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PTU Induction Provide Quick Screening of Hypo and Hyperlipidemia

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Lipids are the small hydrophobic molecules; found in every kind of living organisms and can be categorized as fatty acyls, glycerolipids, glycerophospholipids, gphingolipids, steroids, prenol lipids, saccharolipids and polyketides (Fahy *et al*., 2009). They are the important source of energy and are the part of various cellular membranes. Any disturbance in body's lipid profile, especially production of oxidized lipids can cause disease and disturb the platelet related immune system (Podrez *et al*., 2007). As higher level of lipids, called hyperlipidemia, can increases the risk factors of diseases e.g., myocardial infarction and ischemic heart disease (Nordestgaard *et al*., 2007). It can also cause mortality; in Denmark from 1976-2004, 7818 peoples died due to increased levels of non-fasting cholesterol. Moreover, due to these higher cholesterol levels 1793 become myocardial infarction and 3479 peoples become ischemic heart disease patients. To lower the hyperlipidemia high dosed statin therapy is frequently used, but it can cause muscle disease and limits the activities of patient (Bruckert *et al*., 2005). Its muscle disease onset time due to high dosage was one month in 832 (10.5% of total studied patients) hyperlipidemia patients, thus there is need of more reliable drugs. The efficiency or possible side effects of drugs can be valuably recognized through *in vivo* studies (Doijad *et al*., 2008). But human *in vivo* drug studies are tough and sometimes failed to properly estimate the drug efficiencies because of individual's varying metabolic characteristics (Rostami-Hodjegan and Tucker, 2007). That's why *in vivo* studies, before human trials are performed in small animals (rats). But drug production is often limited by the huge time requirements of animal *in vivo* trials. Because the hyperlipidemic affects producing techniques in rats takes too long time, 2 weeks to 2 months (Bashandy, 2007; Zhu *et al*., 2008). Consequently it delays the drug manufacturing and availability in market; therefore there should be a way to produce the required disease effects quickly in experimental models. This may positively regulate the drug investigation in laboratory trials.

Propylthiouracil (PTU) is well known for its hypothyroidism effects and used as drug to maintain the thyroid hormone production for more than 50 years (Cooper and Rivkees, 2009). It can increase the body lipids when used in combination with bile salts, thus in certain situations it can enhance the lipid levels (Zhang *et al*., 2007). Recently Hasimun *et al*. (2011) recommended PTU as an efficient hyperlipidemic agent to fasten the estimation of drug's efficiency. They orally administrated the rats with 10 mg kg^{-1} b.wt. PTU daily for seven days and add 0.01% PTU in rat's drinking water. They compared these animals with non-PTU adminsitrated and orally induced PTU rat groups. All these rat groups were fed with high cholesterol food 1 h before the examination. A significant difference in these animals was observed, which was due to increased levels of total serum cholesterol. Highest elevation of cholesterol levels occurred in PTU treated animals (Oral + PTU water induction). Its hyperlipidemic property was observable through the increased levels of cholesterol in serum and liver, while its induction caused a decrease in cholesterol secretion through feces. Moreover, a high dose of cholesterol (400 mg kg^{-1} b.wt.) without PTU induction was ineffective in producing hyperlipidemia even after 6 hours of its application. Thus PTU was efficient in rapidly producing hyperlipidemia and showed a significant increase in cholesterol levels after the 2 h of induction. These PTU hyperlipidemic effects were helpful in quick examining of hypolipidemic drugs. As the application of simvastatin and ezetimibe (hypolipidemic drugs) in different PTU hyperlipidemic animals reduced the increased levels of serum cholesterol and maintained them below 100 mg dL^{-1}. Furthermore, these drugs caused a significant reduction in liver cholesterol and increased its secretion through feces, which was observable within 2 h of assessment. According to PTU technique most appreciable hypolipidemic activity was of simvastatin (5 mg kg^{-1} b.wt.), it significantly decreased the liver cholesterol and increased its excretion. On the other hand ezetimibe application was more effective in lowering the serum cholesterol levels. Thus PTU oral and watering application provided excellent results for rapid examination of hypolipidemic and hyperlipidemic effects. As cholesterol food caused hyperlipidemia, was observable shortly after 2 h of its application in PTU treated animals. Whereas its application in non-PTU treated animals required long time to induce

hyperlipidemic. Likewise the hypolipidemic effects of any substitution were also observable in PTU treated animals, which can be determined within 2 h, after drug application.

Hyperlipidemia is a condition of increased cholesterol (lipid) levels in body, which leads towards heart diseases and its related complications. It can be treated through hypolipidemic drugs, but large time requirements of laboratory experiments hindered their rapid production. As the preparations of specific metabolic diseased condition in animals is time consuming procedure. According to Hasimun *et al*. (2011) conducted research PTU application in rat's diet and water could reduce these time expenditures. As PTU application made these animals hyperlipidemic shortly after the application of cholesterol food. It helped in the rapid examination of drugs and estimated the drug efficiency within 2 h. Thus PTU provides a novel approach by constraining the time requirements of hyperlipidemic experimental models and hastens the drug inspection. Its use in experimental trials will helps to positively accelerate the investigation of drugs hypolipidemic property.

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