AB68. Novel regulators of testosterone production

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In recent years, interest in testosterone replacement therapy for the management of male hypogonadism has grown significantly. This development has paralleled increased public awareness of the signs and symptoms of hypogonadism (also known as low T or low serum testosterone) and the opportunity to address this problem with therapeutic interventions. Conventionally, medical treatment of hypogonadism has been met with various formulations of exogenous testosterone therapies, albeit such therapies do carry limitations. Limitations range from challenges with therapeutic delivery to possible adverse effects. As understanding has grown with respect to regulatory mechanisms of testosterone production and possible new targets for endogenous production of testosterone, new avenues are opening for consideration of therapy particularly in males with primary hypogonadism (low intratesticular testosterone, high serum luteinizing hormone (LH) with low serum testosterone). Several novel molecular pathways have received interest recently as potential pharmacologic targets to increase Leydig cell testosterone production. These pathways and/or signaling molecules include phosphodiesterases, the cholesterol translocator protein, the electron transport chain of mitochondria, cyclooxygenases and osteocalcin. The advantages of these new targets are suggested to be: (I) maintain an intratesticular testosterone environment that allows/promotes normal spermatogenesis, (II) avoid side effects of exogenous testosterone supplementation, and (III) maintain the negative feedback mechanism of luteinizing hormone (LH) that prevents testosterone levels from becoming supratherapeutic. These novel options are perceived to offer a more targeted and efficacious approach than other suggested interventions to stimulate Leydig cell testosterone production in individuals with primary hypogonadism, such as exogenous LH, human chorionic gonadotropin, and clomiphene, which all act conventionally through the LH receptor. The proposed novel targets offer opportunities to promote increased endogenous testosterone production through the Leydig cell directly without reliance upon functional LH receptors. This approach may involve the application of small molecules, dietary supplements, or even currently available FDA-approved medications, that may exploit newly refined understanding of signaling pathways at the Leydig cell level. It will be of interest to study all of these potential therapeutic prospects further both with careful animal model experimentation and subsequently in human clinical trials.

Keywords: Testosterone; Novel regulators; luteinizing hormone (LH)

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AB69. Phyto-androgenic androgens in men’s health, sex and aging FX

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In recent years, interest in testosterone replacement therapy for the management of male hypogonadism has grown significantly. This development has paralleled increased public awareness of the signs and symptoms of hypogonadism (also known as low T or low serum testosterone) and the opportunity to address this problem with therapeutic interventions. Conventionally, medical treatment of hypogonadism has been met with various formulations of exogenous testosterone therapies, albeit such therapies do carry limitations. Limitations range from challenges with therapeutic delivery to possible adverse effects. As understanding has grown with respect to regulatory mechanisms of testosterone production and possible new targets for endogenous production of testosterone, new avenues are opening for consideration of therapy particularly in males with primary hypogonadism (low intratesticular testosterone, high serum luteinizing hormone (LH) with low serum testosterone). Several novel molecular pathways have received interest recently as potential pharmacologic targets to increase Leydig cell testosterone production. These pathways and/or signaling molecules include phosphodiesterases, the cholesterol translocator protein, the electron transport chain of mitochondria, cyclooxygenases and osteocalcin. The advantages of these new targets are suggested to be: (I) maintain an intratesticular testosterone environment that allows/promotes normal spermatogenesis, (II) avoid side effects of exogenous testosterone supplementation, and (III) maintain the negative feedback mechanism of luteinizing hormone (LH) that prevents testosterone levels from becoming supratherapeutic. These novel options are perceived to offer a more targeted and efficacious approach than other suggested interventions to stimulate Leydig cell testosterone production in individuals with primary hypogonadism, such as exogenous LH, human chorionic gonadotropin, and clomiphene, which all act conventionally through the LH receptor. The proposed novel targets offer opportunities to promote increased endogenous testosterone production through the Leydig cell directly without reliance upon functional LH receptors. This approach may involve the application of small molecules, dietary supplements, or even currently available FDA-approved medications, that may exploit newly refined understanding of signaling pathways at the Leydig cell level. It will be of interest to study all of these potential therapeutic prospects further both with careful animal model experimentation and subsequently in human clinical trials.

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Protodioscin is a Herbal Steroid Saponin extract derived mainly from Tribulus terrestris L. grown mainly in Bulgaria. This herbal plant begun well known in mainstream medicine since the periods around 1972 in Indonesia when this phytosteroid compound has been proven of having the ability to be converted to DHEA and further to another androgenic androgen (T) in hypogonadal men in the presence of 5-alpha-dehydrogenase (A. Adimoelja, 1976, 1978).

**Biogenic androgens and androgenic androgens**

Testosterone as a product of the male gonads from blood serum cholesterol. Cholesterol is further converted to DHEA. This product is identified as one of the biogenic or endogenic androgens (testosterone, pregnenolone, progesterone, aldosterone, androstendione).

Health disorders are often hampered by the tendencies of men or women to conceal their health (sexual health) conditions due to fear and/or embarrassments. If these conditions are not being soonest medically diagnosed and left to be untreated, another un-healthy condition may appear. (hypertension, high blood serum cholesterol, decrease HDL, CVD). Decrease libido, sex arousal and ED are the first expression of the down-degraded health conditions which may appear (A. Adimoelja 1985).

**Prescription of phytopharmaceuticals in mainstream medicine**

Surprisingly more phyto-pharmaceuticals in mainstream medicine were unconsciously prescribed by physicians (25% of prescriptions, WHO, 1908). Prescriptions were made to support health conditions and promote sexual health problems, most common as aphrodisiacs.

**Protodioscin and health enhancers**

Protodioscin indeed promote health condition in hypogonadic men (A. Adimoelja and Tjajho Djoko Tanojo, 2009). Regretfully most herbal products whih has been promoted as health foods in the market, or sex-tonics are combined with other chemical product(s), some of which combined with erectogenics (W. Pangkahila, 2010). Sharlip ID (USA) too reported in the “Newark Star Ledger in 2002” that 9 out of 10 randomly surveyed herbal extracts on sex performance enhancers did not contain the right compositions as stated in the manual brochures. The addition of illegal chemicals to herbal extracts and traditional herbs which has been proclaimed as sex tonics (erectogenics) or other health conditions (analgetics, cortisone) found in the market.

**Keywords:** Phyto-androgenic androgens; mainstream medicine; health enhancers

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**AB70. Controversies in male hypogonadism**

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**Abstract:** Over the past 5 years the testosterone supplementation therapy (TST) market has grown rapidly. Testosterone is now the second fastest growing medication in the United States. From 2005 to 2009 spending on testosterone jumped 115.5%, and the number of prescriptions filled increased 64.5%. There are many reasons for the rapid growth of the TST market. We have an aging population with the number of U.S. men 65 and older increasing 2-3 times faster than the number of men younger than 65. Furthermore, recent data demonstrate an increased association between poor general health, and possibly mortality, and low serum testosterone levels. There is now less concern for the development of prostate cancer after TST, making it a more attractive treatment option. Finally, new drugs entering the TST market with increased promotion, marketing, and direct-to-consumer advertising, are also driving market growth.

Over the past several decades there have been many controversies surrounding the usage of testosterone. These include concerns that testosterone may lead to prostate cancer, infertility, cardiovascular disease, and benign prostatic hyperplasia. Our understanding of the true relationship of testosterone to these conditions has rapidly expanded over this past decade. This paradigm change has also contributed to the explosive growth of the testosterone market worldwide.

**Keywords:** Controversies; male hypogonadism; testosterone