UTILIZATION OF VITAMIN A IN DIFFERENT CARRIERS 
BY BEEF CATTLE

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AQUATURE of the carrier is known to affect efficiency of utilization of vitamin A by several species. For humans, aqueous dispersions of vitamin A have been found superior to oil solutions for maintaining blood levels and promoting growth (Kramer, 1947; Lewis, 1947, 1950; Sobel, 1949; and their respective coworkers). Kagan et al., (1953) reported that both alcohol and ester forms in aqueous dispersion enter the blood more readily than vitamin A in oil.

Aqueous forms of vitamin A have shown superior bio-availability to oil forms with dairy calves (Jacobson et al., 1954; Wise et al., 1949), with chicks (Halpern and associates, 1947) and with rats (Popper and Volk, 1948; Volk and Popper, 1950; Lewis and Cohlan, 1950; Sobel et al., 1948). Vitamin A dispersed in gelatin beadlets has been found superior to oil solution for liver storage in rats and for growth and liver storage in chicks (Luther et al., 1952), an observation which was recently confirmed in rats by Brüggemann and Tiews (1956) and in chicks by Ascarelli (1957).

Particle size of the vitamin A within the gelatin beadlet affects efficiency of utilization (Luther et al., 1952). It was found that for rats particles of vitamin A of 2 microns or less in diameter dispersed in gelatin beadlets brought about 69% greater liver storage than was obtained with an oil solution. With 5-micron particle size the superiority was 24%, and with 20-micron particle size liver storage was approximately the same as with an oil solution.

The present investigation compares effectiveness for beef cattle of vitamin A in oil solution, in aqueous emulsion and dispersed in gelatin beadlets.

Experimental

Yearling Hereford steers were depleted of vitamin A by self-feeding ground corn cobs and 3 lb. per head per day of a low-vitamin A protein supplement of the following composition: Solvent soybean oil meal 63.8, dry molasses supplement (45% sugar) 28, steamed bone meal 6, trace mineralized salt (1.2 ounces of cobalt chloride added per 100 lb.) 1.7, and vitamin D supplement (1500 U.S.P. units per gm.) 0.5%. The supplement was fed in two equal portions in the morning and afternoon. The animals
were maintained on this feeding program until the blood plasma vitamin A was 10 mcg. per 100 ml. or less. They then were divided into groups for administration of vitamin A doses based on plasma level and body weight. The vitamin A preparations, in gelatin capsules, were administered by a balling gun, usually in the evening for convenience of blood sampling.

The vitamin A sources used were a pharmaceutical grade halibut liver oil (60,000 U.S.P. units per gm., Parke, Davis & Co.); a corn oil concentrate of synthetic vitamin A palmitate containing 1,680,000 U.S.P. units per gm.; an aqueous preparation of vitamin A palmitate prepared by dispersing the oil concentrate of pure synthetic vitamin A palmitate in water solution containing 15% Tween-80;* and Pfizer A-250 or A-250 P, containing 250,000 U.S.P. units of vitamin A per gm. as the pure acetate or palmitate dispersed in gelatin beadlets. In preparing the materials for administration the oil and aqueous preparations were diluted with corn oil and water, respectively. The capsules were filled with the aqueous preparation immediately before dosing. The vitamin A palmitate in gelatin was diluted with soybean meal to approximately 20 ml. volume to nearly fill the gelatin capsules. The preparations were analyzed for vitamin A by the Carr-Price colorimetric and U.S.P. XIV spectrophotometric methods just prior to administration. Dosage levels were based on the Morton-Stubbs corrected U.S.P. spectrophotometric values.

The schedule of dosing and plasma and liver sampling is given in the tables. Blood samples were taken from the jugular vein. Blood and liver samples from individual animals were analyzed for vitamin A using the Carr-Price reaction according to slight modifications of the methods of Kimble (1939) and Gallup and Hoefer (1946), respectively.

The individual blood plasma vitamin A responses at 12 hours and the average blood plasma responses for the total period were subjected to an analysis of variance. Normal assumptions were made that the error of assay was independent of time subsequent to treatment and that errors were randomly distributed.

Results and Discussion

Plasma vitamin A values obtained in eight experiments following several different dosages are presented in table 1. At the lowest dosage level, a single dose of 2800 I.U. per 100 lb. body weight (experiment 1), there was no appreciable rise in plasma vitamin A of animals given the oil solution, but there was an indication of a blood response at 12 hours from aqueous vitamin A and vitamin A in gelatin beadlets. The average response for the entire period was significantly greater for the aqueous and gelatin forms than for the oil solution. With a single dose of 5600 I.U. per 100 lb. body weight (experiment 2, table 1) there was a more rapid response to the

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### TABLE 1. CATTLE PLASMA VITAMIN A FOLLOWING ORAL ADMINISTRATION OF VARIOUS FORMS

<table>
<thead>
<tr>
<th>Experiment no.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
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<tbody>
<tr>
<td>Dose vitamin A,</td>
<td>2,800</td>
<td>5,600</td>
<td>11,000</td>
<td>6,000</td>
<td>36,000</td>
<td>72,000</td>
<td>36,000</td>
<td>36,000</td>
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<td>IU./100 lb.</td>
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<tr>
<td>Form of vitamin A*</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>A</td>
<td>B</td>
<td>A</td>
<td>B</td>
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<td>2</td>
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<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
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<tr>
<td>Plasma vitamin A,</td>
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<td>mcg./100 ml.</td>
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<tr>
<td>Initial</td>
<td>9.45</td>
<td>4.55</td>
<td>7.60</td>
<td>7.60</td>
<td>8.60</td>
<td>6.55</td>
<td>7.90</td>
<td>3.50</td>
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<tr>
<td>12 hours</td>
<td>9.2</td>
<td>6.1</td>
<td>7.9</td>
<td>9.8</td>
<td>10.6</td>
<td>13.8</td>
<td>5.0</td>
<td>5.3</td>
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<tr>
<td>14 hours</td>
<td>10.4</td>
<td>5.8</td>
<td>11.3</td>
<td>9.4</td>
<td>10.0</td>
<td>13.0</td>
<td>4.9</td>
<td>5.5</td>
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<td>16 hours</td>
<td>9.5</td>
<td>10.3</td>
<td>12.9</td>
<td>10.4</td>
<td>14.2</td>
<td>11.4</td>
<td>13.7</td>
<td>10.3</td>
</tr>
<tr>
<td>20 hours</td>
<td>12.8</td>
<td>8.8</td>
<td>12.8</td>
<td>12.2</td>
<td>14.6</td>
<td>14.6</td>
<td>14.2</td>
<td>13.7</td>
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<tr>
<td>24 hours</td>
<td>9.6</td>
<td>7.8</td>
<td>12.9</td>
<td>11.1</td>
<td>15.0</td>
<td>12.7</td>
<td>17.8</td>
<td>17.1</td>
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<tr>
<td>36 hours</td>
<td>11.7</td>
<td>16.8</td>
<td>15.2</td>
<td>21.8</td>
<td>9.0</td>
<td>9.5</td>
<td>14.6</td>
<td>18.1</td>
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<td>48 hours</td>
<td>11.3</td>
<td>17.2</td>
<td>14.6</td>
<td>18.1</td>
<td>13.0</td>
<td>14.0</td>
<td>7.4</td>
<td>7.3</td>
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<td>60 hours</td>
<td>10.2</td>
<td>11.6</td>
<td>20.8</td>
<td>21.8</td>
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<td>9.9</td>
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<td>84 hours</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
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<td>120 hours</td>
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<td>150 hours</td>
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<td>180 hours</td>
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<td>210 hours</td>
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<td>240 hours</td>
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<td>270 hours</td>
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<td>300 hours</td>
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<tr>
<td>Av. plasma response</td>
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<td>mcg./100 ml.</td>
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<td></td>
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<tr>
<td>12 hours</td>
<td>-0.3</td>
<td>1.55</td>
<td>0.3</td>
<td>0.3</td>
<td>1.15</td>
<td>4.05</td>
<td>4.90</td>
<td>1.50</td>
</tr>
<tr>
<td>Total period d</td>
<td>0.85</td>
<td>3.22*</td>
<td>3.96*</td>
<td>3.24</td>
<td>5.83*</td>
<td>5.97</td>
<td>6.90</td>
<td>5.18</td>
</tr>
<tr>
<td>Index (12 hours)</td>
<td>100</td>
<td>384</td>
<td>100</td>
<td>222</td>
<td>100</td>
<td>162</td>
<td>100</td>
<td>596</td>
</tr>
<tr>
<td>Index (total period)</td>
<td>100</td>
<td>375</td>
<td>461</td>
<td>100</td>
<td>180</td>
<td>100</td>
<td>212</td>
<td>100</td>
</tr>
<tr>
<td>L.S.D. (12 hours)*</td>
<td>4.53</td>
<td>4.16</td>
<td>8.80</td>
<td>2.66</td>
<td>6.76</td>
<td>12.15</td>
<td>4.99</td>
<td>4.66</td>
</tr>
<tr>
<td>L.S.D. (total period)*</td>
<td>2.02</td>
<td>1.56</td>
<td>2.78</td>
<td>1.09</td>
<td>2.26</td>
<td>4.96</td>
<td>1.66</td>
<td>1.65</td>
</tr>
</tbody>
</table>

* The forms of vitamin A used were:
A = Vitamin A palmitate in oil
B = Vitamin A palmitate in aqueous dispersion
C = Vitamin A acetate in gelatin beadlet
D = Vitamin A palmitate in gelatin beadlet, Pfizer A-250P
E = Haliver oil, pharmaceutical grade

b 84-hour value in experiment 2B represents one animal.

c 132-hour value in experiment 4A is an average of two animals.
d Values for the average response, total period, are the difference between the initial plasma vitamin A and the average of all values after the initial.
* Significantly different from controls, P = 0.05.
aqueous dispersion than to the oil solution and a significantly greater average response in the animals which received the aqueous dispersion.

When aqueous dispersion (6000 I.U. per 100 lb.) and oil solution (11,000 I.U. per 100 lb.) were compared (experiment 3) the 12-hour plasma response and the average total period response were equal to those produced by the oil even though the level of vitamin A administered in oil was nearly double the level in aqueous dispersion.

A comparison of vitamin A palmitate in oil and in gelatin beadlets, both at 6000 I.U. per 100 lb. body weight (experiment 4), showed a greater increase in plasma A at 12 hours in the animals given the gelatin source as well as a significantly higher average response in plasma vitamin A.

TABLE 2. LIVER VITAMIN A OF STEERS FOLLOWING ADMINISTRATION OF VITAMIN A IN OIL AND GELATIN BEADLETS

<table>
<thead>
<tr>
<th>Source of vitamin A a</th>
<th>No. steers</th>
<th>Before dosing</th>
<th>Days after initial dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palmitate in gel. beadlets</td>
<td>2 b</td>
<td>0.125</td>
<td>12.4 5.0</td>
</tr>
<tr>
<td>Palmitate in oil</td>
<td>3</td>
<td>0.24</td>
<td>9.2 4.7</td>
</tr>
</tbody>
</table>

* L.S.D. = 6.27 for the combined 7- and 24-day values.

a Vitamin A was given in five consecutive daily doses of 36,000 I.U./100 lb.

b There was difficulty in obtaining the 7-day liver sample in one of the three animals which received vitamin A palmitate in gelatin. Liver values for this animal were therefore not included in the average.

With doses of 36,000 I.U. per 100 lb. body weight daily for 5 successive days (experiment 5) the gelatin beadlet form brought a pronounced increase in plasma content in 12 hours after administration of the first dose, whereas oil solution brought no appreciable increase by this time. The plasma vitamin A of animals given the gelatin beadlets was maintained at a higher level than that of those given the oil solution for 84 hours, after which the differences tended to diminish.

With a single dose of 72,000 I.U. per 100 lb. (experiment 6) there was a greater response at 12 hours and for the entire period in the animals given the vitamin A in gelatin than in those given the oil, although the differences were not statistically significant. The higher level of plasma vitamin A in the steers given the vitamin in gelatin beadlets persisted for approximately 24 hours, after which the difference disappeared.

A direct comparison of synthetic vitamin A palmitate in gelatin and natural vitamin A in haliver oil was made in experiment 7, both forms being given in a single dose of 36,000 I.U. per 100 lb. The responses with the synthetic vitamin A in gelatin at 12 hours and for the entire period were significantly greater than the responses with fish liver oil.
In experiment 8 oil solutions of natural vitamin A and synthetic vitamin A were compared to determine whether differences in the isomeric forms of vitamin A occurring in natural and synthetic vitamin A could partially account for the differences in the blood responses obtained in experiment 7. Rat assays in support of the latter possibility show that neo-vitamin A (2-mono-cis), which is present in appreciable amounts in natural sources, is only 75% as potent for rat growth and liver storage as the all-trans form of vitamin A (Ames et al., 1955) occurring in synthetic vitamin A. The results of this comparison with cattle (experiment 8) show no significant differences in the 12-hour and total period responses for the oil solutions of the synthetic and natural vitamin A.

It is possible, however, that small differences in bio-availability of the natural and all-trans synthetic vitamin A could have been masked by the non-vitamin A impurities in the fish liver oil in experiments 7 and 8. The analytical values obtained on the fish liver oil by the Carr-Price and U.S.P. spectrophotometric methods were in a ratio of 1.26, whereas the corresponding Carr-Price: U.S.P. spectrophotometric ratios for the pure synthetic vitamin A in gelatin and in corn oil were all within a range of 1.00–1.05. Assuming that the Carr-Price reacting impurities of the fish liver oil were absorbed by the animals, with dosage levels based on corrected U.S.P. spectrophotometric analyses, the blood plasma vitamin A values determined by the Carr-Price method could have included impurities from fish oil which would not have been present in the plasma of animals treated with synthetic vitamin A.

In consideration of the effect of level of administration of vitamin A upon the sensitivity of the animals to differences in bio-availability of different forms of vitamin A, the data clearly indicate that for the total-period-plasma response, the differences are greater at the lower levels of vitamin A administration and nearly disappeared with the highest level of 72,000 I.U. per 100 lb. For differences in the initial appearance of vitamin A in the plasma at 12 hours, difference in dosage level did not appear consistently to influence the results although at the lowest level, 2800 I.U. per 100 lb., the response curve was too gradual for differences to be demonstrated.

Liver storage studies were carried out in the cattle used in experiment 5. Liver samples of approximately 2 gm. size were removed by a biopsy instrument just before dosing, at 7 days (2 days after the animals had received the last of five daily doses of 36,000 I.U. vitamin A per 100 lb.) and 24 days after the initial dose. The initial liver content of vitamin A averaged less than 0.25 mcg. per gm. in both groups of cattle. The average 7-day liver vitamin A of the animals given vitamin A in gelatin was over 30% higher than the corresponding value for the group which received an oil solution. Due to variability in the animals in liver responses and the
limited number of animals, however, this difference was not statistically
significant although the difference in total blood response was significant.

Summary

1. Vitamin A depleted cattle were given orally pure synthetic vitamin A
esters in the forms of aqueous dispersion, oil solution and gelatin beadlets
at levels of 2800–72,000 I.U. per 100 lb. body weight. The aqueous and
gelatin beadlet forms of vitamin A produced greater blood plasma vitamin
A responses at 12 hours after dosing and greater average plasma responses
for the entire period following dosing than did the oil solutions of vitamin
A.

2. Oil solutions of synthetic vitamin A and natural vitamin A (fish oil)
when administered in equal doses produced blood plasma responses which
were not significantly different at 12 hours or for the entire period.

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