It is well established that hyperlipidemia is commonly associated with an increased risk for the development of atherosclerosis and consequently cardiovascular diseases, as well as, of type-2 diabetes. In addition, many agents having cyclic imides functions were reported to possess hypolipidemic action superior in many cases to the lipid-modifying drug Clofibrate (I) which is the first generation of Fibrate drugs. These imides; phthalimide (a), 1,8-naphthalimide (b),and diphenimide (c); were generally potent hypolipidemic agents; lowering serum cholesterol levels on an average of 35% and serum triglyceride levels on an average of 29% after 16 days dosing at 20 mg/kg/day intrapretonially in mice. Therefore, certain new nitrogen substituted derivatives of these cyclic imides were synthesized, aiming to obtain potent hypolipidemic agents of high therapeutic index and minimal side effects in comparison with the widely used and commercially available Fibrate drugs. Thus, 2-(N-imido)propionic acids, 2-(N-phthalimido)-2-methylpropionic acid, and their ethyl esters were synthesized (Target derivative A). In addition, N-substituted-2-(N-imido)propionamides, and 2-(N-phthalimido)-2-methylpropionamides; (Target derivative B) were prepared. The structures of the new compounds were confirmed by microanalyses and $^1$HNMR spectroscopy. Some of them were subjected to 3D studies and were found to be superimposed on compound (I). The preliminary evaluation of hypolipidemic activity of the newly prepared compounds against triton WR-1339 induced hyperlipidemia in rat showed that several derivatives have demonstrated significant lowering of serum total cholesterol and triglyceride levels at dose of 150mg/kg/ i.p.comparing to Feno fibrate which is one of the second generation of Fibrate drugs.
Cloribrate (I)  

Target Derivatives (A)  

Target Derivatives (B)  

R¹, R² = H, CH₃  
R³ = C₂H₅, n-C₃H₇, CH(CH₃)₂,  
C₆H₅, C₆H₅-CH₂, C₆H₅-(CH₂)₂,