This invention relates to new therapeutically active preparations and has particular relation to compositions containing sex hormones in mixture with other active ingredients.

The main object of my present invention is to provide pharmaceutical compositions which contain sex hormones such as androgens, estrogens and progestins, in mixture with other active ingredients which are adapted to prevent or reduce undesired side effects caused by sex hormones, without adversely affecting the beneficial effects of the latter.

The term "sex hormone" is used in the present specification and claims to include naturally occurring sex hormones, which are obtainable from natural sources or by synthesis, chemically modified forms of naturally occurring hormones, and also synthetic substances, the composition of which is not identical with that of natural sex hormones, which, however, show activities similar to that of the sex hormones proper. As examples of such substances which may be used in carrying out the present invention, the following may be mentioned: androgens, such as testosterone, testosterone propionate, methyltestosterone, androsterone, dehydroandrosterone; estrogens, such as estradiol, estriol, estrone, non-crystalline estrogen preparations containing substantially estrone, diethylstilbestrol, hexestrol, benzestrol, triphenyl ethylene, ethynil estradiol, and progestins, such as progesterone and ethynil testosterone.

The above substances have been used in various clinical applications with beneficial effects, but it has been known that their administration may cause certain undesired or even dangerous secondary effects, such as cancer of the sex organs or organs controlled by them, liver dysfunction, and liver cirrhosis, particularly if the amount of the sex hormone administered to the patient exceeds certain narrow limits. I have now found that such secondary effects may be prevented or considerably reduced by administering the sex

hormone or hormones in form of mixtures with vitamin B compounds of the type described hereinafter. In addition to said vitamins, the preparations according to my present invention preferably contain other active ingredients, particularly ingredients supporting the effect of B-vitamins, and they may also contain substances increasing the stability of the preparations, or other suitable additions.

According to the preferred embodiment of my present invention, as substances supporting the beneficial effect of B-vitamins on sex hormones, certain specific amino acids are used. The specific amino acids are: betaine, glutamic acid, glycine, histidine, methionine, tyrosine and cysteine. One single of these amino acids or preferably a mixture of two or more of them may be used. The term "amino acid" is used in the present specification and claims to include the beforementioned free amino acids as well as their salts. Another substance supporting the beneficial effect of B-vitamins on sex hormones is choline.

In the preparations according to my present invention, the proportion between the sex hormones and the B-vitamins depends on the desired therapeutic effects. The amount of B-vitamins to be administered daily in the compositions according to the invention may vary between the known daily requirements and many times their equivalent in cases of liver dysfunction, malnutrition or deficiencies, in infections, malabsorption for instance in colitis, intestinal obstruction, secretion disturbances of the stomach or pancreas, or the like.

The compositions according to this invention may be applied by oral or parenteral administration.

The following examples serve to illustrate some preferred embodiments of my invention without limiting the same to the specific ingredients, proportions, and other details.

Example 1. A 2cc solution for intramuscular injection is prepared by dissolving in propylene glycol

Testosterone	10 mg
Vitamin B^1	10 mg
Vitamin B^2	5 mg
Calcium pantothenate	1 mg
Nicotinic acid	50 mg

Example 2. Capsules to be used by oral administration consist of

Testosterone	5 mg
Methyltestosterone	20 mg
Vitamin A (Fish Liver Oil)	4000 USP units
Vitamin D (Irradiated Ergosterol)	400 USP units
Vitamin B^1 (Thiamine HCl, 666 USP units)	2 mg
Vitamin B^2 (Riboflavin)	2 mg
Vitamin B^6 (Pyridoxine HCl)	0.1 mg
Vitamin C (Ascorbic acid, 750 USP units)	37.5 mg
Niacin amide	20.0 mg
Calcium pantothenate	1 mg
Cysteine hydrochloride	8 mg
Urea	75 mg
Tyrosine	60 mg
Choline	30 mg
Glutamic acid	60 mg
Liver conc. 1:20	25 mg
Yeast dried USP	50 mg

Example 3. A 2cc solution for intramuscular injection is prepared from the following ingredients:

Progesterone	2 mg
Vitamin B^1	20 mg
Vitamin B^2	5 mg
Vitamin B^6	10 mg
Niacinamide	50 mg
Urea	200 mg
Histidine HCl	40 mg

Sodium glutamate	100 mg
Choline citrate	20 mg
Methionine	40 mg
Benzyl alcohol	2% of the total weight
Chlorobutanol	0.4% of the total weight
Propylene glycol	25-50% of the total weight.

Example 4. A 2cc solution for intramuscular injection is prepared by dissolving

0.2 mg diethylstilbestrol
5 mg vitamin B^1
5 mg vitamin B^2
0.5 mg vitamin B^6
25.0 mg nicotine amide, and
2.0 mg calcium pantothenate

in sterile propylene glycol.

Example 5. A composition is prepared by mixing

0.2 mg diethyl stilbestrol
100 mg cystein hydrochloride
300 mg glutamic acid hydrochloride
5 mg vitamin B^1
5 mg vitamin B^2
40 mg vitamin C
30 mg choline
170 mg vitamin B filtrate factor of liver
170 mg rice polish
170 mg yeast.

Example 6. A composition is prepared by mixing

0.05 mg ethynil estradiol
100 mg cysteine
300 mg methionine
5 mg vitamin B^1
5 mg vitamin B^2

40 mg vitamin C

30 mg choline

170 mg vitamin B filtrate factor of liver

170 mg yeast

170 mg rice polish.

Example 7. A 2cc solution for intramuscular injection is prepared by dissolving

2 mg hexestrol

80 mg methionine

20 mg vitamin B^1

5 mg vitamin B^2

10 mg vitamin B^6

30 mg nicotinamide

2 mg calcium pantothenate

in sterile methyl acetamide.

Example 8. A 2cc solution for intramuscular injection is prepared by dissolving

2 mg hexestrol

80 mg histidine hydrochloride

5-10 mg vitamin B^1

5 mg vitamin B^2

0.5-1.0 mg vitamin B^6

20-30.0 mg niacin amide

2.0 mg calcium pantothenate

400 mg urea

667.0 mg propylene glycol

40.0 mg Na_2HPO_4

6.0 mg H_3PO_4 (85%)

100 mg benzyl alcohol

80 mg chlorobutanol

0.71 mg nipagin,

in methyl acetamide.

The above described compositions may also be administered in the form of ointments or cosmetic creams, or the like in which the above described compositions are homogeneously incorporated in a manner known by itself. Oil solutions containing sex hormone products and/or vitamins may also be used in carrying out my invention.

In order to increase the stability of the compositions according to the present invention and avoid undesirable changes in the same, I prefer to add to these compositions a small amount, i.e. 0.01-0.05% of p-hydroxybenzoic methyl ester ($HO-C_6H_4.COO.CH_3$) or p-hydroxybenzoic ethyl ester ($HO-C_6H_4.COO.C_2H_5$). Such amounts of these substances may be added to any of the compositions described in the above examples. Mixtures of the two esters may also be used as stabilizers.

It will be understood that the invention is not limited to the proportions, ingredients or other details described above and permits of various modifications, substitutions and additions without departing from the scope of the invention as defined in the appended claims. It is essential in this invention that the individual groups of ingredients, i.e. hormones, B-vitamins and amino-acids co-act to bring about a result which cannot be obtained by the separate use of said ingredients.