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The Effect of Fenofibrate Treatment on Lipid Profile

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ABSTRACT

Fenofibrate chemically known as 2-[4-(4-chlorobezoyl) phenoxy]-2-methylpropionic acid 1-methylethyl ester, its formula $C_{20}H_{21}ClO_4$, fenofibrate is a lipophilic antihyperlipoproteinemic agent. It is a nonelectrolyte with low aqueous solubility (<3 mg/mL) and fairly high octanol/ water partition coefficient (log P 4.6). Fenofibrate is a drug of the fibrate class. It is mainly used to reduce cholesterol levels in patients at risk of cardiovascular disease. The function of fenofibrate is to reduce the production of total cholesterol, Low-Density Lipoprotein (LDL), apolipoprotein B, total triglycerides and triglyceride rich Very-Low-Density Lipoprotein (VLDL) in treated patients. Furthermore, treatment with fenofibrate results in increase in High Density Lipoprotein (HDL) and apoproteins apoAI. Fenofibrate as generic products has been very available recently to fulfill the demand of the global healthcare market.

1. Introduction

Fenofibrate chemically known as 2-[4-(4-chlorobezoyl) phenoxy]-2-methylpropionic acid 1-methylethyl ester, its formula $C_{20}H_{21}ClO_4$, fenofibrate is a lipophilic antihyperlipoproteinemic agent [1]. It is a nonelectrolyte with low aqueous solubility (<3 mg/mL) and fairly high octanol/ water partition coefficient (log P 4.6). Fenofibrate is a drug of the fibrate class. It is mainly used to reduce cholesterol levels in patients at risk of cardiovascular disease [2]. The function of fenofibrate is to reduce the production of total cholesterol, Low-Density Lipoprotein (LDL), apolipoprotein B, total triglycerides and triglyceride rich Very-Low-Density Lipoprotein (VLDL) in treated patients. Furthermore, treatment with fenofibrate results in increase in High Density Lipoprotein (HDL) [3] and apoproteins apoAI [4]. Fenofibrate as generic products has been very available recently to fulfill the demand of the global healthcare market.

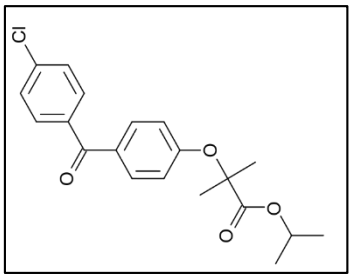
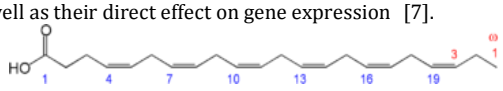


Fig. 1 The structure of fenofibrate

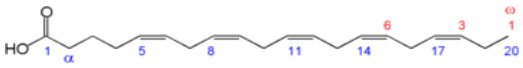
Fenofibrate is mainly used for primary hypercholesterolemia or mixed dyslipidemia. Fenofibrate appears to decrease the risk of cardiovascular disease and possibly diabetic retinopathy in those with diabetes mellitus [5].

It is used in addition to diet for treatment of adults with severe hypertriglyceridemia. Improving glycemic control in diabetics showing fasting chylomicronemia will usually decrease the need for pharmacologic intervention.

Omega bio-marine (concentrated fish oil softgel capsules, preparation in the form of free fatty acids with a maximised content of EPA and DHA) [6], omega-3 fatty acids are a family of naturally occurring polyunsaturated fatty acids (PUFAs). Humans do not have the essential metabolic pathways to synthesis the precursor fatty acids (α-linolenic acid), which is vital for the production of the longer bioactive ω-3 Fatty Acids. Consequently, the long-chain poly unsaturate fatty acids must be gained from either plant sources or by direct intake of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) from marine or industrial products [7]. EPA and DHA are mostly found in seafood, but fish do not actually produce these fatty acids [8]. The benefit of the high ω-3 fatty acid intake is attributed to their capacity to modulate cellular metabolic functions and gene expression [9]. These actions include the alteration of inflammatory processes in which eicosanoid participate, alterations of cellular membrane structure and functions induced by the incorporation of ω-3 Fatty Acids into membrane phospholipids, modulation of various signalling pathways involved in normal and pathological cell functions, as well as their direct effect on gene expression [7].



DHA
Docosahexaenoic acid



EPA
Eicosapentaenoic acid

2. Experimental Methods

The study designed to investigate the effect of fenofibrate and omega 3 (30% EPA and 20% DHA) on the levels of lipid profile so the subject used fenofibrate (200 mg) supplied by Recipharm Fontaine, France and omega 3 (1000 mg) supplied by Pharma Nord, Canada. The lipid profile measurement done with Reflotron plus EN device from German with Reflotron strip. The samples collected before taken the fenofibrate and omega 3 and after 20, 44, 55 and 72 days the measurements done and the results showed in the Figs. 2 - 7.

3. Results and Discussion

The results reveal the effect of finofibrate treatment with combination of omega 3 supplyment, as shown in the figures, there is clear decrease in the level of trigycerides, VLDL and atherogenic ratio while there is increase in the level of HDL. Fenofibrate is known to inhibit hepatic VLDL

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synthesis and secretion, and to promote the lipolysis of trigycerides-rich lipoproteins through stimulation of lipoprotein lipase activity, by activation of peroxisome proliferator-activated receptor alpha (PPARα), PPARα activates lipoprotein lipase and reduces apoprotein CIII, which increases lipolysis and elimination of triglyceride-rich particles from plasma. PPARα also increases apoproteins AI and AII, reduces very low-density lipoprotein (VLDL) and low-density lipoprotein (LDL) containing apoprotein B, and increases high-density lipoprotein (HDL) containing apoprotein AI and AII.

In addition, by reducing the synthesis and increasing the catabolism of VLDL, fenofibrate increases LDL clearance and reduces small and dense LDL, which are associated with coronary heart disease [10] and to promote catabolism of LDL particles via the LDL receptor–mediated pathway. Evidence suggests that fibrates increase excretion of hepatic cholesterol in bile and that endogenous hepatic cholesterol synthesis may be decreased [11].

A major feature of hypolipidemic action involves modulation of the de novo synthesis, intravascular remodeling, and cellular degradation of plasma lipoproteins. More specifically, fenofibrate not only reduces absolute circulating concentrations of VLDL but also induces a reduction in the size of VLDL particles of hepatic origin; as a consequence of the intravascular remodeling of such VLDLs, receptor-active LDLs are formed, thereby resulting in an increase in the proportion of plasma LDLs that are catabolized by the nonatherogenic LDL receptor pathway. These latter effects have been demonstrated in vivo both in hypertriglyceridemic and hypercholesterolemic patients. It must be emphasized, however, that the precise mechanisms that underlie the fenofibrate-mediated enhanced formation of LDL receptor–active LDL subspecies are as yet undetermined, although some evidence for drug-induced changes in LDL chemical composition and particle size has been provided [12].

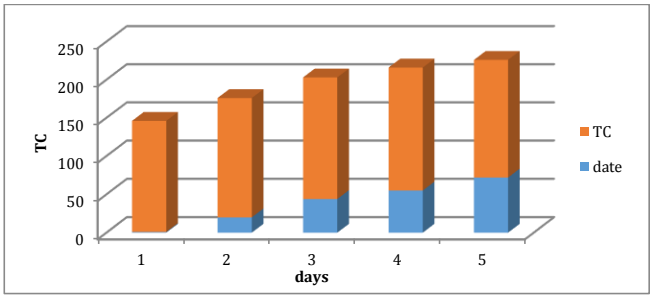

Fig. 2 The change in the level of total cholesterol with time

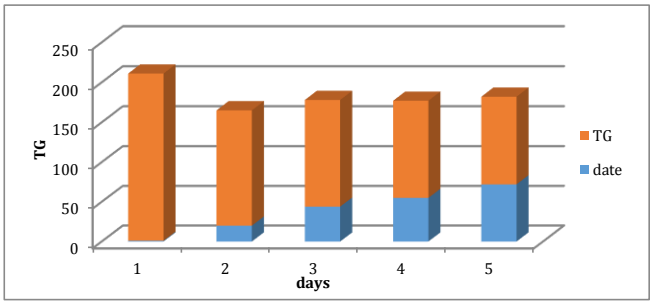

Fig. 3 The change in the level of trigycerides with time

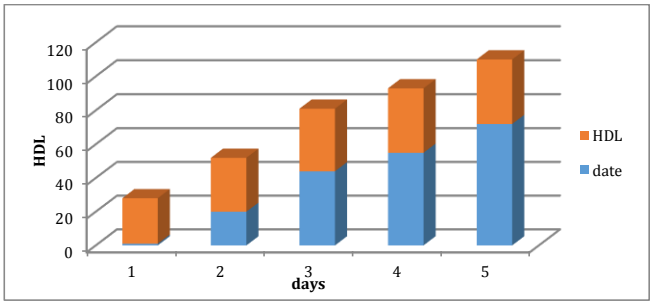

Fig. 4 The change in the level of HDL with time

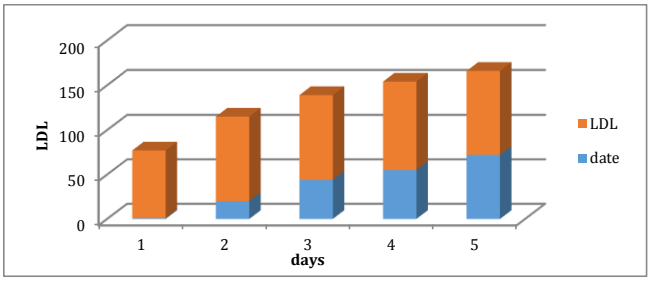

Fig. 5 The change in the level of LDL with time

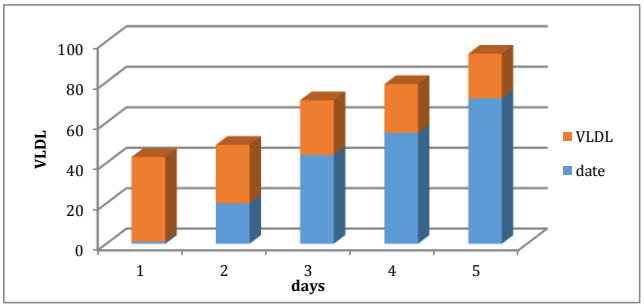

Fig. 6 The change in the level of VLDL with time

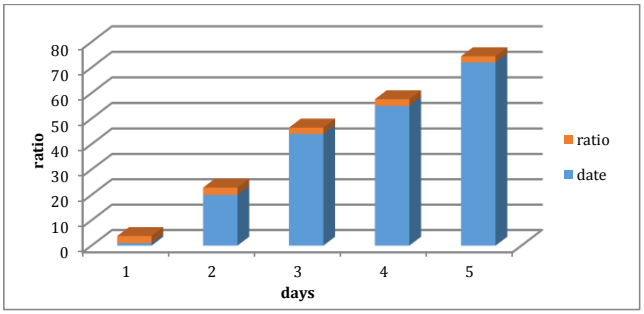

Fig. 7 The change in Atherogenic ratio with time

This study designed to investigate the effect of omega 3 on lipids profile, the study revealed in Figs. 2 - 7 that there were positive effect of omega 3 on triglcerids by reduce triglycerids level.

High triglyceride (TG) levels have been recognised as an independent risk factor for coronary heart disease (CHD), while severe hypertriglyceridaemia) fasting TGs ≥500 mg/dL) significantly increases the risk of acute pancreatitis, a potentially deadly complication [13]. Moreover, a key feature of the dyslipidaemia associated with the metabolic syndrome as well as diabetes is elevated TG levels. Fish oil can have a favorable role in the treatment of noticeable hypertriglyceridaemia [14]. According to the American Heart Association, omega-3 fatty acids benefit the heart of healthy people, and those at high risk of-or who have-cardiovascular disease. Research has shown that omega-3 fatty acids decrease risk of arrhythmias, which can lead to sudden death. Omega-3 fatty acids as well decrease triglyceride levels as shown in this study in Figs. 2 – 7, also omega 3 fatty acids can slow the growth rate of the atherosclerotic plaque, and produce modest reductions in blood pressure. The omega-3 fatty acids in fish oil seem to be able to expand blood vessels, and this brings blood pressure down.

DHA is far more abundant than EPA in the myocardium. DHA alone or in combination with EPA may be more important for protection against dysrhythmias and cardiovascular disease than EPA alone [15]. Omega 3 fatty acids act on triglycerids metabolism primarily include the suppression of hepatic very low density lipoprrptein synthesis and discharge [6].

Additionally, the conversions of very low density lipoprrptein (VLDL) to intermediate-density lipoprotein (IDL), VLDL to LDL, and IDL to low density lipoprrptein (LDL) are significantly increased; this may partly explain the increase in LDL-C levels observed in ω -3 FA-treated patients [8]. On the other hand, ω-3 FAs do not significantly change the fractional catabolic rates of apolipoprotein (apo B) in VLDL, IDL, or LDL or change the catabolism of the chylomicron remnants. Consequently ω-3 Fatty Acids effectively decrease the plasma concentration of Triglycerids, mainly by reducing VLDL production but not by altering the catabolism of apo B-containing lipoprotein or chylomicron remnants [16].

4. Conclusion

Finofibarte treatment can lead to clinically decrease in the atherogenic ratio value and triglycerids level and increase in the level of HDL so that finofibarte consider as cardioprotctive drugs.

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