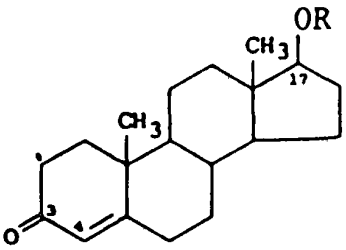
TESTOSTERONE

IDENTITY

Chemical name: 17β-hydroxyandrost-4-en-3-one
Δ-4-androsten-17β-ol-3-one

Synonyms: trans-testosterone

Structural formula:



R = H, testosterone

R = $OCCH_2CH_3$, testosterone propionate

Molecular formula: $C_{19}H_{28}O_2$ (testosterone)

$C_{22}H_{32}O_3$ (testosterone propionate)

Molecular weight: 288.41 (testosterone)
344.48 (testosterone propionate)

OTHER INFORMATION ON IDENTITY AND PROPERTIES

Pure active ingredient:

	Testosterone	Testosterone propionate
Description:	needles	prisms
Melting Point:	155°C	118-122°C
Optical Rotation:	$[\alpha]_D^{24}$ = + 109° (c=4 in alc)	$[\alpha]_D^{25}$ = + 83° to 90° (c=1 in dioxane)

UV_{max}: 238 nm

(Windholz, 1983)

Technical active ingredient:

USP Grade: >97% purity

RESIDUES IN ANIMALS AND THEIR EVALUATION

CONDITIONS OF USE

General:

Testosterone or testosterone propionate are used primarily as growth promotants in cattle in combination with estradiol or esters of estradiol. Administration is by subcutaneous implant in the ear. The ear, along with any residual drug, is discarded at slaughter.

Dosages:

Synovex-H (200 mg testosterone propionate + 20 mg estradiol benzoate) = heifers
Heifer-oid (200 mg testosterone propionate + 20 mg estradiol benzoate) = heifers
Implix BF (200 mg testosterone + 20 mg estradiol) = heifers

RADIOLABELED RESIDUE STUDIES

General:

When administered exogeneously, testosterone enters the same metabolic pathways and is indistinguishable from the endogenously produced molecule. (Hoffman and Evers, 1986)

RESIDUE STUDIES

Non-pregnant and Pregnant Heifers

Concentrations of testosterone were measured in muscle, liver, kidney, and fat from non-pregnant control heifers and non-pregnant heifers implanted with SYNOVEX-H. Samples were taken at slaughter at 30, 61, 90, or 120 days after implantation (see Table I). Testosterone levels were also determined in muscle, liver, kidney, and fat obtained from pregnant heifers (control and implanted with SYNOVEX-H for 61 days). At the time of slaughter, animals were approximately 120, 180, or 240 days of gestation (see Table II).

The results obtained for testosterone in non-pregnant heifers differ from those for the other steroids in that the highest concentrations were found in kidney rather than in fat. (Kushinsky, 1983)

Table I. Testosterone Mean Tissue Concentrations in Heifers Implanted with SYNOVEX-H (ng/kg)

	Tissue			
	Muscle	Liver	Kidney	Fat
Control	19.6 ± 7.09	12.9 ± 1.96	189 ± 91.6	25.5 ± 6.94
30 Days	102* ± 48.1	34.1* ± 9.98	451* ± 201	339* ± 228*
61 Days	46.7* ± 22.3	15.7* ± 3.35	228* ± 143	142* ± 104*
90 Days	56.7* ± 34.2	22.6* ± 7.89	371* ± 267	115* ± 69.8
120 Days	31.3* ± 12.4	16.1 ± 5.26	307* ± 89.3	32.1* ± 12.1

* Significantly higher than controls.

Table II. Testosterone Mean Tissue Concentrations in Pregnant Heifers Implanted with SYNOVEX-H (ng/kg)

	Tissue			
	Muscle	Liver	Kidney	Fat
120-Day Gestation				
Control**	267 ± 101	52.8 ± 10.1	1513 ± 331	590 ± 176
61-Day	357 ± 130	37.6 ± 6.9*	1856 ± 426	751 ± 198
180-Day Gestation				
Control**	343 ± 117	121 ± 19.4	3505 ± 1537	751 ± 174
61-Day	356 ± 81.4	60.6 ± 8.0	1974 ± 510*	1047 ± 274*
240-Day Gestation				
Control**	418 ± 180	274 ± 69.4	4014 ± 2269	694 ± 231
61-Day	370 ± 89	90.2 ± 8.8	2914 ± 1057	119 ± 155*

* Significantly different from synchronized controls.
** Control pregnant heifers were synchronized with fenprostalene.

Female Calves

Nine female calves were implanted with 20 mg estradiol and 200 mg testosterone at three weeks of age. Three animals were sacrificed at each of three withholding times: 15, 30 and 50 days. Two female calves served as controls. The concentrations of testosterone as determined by a RIA procedure are in Table III. (Roberts and Cameron, 1986)

Table III. Testosterone Mean Tissue Concentrations in Female Calves Treated with Implix BF (ng/kg)

	Tissue			
	Muscle	Liver	Kidney	Fat
Control	6 ± .3	108 ± 18	96 ± 53	22 ± 1
15 Day	360 ± 58	196 ± 104	588 ± 153	1027 ± 620
30 Day	245 ± 28	66 ± 7	564 ± 125	1258 ± 600
50 Day	225 ± 87	71 ± 22	515 ± 117	750 ± 157

Bulls, Heifers and Female Veal Calves

Free and conjugated testosterone were determined in the tissues of bulls and feedlot heifers by RIA. In addition, tissue levels for free and conjugated testosterone were determined in female veal calves implanted with 20 mg estradiol and 200 mg of testosterone. (Hoffman and Rattenberger, 1977)

Table IV. Testosterone Mean Tissue Concentrations of Untreated and Treated Cattle (ng/kg)

Type of Animal	Muscle	Liver	Kidney	Fat
Bull	535 ± 525	749 ± 405	2783 ± 2192	10,950 ± 8683
Heifer	92 ± 29	193 ± 101	595 ± 650	250 ± 64
Female veal calf	16 ± 13	39 ± 18	256 ± 110	178 ± 118
Female veal calf, untreated[1]	70 ± 43	47 ± 12	685 ± 54	340 ± 265

[1] Withholding period of 77 days.

APPRAISAL

Residues occur in the edible tissues of non-pregnant and pregnant heifers and female calves. Although not a component of implants that are used in bulls, endogenous levels of testosterone have been determined in the tissues of bulls.

Thirty days after implantation of testosterone and estradiol-17β in non-pregnant heifers, mean levels of testosterone in fat had increased from 26 to 340 ng/kg, in muscle from 20 to 100 ng/kg, in liver from 13 to 34 ng/kg, and in kidney from 190 to 450 ng/kg. These levels then progressively decreased to reach levels expected for the endogenous hormone only at 130 days. The maximum levels of testosterone in all tissues of treated heifers are less than the levels found in untreated pregnant heifers. In kidney, this difference is of the order of 3 to 8-fold depending on the length of pregnancy. Similar differences are seen in the kidney of treated heifers and untreated bulls; however, the difference in the fat of treated heifers and untreated bulls is approximately 30-fold.

Testosterone is normally produced in all mammalian species. When heifers are treated in accordance with good animal husbandry practice, the levels of residues in edible tissues about twofold, but these levels are extremely low when compared with the amounts of testosterone normally produced by human beings. The daily production rate of testosterone in human beings is given in Table V (Farber and Arcos, 1983). Even in prepubertal girls, the amount of endogenous testosterone produced daily is almost a thousand times the amount of testosterone that would be ingested in a 500 g portion of meat derived from a treated animal (40 ng).

Table V. Testosterone Production Rate in Humans

Women	mg/day
Non-pregnant	0.24
Late pregnant	0.32
Postmenopausal	0.14
Prepubertal girls	0.032
Men	
Adult	6.48
Prepubertal boys	0.065

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