acid is due to contamination with small amounts of other compounds which promote its growth (table 1), the same sample of quinic acid was filter sterilized and tested at 1- and 5-mg. levels against each of the other mutants listed in table 1. None grew at either concentration of quinic acid.

TABLE 1

COMPOUNDS UTILIZED BY VARIOUS NEUROSPORA MUTANTS

STRAIN	TYROSINE OR *trans*-CINNAMIC ACID	PHENYL-ALANINE	ANTHRA-NILIC ACID	INDOLE	TRYPTO-PHAN	KYNURE-NINE	3-OH-KYNURE-NINE	3-OH-ANTHRA-NILIC ACID	NICO-TINIC ACID
C-86	+	+	+	+	+	+	+	+	+
E-5212	−	+	−	−	−	−	−	−	−
B-1312	−	−	+	+	+	+	−	−	−
39401	−	−	−	+	+	+	+	+	+
10575	−	−	−	+	+	−	−	−	−
C-83	−	−	−	−	+	−	−	−	−
E-5029	−	−	−	−	−	−	+	+	+
4540	−	−	−	−	−	−	−	−	+

TABLE 2

GROWTH OF NEUROSPORA MUTANT C-86 IN THE PRESENCE OF (−)-QUINIC ACID AND *L*-TRYPTOPHAN

γ	DRY WT. OF MOLD, MG.	
	L-TRYPTOPHAN	(−)-QUINIC ACID
25	15.8	...
50	22.8	...
100	33.6	...
250	...	2.0
500	69.2	7.6
1000	...	21.8
3000	...	38.4
5000	...	48.2

Discussion.—These experiments demonstrate three main differences between the shikimic acid and quinic acid mutants of Neurospora.

(1) The mutant which utilizes shikimic acid cannot utilize quinic acid and vice versa.

(2) C-86 grows in the presence of any one of a number of compounds which presumably are related metabolically. The shikimic acid mutant requires four aromatic compounds for growth in the absence of shikimic acid.

(3) *p*-Aminobenzoic acid has no effect on C-86, while it is an absolute requirement for the shikimic acid mutant in the absence of shikimic acid.

The apparent lack of correlation between the results obtained with C-86 and the shikimic acid mutant can be explained by one of several schemes. However, the data presently available do not warrant extensive speculation about the presumed metabolic relationship between quinic acid and shikimic acid, between them and glucose or between them and the aromatic compounds they replace. The evidence would nevertheless seem to favor the view that at least several of the aromatic compounds found in Neurospora arise from a common non-aromatic, cyclical intermediate.

Summary.—Quinic acid promotes the growth of Neurospora, strain C-86, which otherwise requires for growth any one of several aromatic compounds. The closely related shikimic acid is completely without activity for this strain.

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