1. INTRODUCTION

More than 40 percent of the drug coming from high-throughput screening are poorly soluble in water (Lipinski 2002) Compounds with poor solubility are increasingly posing challenges in the development of new drugs, since a large number of drugs coming directly from synthesis or from high throughput screening have a very poor solubility (Ohara et al 2005). It is well known that drug efficacy can be severely limited by poor aqueous solubility, leading to low dissolution rate and thus results in low absorption in the gastrointestinal tract after oral administration hence comprising oral bioavailability. The ability to increase aqueous solubility is thus a valuable aid to increase the efficacy for certain drugs (Yalkowsky S 1981).

The Biopharmaceutical Classification System divides drugs into four classes depending on in vitro and in vivo permeability data. (Amidon G.L. 1995) Four classes of compound can be distinguished: I (high solubility, high permeability), II (low solubility, high permeability), III (high solubility, low permeability) and IV (low solubility and low permeability). Class I compounds are typical examples for waiving bioequivalence studies. In the selection process, new chemical compound with low aqueous solubility and low permeability are preferably filtered out since they might pose problems during pharmaceutical development. For class II drugs dissolution/solubility and for Class III drug permeability limits the oral drug absorption.

It is obvious that class II drugs the low ability to dissolve is a more important limitation to their overall rate and extent of absorption than their ability to permeate through the intestinal epithelia. There are several pharmaceutical strategies available to improve the aqueous solubility of poorly soluble drugs solid dispersion, solubilization using surfactant, the use of co-solvent, reduction of particle size, hydrotropy and the use of aqueous soluble derivatives or salts.
Among all technique solid dispersion (SD), is the most efficient technique from the dispersion in carrier more specially (Chiou WL 1971) define the system has the dispersion of the one or more active ingredient in an inert matrix at solid state perform by melting method, solvent evaporation method and melting solvent. (Craig DQ 2002) Since long, many investigators have studied SDs of poorly water-soluble drugs with various pharmacologically inert carriers to increase the dissolution and oral absorption of poorly water–soluble drugs, however, only a few system are useful commercially. (Ghebremeskel AN et al 2007; Yung-Kuang L et al 2007)

Poloxamer have been recently widely used as wetting and solubilizing agents as well as surface adsorption excipients. They have been employed to enhance the solubility, dissolution and bioavailability of many hydrophobic drugs using various techniques, for some drugs, the improvement in solubility using poloxamer was higher compared to the other meltable polymers such as PEGs and complex forming agents such as cyclodextrins. (Chen Y et al 2004) In the present study, poloxamer was thus empirically selected as a hydrophilic carrier for its excellent surfactant properties and oral safety.

The main possibilities for improving dissolution according to analysis are to increase the surface area available for dissolution rate by decreasing the particle size of the solid compound and or by optimizing the wetting characteristics of the compound surface, to decrease the boundary layer thickness ,to ensure sink condition for dissolution and last but definitely not least ,to improve the apparent solubility of drug under physiologically relevant condition.(Noyes AA et al 1897; Leuner C et al 2000) . As solubility and permeability is the deciding factor for the in-vivo absorption of the drug ,these can altered or modified by enhancement technique like the novel approach for particle size reduction on basis of crystallization by using ultrasound is sonocrystallization this utilizes ultrasound power characterized by a frequency range of 20-100KHz for inducing crystallization its not only enhances the nucleation rate but also an effective means of size reduction and controlling size distribution of the active pharmaceutical ingredients (API).(US patent 20020031577)

Most application used ultrasound in the range 20-5MHz. There are reports on application of ultrasonic (US) energy during crystallization i.e. sonocrystallization. US
energy has been used to achieve nucleation at moderate super saturation during crystallization process or terminal treatment to achieve deagglomeration and to obtain crystal habit. (Fini A et al 1997)

Melt sono crystallization (MSC) is particle engineering technique are developing to modify the physicochemical and biopharmaceutical properties of drug, for above mentioned both techniques BCS Class II drugs are selected because low solubility and high permeability like antidiabetic drugs. Antidiabetic drugs to be absorbed must be present in the form of an aqueous solution at the site of absorption for their hypoglycemic activity so solubility enhancement techniques are more essential for drugs like Pioglitazone, (+)-5-[P-(2-(5-Ethyl-2 Pyridyl) ethoxy ]benzyl 1]-2-4thiazolinedione monohydrochloride, is thiazolidinedione antidiabetic agent that depends on the presence of insulin for its mechanism of action decreases insulin resistance in the periphery and in the liver resulting in increased insulin dependent glucose disposal and decreased hepatic glucose output , unlike sulphonyl urea .Pioglitazone is highly selective agonist for peroxisome proliferators activated receptor –gamma (PPARγ). (Pioglitazone monographs Mosby’s Drug consult 2005) for this reason Pioglitazone is an oral antidiabetic agent that acts primarily by decreasing insulin resistance. and Rosiglitazone-(RS)-5-[4-(2 [methyl (pyridine-2-yl)amino]ethoxy benzyl]thiozolidione-2-4-dione is oral hypoglycemic agent in the thiazolidinedione class of drug. It works as an insulin sensitizer, by binding to the PPAR receptor in fat cell and making the cells more responsive to insulin. (Ajjan RA et al 2008)

however, the drawback of this potentially useful hypoglycemic agent is that it is highly hydrophobic and practically insoluble in water. (Chawdhary KPR, Vijayasrinivas S.et al 2004)

The present research work thus deals with the techniques of enhancement of solubility as well as dissolution and bioavailability of poorly aqueous soluble drugs like pioglitazone and rosiglitazone.