

On the basis of the lack of constancy of certain elemental ratios, there is no evidence of a defective crystal lattice other than the proxy of Ca for Na and Al for Si. That is, there is no evidence of vacant positions in the lattice. Nevertheless, precisely this type of evidence (lack of constancy of Ca/P ratios) has been used by numerous non-mineralogists in order to demonstrate "defects" in the lattice of apatite when considering the mineral substance of tooth and bone. Thus, for example, the so-called "defect series" of apatites postulated by POSNER, FABRY AND DALLEMAGNE<sup>1</sup> is completely meaningless in the sense in which they have attempted to use it to describe these structures. That extensive isomorphic substitution does take place in the apatite structure was clearly demonstrated by the writer in 1938<sup>2</sup>, and has been confirmed by numerous investigators<sup>3,4,5</sup>.

There are two glaring omissions in their experimental results on the "defect" hydroxy-apatites with various ratios Ca/P, namely, (1) determination of the water content and (2) determination of the carbon dioxide. These omissions should be quickly recognizable in view of the isomorphic substitutions involving  $\text{PO}_4^{3-} \rightarrow \text{H}_2\text{O}_4^{4-}$ ,  $[\text{3PO}_4]^{9-} \rightarrow [\text{4CO}_3]^{8-}$  and  $\text{Ca}^{2+} \rightarrow \text{H}_3\text{O}^+$  or  $\text{H}_2\text{O}$ , as suggested<sup>6,7</sup>. Francolite from Staffell, it will be recalled, contains F,  $\text{CO}_2$  and  $\text{H}_2\text{O}$  (above 300° C) in the amounts 4.11, 3.36 and 0.90 weight per cents, respectively<sup>8</sup>. The quantity of fluorine alone is slightly in excess of the amount required to fill all fluorine positions of the fluorapatite structure.

The question of how the carbonate ion occurs within the crystal lattice of mineral carbonate-apatites has not been demonstrated rigorously, but a hypothesis that qualitatively fits all of the experimental data has been presented<sup>6,7</sup>. Certainly it must be fully as obvious now as it was in 1937<sup>8</sup> that the carbonate group does not substitute for fluorine of fluorapatite and, whatever the structural formula for carbonate-apatite may be, it cannot be  $\text{Ca}_{10}\text{CO}_3(\text{PO}_4)_6$ . Furthermore, it should be obvious that constant ratios of C:P:Ca would not be expected, and the fact that they are not found does not demonstrate either a defect structure or the presence of more than one phase.

The question of the existence of a carbonate-apatite probably first arose in 1822, when HAÜY<sup>9</sup> questions the validity of WERNER's supposition that certain apatites were not merely mixtures. During the intervening 133 years, there has been no straightforward demonstration that small, water-clear crystals of francolite consist of more than a single phase. The conclusion of POSNER AND DUYCKAERTS<sup>10</sup>, that two phases are indicated by their infrared absorption data is a *non sequitur*, and must be disregarded completely in view of the fact that such data as they present cannot possibly yield information concerning the configuration of other atoms in the vicinity of the  $\text{CO}_3$  groups.

There have been many attempts to demonstrate the presence of two phases, but all have been completely unsuccessful in demonstrating even a trace of any solid form of  $\text{CaCO}_3$ . It must, furthermore, be recalled that the carbonate content of francolite is sufficient to require about 10 % of  $\text{CaCO}_3$ . In light of the fact that impurities amounting to less than 0.5 % are readily detectable in many clear, colorless crystals, it must be concluded that some of these persons are quite naive with regard to mineralogical matters. It should be emphasized, moreover, that the properties of francolite differ from those of fluorapatite in several important respects, and these differences cannot be explained by assuming the presence of a second phase. One of these differences is a distinctly smaller lattice periodicity for the *a* direction of francolite as compared with fluorapatite<sup>6</sup>. Optical differences have been reported by many mineralogists<sup>5</sup>.

That certain non-mineralogists are likely to make fundamental contributions to knowledge on the mineral, francolite, through the complete disregard of well-established mineralogical concepts seems highly unlikely, although there appears to be no interruption in the output of their misleading interpretations on these matters.

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Received April 15th, 1955

## The participation of the oxidative pathway in the glucose metabolism of mouse tumors

Following the pioneer investigations of WARBURG AND DICKENS, the existence of an oxidative pathway in glucose metabolism as distinct from the glycolytic pathway, seems now well established for a number of normal animal tissues<sup>1-5</sup>.

A recent communication dealing with this extraglycolytic route in hepatomas<sup>5</sup> prompted us to report on similar findings made in our laboratory.

By comparing the percentage <sup>14</sup>C recoveries in <sup>14</sup>CO<sub>2</sub> after incubation of fresh tumor slices with glucose-1-<sup>14</sup>C and glucose-6-<sup>14</sup>C in Krebs-Ringer phosphate buffer, evidence of the participation of the oxidative pathway in the glucose metabolism of all tumors studied so far, has been obtained (Table I). This method is based on the consideration that the carbon dioxide originating from the breakdown of specifically labelled glucose is initially richer in carbon atom 1 than carbon atom 6, if the oxidative pathway is operative. The carbon atoms 1 and 6 are expected to appear in equal rates in the carbon dioxide if the glycolytic scheme is the only route along which glucose breakdown starts. The ratio  $R_6/R_1$  was found to be 0.70 for mouse liver and 1.1 for rat diaphragm, in accord with previous findings<sup>1,5</sup>.

TABLE I

INCORPORATION OF CARBON ATOMS 1 AND 6 OF SPECIFICALLY LABELLED GLUCOSE INTO CO<sub>2</sub>

1 g of slices were incubated for 1 hour at 37° C. The medium consisted of 5 ml of Krebs-Ringer phosphate buffer (pH 7.4) containing 3 mg of the labelled glucose. The specific activity of both

<i>Tumor</i>	<i>Substrate</i> <i>G-n-C<sup>14</sup>*</i>		<i>R<sub>n</sub>**</i>		<i>R<sub>6</sub></i> <i>R<sub>1</sub></i>
	<i>n</i>	<i>per cent</i>			
T 49985 - mammary carcinoma	6	3.3	3.7	3.9	0.47, 0.44, 0.47
	1	7.1	8.4	8.2	
	6	3.7	2.6	2.4	
	1	8.7	6.8	7.4	
Spontaneous (C <sub>3</sub> H) mammary carcinoma	6	2.8			0.54
	1	5.2			
T 26473-hepatoma	6	0.86	0.92	1.8	0.36, 0.35, 0.49
	1	2.4	2.6	3.7	
T 5441-ovarium tumor (granulosa cell type)	6	1.8	2.6		0.69, 0.70
	1	2.6	3.7		
T 26567-ovarium tumor (sarcomatoid type)	6	5.7	5.1		0.56, 0.49
	1	10.1	10.3		
UV256-sarcoma	6	3.1	2.7		0.65, 0.43
	1	4.8	6.3		

\* G = glucose, n = position labelled with <sup>14</sup>C.

\*\* Radioactivity recovered as <sup>14</sup>CO<sub>2</sub>.

In order to collect more quantitative information regarding this pathway in neoplastic tissues, lactic acid was isolated by silicagel chromatography<sup>6</sup> from the incubation mixtures to which glucose-1-<sup>14</sup>C was added. After titration with 0.1 N NaOH, sodium lactate was isolated and converted to the free acid with the aid of Dowex-50. Half the quantity of this lactic acid was combusted directly<sup>7</sup>, while the other part was converted to the zinc salt, purified and combusted. Identical specific activities were found and corrections were made for any lactic acid endogenously produced or already present.

Following this procedure it was calculated, on the assumption that no intermediates during the conversion of glucose to lactic acid were lost, that approximately 70% of the glucose-1-<sup>14</sup>C molecules giving rise to lactic acid had followed the oxidative pathway in the case of the transplanted mammary carcinomas (average of 3 experiments) and 50% in the case of the ovarium tumors of the sarcomatoid type (average of 5 experiments).

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Received April 16th, 1955