

FSLYM 192050 A Novel Drug in Reproductive Medicine (Pharmacokinetics and Pharmacodynamics studies)Ali Farid Mohamed Ali¹, Lila Farid², Sana Elshayb³ and Mohamed Ali Farid²¹Heliopolis research center²Faculty of Medicine Ain Shams University³Veterinary faculty of Medicine Kafr El Sheikh University, Egyptelshayb1950@yahoo.com

Abstract: In this review we introduced for the first time in literature a new drug which is prepared in the laboratory using multiple biochemical reactions include. Cell culture and cytotoxicity assay, DNA fragmentation for detection of cell apoptosis flow cytometry, stable free radical scavenging capacity cell culture, RT-PCR, Zymography, fluorometric assay, cell invasion and motility assay, NHR spectral evidence. HPLC analysis and LC/EST – MS Method. This review include all the details of this new drug: Pharmacodynamics, Pharmacokinetics studies, drug interaction, contraindication, cost, and dosage.

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Keyword: FSLYM 192050, Zymography, apoptosis, DNA fragmentation, HPLC analysis

1. Introduction:

FSLYM 192050, Patent No 698/2014, A New Substance prepared in the laboratory using multiple biochemical reactions include: cell culture and cytotoxicity assay, DNA fragmentation for detection

of cell apoptosis flow cytometry, stable free radical scavenging capacity cell culture, RT-PCR, Zymography, fluorometric assay, cell invasion and motility assay, NHR spectral evidence, HPLC analysis and LC/ESI – MS. Method. ^{(1),(2)}

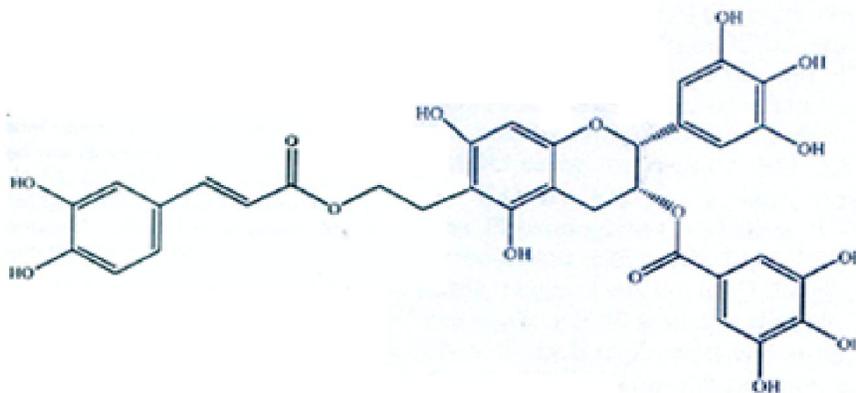


Figure 1. Chemical structure of FSLYM 192050

Pharmacokinetic properties:**Absorption and distribution:**

Fully absorbed after oral administration, Oral bioavailability being 95%, Absorption is rapid, Compared with the fasting state a high fat meal did not markedly alter the bioavailability of oral dose, 95% bound to albumin in plasma apparent volume of distribution is 45L.

Metabolism and elimination:

Fully metabolized by hydroxylation, Cytochrome P450 (CYP) 3 A4 is the major enzyme involved in metabolism, Metabolites are rapidly

cleaved from the plasma, Terminal elimination half life of single or multiple dose is 10 hours, Metabolic clearance rate from serum is 64 ml/min, The main route of excretion is urine, Bulk of metabolites elimination is the first 24 hours, Half life of excretion of urinary metabolites is 14 hours, 63% → eliminated in urine, 23% → in feces.

Drug interaction:

Not excreted in milk, No drug interaction, No effect with renal or hepatic impairment.

Contraindication:

No contraindication

Cost:

Excellent cost benefit ratio.

DOSE:

45 mg/kg/over 8 weeks.

Pharmacodynamic properties:

Moderate affinity for human progesterone receptors (invitro), Highly selective for progesterone receptor, Antagonistic activity on androgen receptor, Neither agonist nor antagonist activity on glucocorticoid or mineralocorticoid receptors, Does not activate estrogen receptors (α , β)

In vivo:

Strong progestational effect, Moderate antigonadotrophic effects, No androgenic, glucocorticoid, mineralocorticoid activity, inhibit rises in serum estradiol by inhibiting the development of ovarian follicles, it is moderately suppresses serum estradiol levels and affection of endometrial wave⁽³⁾, Dose dependent activity, Inhibit protein kinase activity⁽⁴⁾, Suppressing cyclin digene expression⁽⁵⁾, Normalize natural killer cell activity⁽⁶⁾, No effect on bone mineral activity, after 6 months: no effect on liver, lipid, carbohydrate metabolism⁽⁷⁾, Delay in oocyte aging in mice⁽⁷⁾, It inhibit interleukin 33 this inter leukin had a myolysis effect also, CD 147 which had Apoptosis⁽⁸⁾, It attenuates nuclear factor KB activation, cyclooxygenase 2 expression and prostaglandin E2⁽⁹⁾, Micro RNA expression and their relation to angiogenic factors miRNAs (miR-156, -16, -17 -5p, -209, 21, 125a 221, 222, vascular endothelial growth factor A thrombospondin I, miR-17-92-miR-17-5P) moreover reduced microvascular density⁽¹⁰⁾, Trapping of reactive diacarbonyl compound (methyl glyoxol MGO, glyoxal (GO) which causes production of advanced glycation end products (AGEs)⁽¹¹⁾, Inhibition of macrophage migration inhibitory factor (MIF)⁽¹¹⁾, Acton ephrin A, B system⁽¹²⁾, Stimulation of histone deacetylase inhibitors⁽¹³⁾, It inhibit hypoxia mediated activation of Erk/2 and Akt resulting in decrease expression of hypoxia inducible factor -1a⁽¹⁴⁾, Reduce the activity of matrix metalloproteinase 2, 9.⁽¹⁵⁾, Affection of mitochondrial biomarkers by using surface enhanced laser desorption / ionization time of light mass spectrometry⁽¹⁶⁾, Affection of iron storage in peritoneal macrophages it is known that iron storage is increased in the peritoneal macrophages in patients with endometriosis and correlates with iron over load in peritoneal fluid and serum⁽¹⁷⁾, Correction of mitochondrial displacement D-loop, it is known that there is association of mitochondrial displacement D-loop alteration and endometriosis⁽¹⁷⁾, Increasing expression of glyoxalase 1-reduces ROS production and increases life span⁽¹⁸⁾, Reduced advanced glycation end products⁽¹⁹⁾, Reduction of methyl glyoxal which has injurious effects on maturation of

oocytes fertilization, fetal development via apoptosis⁽¹⁹⁾, Anticancer cell metastasis by down regulation of matrix metalloproteinase expression⁽²⁰⁾, Antitumor, antioxidant antibacterial, antiviral, antifungal and anti-inflammatory activities⁽²⁰⁾, Affection of telomerase and telomere length⁽²¹⁾, Stimulation of pigment epithelium derijved factor (PEDF) which is a 50 kDa secreted glycoprotein that possesses a potent antiangiogenic activity⁽²²⁾, Induce apoptosis and G0/G1 cell cycle arrest⁽²³⁾, It is considered as apoptosis inducing agent⁽²²⁾, suppressing antiapoptotic proteins⁽²⁴⁾, It has antithrombotic, antihuman immunodeficiency virus activities⁽²⁴⁾, Suppression of the polo like kinase/activity⁽²⁴⁾, Suppression of mitochondrial tumour necrosis factor receptor associated protein expression⁽²⁴⁾, Activation of MAP kinases⁽²⁴⁾, Inhibits certain enzyme activities such lipoxigenases cyclooxygenase, glutathione S transferase, xanthine oxidase⁽²⁴⁾.

Supposed Therapeutic Indications:

Endometriosis, Fibroid, PCO, Failed IVF, Premature ovarian failure, Improve endometrial receptivity, Poor ovarian response, improved endometrial thickness, It can be used in the field of medicine and surgery industrial, agriculture and nano technology.

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