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GROWTH PROMOTANT SUBSTANCES

Alan B. Rogers, Evergreen Park, and John F. Roland, Jr., Glenview, Ill., assignors to Armour and Company, Chicago, Ill., a corporation of Illinois

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This invention relates to growth-promotant substances. The growth-promotant substances of this invention have particular value in growing and fattening chickens and hogs, but they can also be used advantageously with other animals.

In recent years a few substances have been found to have the property of stimulating animal growth, although these substances are apparently not a normal nutritional requirement of the animals. Perhaps the best established of these substances are certain growth-stimulating antibiotics such as aureomycin. In addition, as reported in the literature in this field, there have been experimental indications that other non-nutritional substances, principally surfactants, under some conditions may also stimulate growth, although not to the extent of or as reliably as the antibiotics. However, as the animal raising art stands at present, only certain antibiotics have been accepted generally as additives to animal feeds, while surfactants have not been felt to be of sufficient value to justify their use in commercial feeding operations. Therefore, there is still a considerable need for more effective and less expensive animal growth promotants.

It is therefore a general object of this invention to provide animal feeds containing novel growth-promotant substances which compare favorably with the antibiotics both as to cost and results obtained. Further objects and advantages will appear as the specification proceeds.

Heretofore it has been postulated that the growth-promoting properties of antibiotics and surfactants may be related to their bactericidal and bacteriostatic properties. It has also been suggested, particularly in the case of surfactants, that growth stimulation may correlate in some way with surface activity. Therefore, the present invention to a considerable extent goes against this prior thinking in the field and, in fact, probably requires the explanations previously advanced for the growth-stimulating effect of surfactants to be either modified or abandoned. This is true because the present invention is based on the discovery that certain classes of surfactants which have been chemically modified so as to display virtually no surface activtiy in water and also so as to possess little or no bactericidal and bacteriostatic properties not only continue to act as growth stimulants for animals, but even more surprisingly have proven to be greatly superior growth promotants over the unmodified surfactants from which they are formed, and to compare with the growth-promoting antibiotics.

The general class of compounds which have utility for the purpose of this invention can be designated as the reaction product of the cationic fragment of a cationic surfactant with the anionic fragment of an anionic surfactant. For example, the cationic fragment of trimethyl octadecyl ammonium chloride can be chemically combined with the anionic fragment of sodium stearate to produce trimethyl octadecyl ammonium stearate, which new compound is then employed for the purpose of this invention.

The available experimental evidence indicates the operability for the purposes of this inveniton of the class of substances defined above. However, certain sub-classes are preferred. For example, it is preferred that the cationic fragment of the reaction product be derived from a surface active quaternay ammonium salt such as the dimethyl dialkyl ammonium halides of the trimethyl alkyl ammonium halides where the alkyl group (or groups) can contain from 8 to 22 carbon atoms and can be saturated or unsaturated. Instead of an alkyl group of the character described, the surface active quaternary ammonium compound can contain an aromatic group such as a benzyl group. By way of specific example, such cationic surfactants may be mentioned as: dimethyl didodecyl ammonium chloride, trimethyl dodecyl ammonium chloride, diemthyl dioctadecyl ammonium chloride, trimethyl octadecyl ammonium chloride, dodecyl dimethyl benzyl ammonium chloride, octadecyl dimethyl benzyl ammonium chloride, etc. Also, mixtures of different cationic surfactants can be employed, such as the naturally occurring mixtures where the quaternary ammonium compound is prepared from a natural fatty acid source. For example, trimethyl coco ammonium chloride, dimethyl ditallow ammonium chloride, trimethyl soya ammonium chloride, etc. are suitable sources for the ctaionic fragments. In addition, other cationic surfactants can be used to provide the cationic fragments, such as various surface active primary, secondary and tertiary amines. Usually such amines should contain at least 1 alkyl chain having from 8 to 22 carbon atoms. By way of specific example may be mentioned: octadecyl amine, dimethyl octadecyl amine, bis-hydroxyethyl octadecyl amine, metehyl dioctadecyl amine, dioctadecyl amine, etc. If desired, polyamines like dodecyl trimethylene diamine or cyclic nitrogen compounds like octadecyl pyridinium chloride can also be used.

Various anionic surfactants can be used as the source of the anionic fragment in the compounds of this invention. Common soaps, that is, sodium or potassium salts of the higher fatty acids, have proven satisfactory, as for example, sodium stearate or sodium laurate or other salts of fatty acids containing from 8 to 22 carbon atoms in which the hydrocarbon chains are either saturated or unsaturated. Anionic detergents are also quite satisfactory, like the alkyl sulphates or sulphonates, as well as the alkyl aryl sulphonates. Also, the alkyl methyl taurides may be mentioned. By way of specific example of the type of anionic detergents useful in forming the compounds of this invention may be mentioned: dodecyl sulphate, octadecyl benzene sodium sulphonate, the ester of oleic acid and hydroxy ethane sodium sulphonate, etc. The quaternary ammonium soaps can be considered as typical of the compounds of this invention, that is, as the reaction product of a surface active quaternary ammonium compound and a soap. Such reaction products are quite insoluble in water and display substantially no surface activity in water as distinguished from both the anionic and cationic surfactants from which they are formed. Further, these reaction products have little germicidal activity as compared with the compounds from which they are formed. In spite of these modified properties, however, it has been found that these reaction products are surprisingly effective in promoting the growth of various animals and, in particular, in promoting the growth of hogs and chickens.

In practicing this invention, the reaction products described above are orally administered to the growing animal. In the case of non-ruminant animals such as chickens and hogs, it has been found that the range is rather wide for the amount of the reaction products which can be administered while promoting the growth

of the animals without having any undesirable toxic effect on the animal. Therefore, it is relatively easy to practice the invention by incorporating the compounds in animal feeds or other nutrient materials which will be consumed by the animals. In this way it has been found possible to increase the rate of weight gain as much as 8 to 15% on the average in chickens, and a comparable although somewhat lesser amount in hogs. The "feed efficiency" is also significantly improved, i. e., the pounds of feed required to produce one pound of weight gain are decreased.

The following examples more fully illustrate this invention by describing tests with animal feed materials characterized by containing as an essential ingredient therein at least one compound composed of the cationic fragment of a cationic surfactant and an anionic fragment of an anionic surfactant.

EXAMPLE I

Trimethyl octadecyl ammonium stearate was tested as a growth promotion for baby pigs fed on synthetic milk. The results of these tests are summarized below:

Lot	No. of Pigs	Average Weekly Gains Over Preceding Week, lbs.				
		1 Week	2 Weeks	3 Weeks	4 Weeks	5 Weeks
1	4	0.51	0.70	1.72	2.61	3.86
2	4	0.39	1.08	2.03	2.78	3.45
3	3	0.41	0.79	1.92	2.53	3.54

Lot	No. of Pigs	Feed Efficiency (lbs. dry matter fed/lb. gain), lbs.				
		1 Week	2 Weeks	3 Weeks	4 Weeks	5 Weeks
1	4	1.69	1.77	1.11	1.19	1.17
2	4	2.69	1.37	1.04	1.13	1.24
3	3	2.25	1.64	0.78	1.80	1.23

Lot 1—Fed synthetic milk plus trimethyl octadecyl ammonium stearate
Lot 2—Fed synthetic milk plus aureomycin
Lot 3—Fed synthetic milk only
Levels of promotant fed milk (dry matter):
Trimethyl octadecyl ammonium stearate @ 50 mg./kg. for first three weeks, @ 500 mg./kg. after three weeks
Aureomycin @ 50 mg./kg. throughout the five-week period

Average gain and feed efficiency for 3-week period (weeks 1, 2 and 3)

	Gain, lbs.	Efficiency
Lot 1	2.93	1.37
Lot 2	3.50	1.39
Lot 3	3.13	1.19

Average gains and feed efficiency for 4th and 5th weeks of test

	Gain lbs.	Efficiency
Lot 1	6.47	1.18
Lot 2	6.23	1.19
Lot 3	6.07	1.26

The above data indicate that for the baby pig on a milk diet trimethyl octadecyl ammonium stearate is preferably used at concentrations above 50 mg. per kilogram of dry matter and is effective at concentrations up to at least 500 mg. per kg.

EXAMPLE II

Further tests were made with trimethyl octadecyl ammonium stearate on weanling pigs with the following results:

Lot	Ave. Initial Wt., Lbs.	Average Daily Gains Over Initial Wt., Lbs.				
		2 Weeks	4 Weeks	6 Weeks	8 Weeks	10 Weeks
1	27.0	0.63	0.81	0.95	1.08	1.17
2	26.8	0.86	1.05	1.18	1.29	1.35
6	26.8	0.98	1.10	1.25	1.36	1.41
5	26.8	0.75	0.90	1.03	1.12	1.20

Lot	Feed Efficiency (lbs. feed/lbs. gain)				
	2 Weeks	4 Weeks	6 Weeks	8 Weeks	10 Weeks
1	2.37	2.56	2.64	2.76	2.94
2	2.26	2.46	2.63	2.84	3.03
6	2.18	2.44	2.55	2.72	2.90
5	2.28	2.52	2.61	2.81	3.02

Lot 1—Fed basal ration
Lot 2—Fed basal ration plus Aurofac @ 5 lbs./ton
Lot 6—Fed basal ration plus trimethyl ostadecyl ammonium stearate @ 50 gm./ton
Lot 5—Fed basal ration plus trimethyl octadecyl ammonium stearate @ 25 gm./ton

Basal ration:	Lbs.
Corn	780
Soy bean oil meal	140
Meat and bone scrap	50
Fish solubles	10
Limestone	5
Dicalcium phosphate	9
Iodized salt	5
Trace minerals	1
Vitamins A and D	0.5
Fortafeed 2-49-C	1

EXAMPLE III

The effect of trimethyl octadecyl ammonium stearate on the growth of chicks was shown in the following test:

Test No.	Lot	Average Gains in Weight		Feed Eff. to 8 wks.
		4 weeks, gm.	8 weeks, gm.	
1	Basal	462	1,154	2.72
1	Basal plus trimethyl octadecyl ammonium stearate[1]	514	1,231	2.52
2	Basal	536	1,387	2.81
2	Basal plus trimethyl octadecyl ammonium stearate[1]	512	1,416	2.64

[1] Trimethyl ostadecyl ammonium stearate added to ration @ 12½ mg./lb.

Composition of basal ration:	
Gr. yellow corn	64.0
Soy bean meal	23.5
Dried sk. milk	2.0
Meat scraps	4.0
Alfalfa meal	2.5
St. bone meal	1.5
Limestone	1.0
Salt (Mn+I)	0.5
Vitamin pre-mix [2]	1.0
	100.0

[2] Provides per pound of diet: Riboflavin 1 mg., Niacin 17 mg., Ca pantothenate 2.5 mg., vitamin B_{12} 1.5 mcg., choline chloride 227 mg., A 1500 units, D 200 ICU.

EXAMPLE IV

Further tests were made as described in Example III, except that the basal ration contained 62.0% yellow corn and 2.0% animal fat. The results were as follows:

Average gains in weight

Test No.	Lot	4 weeks, gm.	8 weeks, gm.
3	Basal	514	1,16
3	Basal plus trimethyl octadecyl ammonium stearate [1]	532	1,28

Feed efficiency

Test No.	Lot	8 weeks
3	Basal	2.67
3	Basal plus trimethyl octadecyl ammonium stearate [1]	2.55

[1] Trimethyl octadecyl ammonium stearate added to ration @ 12½ mg./lb.

EXAMPLE V

The following compounds were incorporated in the basal diet of weanling rats to determine their effect as growth stimultants:

(*a*) Trimethyl octadecyl ammonium stearate;
(*b*) Trimethyl octadecyl ammonium dodecyl sulphate;
(*c*) Trimethyl octadecyl ammonium alkyl benzene sulphonate; and
(*d*) Trimethyl octadecyl ammonium oleylmethyl tauride.

Eight rats per lot were tested, and the data given below reports the results on the second week of the tests. There is always a readjustment period when placing weanling rats on a diet and it is thus considered that the data on the first week may not be significant. The rats were taken off test after the 2-week period:

Promotant	Level mg./kilo of feed	Gain in Wt. (7 to 14th day), Grams
None		0.8
(*a*)	94.5	4.7
(*b*)	92.0	3.4
(*c*)	100.0	4.0
(*d*)	115.0	3.7

Basal diet: Casein to provide 9% protein, Cerelose 58%, lard 28.0% salt mix U. S. P. No. 2, 4%, and adequate amounts of essential vitamins.

EXAMPLE VI

A number of additional tests were run employing compounds falling within the scope of this invention as additives to chicken feed composed of a basal ration similar to that described in Example III. A summary of these tests is set out below, the weights at 4, 6, and 8 weeks being given in grams.

Age (Weeks)	4	6	8
Basal	415	754	1,215
Basal + A–1 50 mg./lb.	431	768	1,240
Basal + A–1 75 mg./lb.	439	781	1,253
Basal + A–2 50 mg./lb.	426	755	1,220
Basal + A–2 75 mg./lb.	424	780	1,257
Basal + A–3 50 mg./lb.	454	789	1,241
Basal + A–3 75 mg./lb.	452	811	1,298
Basal + A–4 50 mg./lb.	459	784	1,257
Basal + A–4 75 mg./lb.	442	804	1,256

Summary of feed efficiency in above experiment:

	Feed/pound gain to 8 weeks
Basal	2.86
Basal+A–1	2.71
Basal+A–2	2.72
Basal+A–3	2.79
Basal+A–4	2.64

Summary of growth response in grams of chicks to additions of A–2 to the diet:

Age (Weeks)	4	6	8
Basal	377	666	1,115
Basal + A–2 40 mg./lb.	396	688	1,134
Basal + A–2 80 mg./lb.	426	740	1,222
Basal + A–2 160 mg./lb.	408	715	1,138
Basal + A–2 40 mg./lb. to 4 wks; 160 mg./lb. 4–8 wks.	403	728	1,197

The compound identification symbols used in this example have the following meaning:

A–1—trimethyl octadecyl ammonium stearate
A–2—trimethyl octadecyl ammonium dodecyl sulphate
A–3—trimethyl octadecyl ammonium dodecyl benzene sulphonate
A–4—trimethyl octadecyl ammonium oleylmethyl tauride

In preparing the hog and chicken feed materials described in the above examples, the growth-promotant substance, such as trimethyl octadecyl ammonium stearate, were intimately mixed with another feed ingredient, such as one of the commonly used feed ingredients like bone meal or limestone, to produce 5% to 10% premix. An appropriate amount of this premix was then distributed throughout the entire feed in a feed mixer. The premix can be made conveniently in any mixer which provides a grinding action in addition to stirring. Alternatively the growth-promotant substance can be dissolved in a solvent, such as ethanol, propanol-2, etc., and the solubilized material mixed with the bone meal or other commonly used feed ingredient as described above.

The range of effectiveness of the growth-promotant substances of this invention depends on the age and species of the animal being fed. Experiments have shown response from 12 grams up to 500 grams per ton of feed. A favorable range for growing poultry and swine appears to be about 25 to 200 grams per ton of feed. However, greater or lesser amounts can be employed with considerable success.

The growth-promotant substances described herein not only speed up growth of the animal, but also improve the efficiency of feed conversion. This is an important advantage, since it makes the growing process more economical for animal raisers by requiring less feed per pound of weight gain.

While in the foregoing specification this invention has been described in relation to certain specific embodiments thereof and many details have been set forth for purpose of illustration, it will be apparent to those skilled in the art that the invention is susceptible to other embodiments than those set forth and that many of the specific details can be varied widely without departing from the basic concepts of the invention.

We claim:

1. An animal nutrient material characterized by containing as an essential ingredient therein at least one compound composed of the cationic fragment of a quaternary ammonium surfactant and the anionic fragment of an anionic surfactant, said compound being substantially insoluble and non-surface active in water.

2. The animal nutrient material of claim 1, in which said quaternary ammonium surfactant is a trimethyl octadecyl ammonium surfactant.

3. The animal nutrient material of claim 1, in which said compound is trimethyl octadecyl ammonium stearate.

4. A hog feed material characterized by containing as an essential ingredient therein at least one compound composed of the cationic fragment of a quaternary ammonium surfactant and the anionic fragment of an anionic surfactant, said compound having the function of a growth promotant in said feed material while being substantially insoluble and non-surface active in water.

5. A chicken feed material characterized by containing as an essential ingredient therein at least one compound composed of the cationic fragment of a quaternary ammonium surfactant and the anionic fragment of an anionic surfactant, said compound having the function of a growth promotant in said feed material while being substantially insoluble and non-surface active in water.

6. The animal nutrient material of claim 1, in which said quaternary ammonium surfactant is trimethyl alkyl ammonium salt inn which the alkyl group contains from 8 to 22 carbon atoms.

7. An animal feed material characterized by contain-

ing as an essential ingredient therein at least one compound composed of the cationic fragment of a cationic surfactant and the anionic fragment of an anionic surfactant, said cationic surfactant being selected from the group consisting of quaternary ammonium surfactants and cyclic nitrogen surfactants, said anionic surfactant being selected from the group consisting of fatty acid salt surfactants, alkyl sulphate surfactants, alkyl aryl surfactants, and alkyl methyl tauride surfactants.

8. The animal feed material of claim 7 in which the ingredient is a quaternary ammonium soap, said ingredient being substantially insoluble and non-surface active in water.

9. The animal feed material of claim 7 in which the ingredient is trimethyl ammonium dodecyl sulphate.

10. The animal feed material of claim 7 in which the ingredient is trimethyl octadecyl ammonium dodecyl benzene sulfonate.

11. The animal feed material of claim 7 in which the ingredient is trimethyl octadecyl ammonium oleylmethyl tauride.

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