REVIEW OF LITERATURE:

1. **Piyush M. P et al 2012**\(^{17}\) studied the *in vitro* hepatoprotective activity of different herbal drugs was evaluated using isolated rat hepatocytes. The liver function tests like serum glutamate pyruvate transaminase (SGPT), serum glutamate oxaloacetate transaminase (SGOT), serum alkaline phosphatase (SAKP), serum bilirubin (SB) were assayed according to standard method.

2. **Jingling tang et al 2011**\(^{18}\) Evaluate to improvise the oral biodisponibility of genistein due to their poor solubility in aqueous medium. Genistein nanoparticle was prepared by nanoprecipitation method using the unique carrier (Eudragit) and got significant particle size was about 120nm when diluted with 100 times of distilled water, he observed the drug loaded nanoparticles were spherical in shape and got significant encapsulation efficiency and drug entrapping of genistein loaded nanoparticles were 50.61% and 5.02% respectively and Invitro releasing pattern was two time greater than the conventional product. In addition to that he studied relative bioavailability of genistein from the nanoparticles compared with the standard suspension was 241.8%.

3. **Lovely Thakur et al (2011)**\(^{19}\) Reported that Natural medicines are constantly gaining attention as the therapy for many of the degenerative ailments in the modern era. Thus, it becomes the prime responsibility of the herbal drug manufacturer to provide adequate stability for long-term storage and safety for consumption by the patients. As the phytoformulation is a mixture of more than one active ingredient, care should be taken to the determination of the stability profile for natural medicines. A stable formulation will gain confidence in the modern patient compliance.

4. **Yadav D et al 2011**\(^{20}\) Developed a nanomicellar system, nanotubes, and colloidal nanogels for curcumin to be used alone as well as in combination with other chemotherapeutic agents like paclitaxel. *Cuscuta chinensis* is a commonly
used traditional Chinese medicine to nourish the liver and kidney. Due to the poor water solubility of its major constituents such as flavonoids and lignans, its absorption upon oral administration could be limited. So, the nanoparticles for the same were developed.

5. **C.Moorthi et al 2012** Documented that curcumin-piperine, or curcumin-quercetin or curcumin–silibinin dual drug loaded nanoparticulate combinational therapy to target and treat the multi drug cancers.

6. **Magda et al 2011** assessed that the synergistic hepatoprotective effect of curcumin and a ginger against carbon tetrachloride induced liver damage in rat model. Liver enzymes oxidative status and histopathological studies shows that coadministration of curcumin and ginger extensively arrested the progression of Liver fibrosis. Elevated liver biomarkers like SGPT, SGOT and ALP levels Remarkably reduced. In addition that this combinational treatment shows Significant reduction of GSH, SOD, TNF-α and catalase.

7. **Asth Mehta et al 2012** Performed that piperine and quercetin enhance antioxidant and hepatoprotective effect of curcumin in Paracetamol induced oxidative stress in suitable animal model. In this study we found that piperine and Quercetin were combined with curcumin enhances oral bioavailability by inhibiting The metabolic enzymes. *Invitro* and *ex vivo* studies shown statistical significance of IC$_{50}$ result with 50% enhancement activity by combinatorial extract. In addition Serum level of ALT, AST and ALP were significantly reduced by 53%, 35% and Respectively after treatment with combinational extract (CPQ).

8. **Khalid H.Janbaz et al 2001** Investigated that protective effect of rutin on Paracetamol and CCL$_4$ – induced hepatotoxicity in rodent model. This study shows Significantly reduced the serum enzymes at the dose level of 20 mg/kg. Rutin also Prevented the CCL$_4$ induced prolongation in pentobarbital sleeping time conforming its hepatoprotection. Hence result indicate that rutin posses the hepatoprotective activity.

9. **Fawn S. Hogan et al 2007** Performed that Silibinin inhibits proliferation and promotes cell-cycle arrest of human colon cancer. Result shows that silibinin
significantly inhibits proliferation through cell-cycle arrest via inhibition of cyclinCDK promoter activity.

10. **Vidyavathi Maravaihala et al 2012** discussed the various techniques for the fabrication of nano drug delivery system (NDDS) like nanoparticles, nanocrystals, nanosuspension, and nanoemulsions by various techniques such as bottom-up (Microprecipitation, microemulsion and melt emulsification) top–down method (High pressure homogenization and milling method).

11. **Houli LI et al 2006** studied on the preparation of quercetin solid lipid nanoparticles and oral absorption in mice model. In this study nanoparticles prepared by emulsion evaporation at a high temperature and solidification method at a low temperature. Result shows QT-SLN morphology was sphere like and smooth in nature. Mean diameter was 217.3 nm entrapment efficiency was 48.50%. The mice oral absorption of QT-SLN was much better than the quercetin solution.

12. **Savita Bisht et al** formulated the polymeric nanoparticle of curcumin ameliorates CCl₄ induced hepatic injury model. Result was sustain intrahepatic curcumin levels that can be found in both hepatocytes and parenchymal cell. Curcumin nanoparticle significantly inhibits CCl₄ induced hepatic cell, synthesis of pro-inflammatory cytokines and fibrosis. NanoCure™ enhances antioxidant level in hepatic cell.

13. **Houli Li et al** performed the enhancement of GI absorption of quercetin by solid lipid nanoparticles. Result revealed that the QT-SLNs was spherical in shape under TEM, with average size about 155.3 nm. The average entrapment efficiency, drug loading and zeta potential were 91.1%, 13.2% and -32.2 mV respectively. In addition to that pharmacokinetic parameters like relative bioavailability of QT-SLNs as compare to quercetin suspension was 571.4%. The T_max and MRT for quercetin in plasma was delayed.

14. **Deepak Chitkara et al 2012** developed the quercetin nanofabrication and in vivo evaluation using STZ induced diabetic rat model. This formulation by emulsion–diffusion–evaporation method using a well known poly (lactic-co-
glycolic acid ) (PLGA). Result shows that particle size was 179.9 ±11.2 nm with 0.128 polydispersity Index and more than 86% drug entrapment efficiency, and zeta potential was -6.06 ±1.51mV. In addition to that the efficacy of quercetin nanoparticle shows a better in reduction of glucose level as compare with unloaded quercetin suspension.

15. Narendran Krishnakumar et al 31 done that enhanced anti cancer activity of Naringenin loaded nanoparticle in human cervical (HeLa) cancer cell. The study result reveled that *in vitro* drug release by UV showed there was sustained drug delivery pattern of Naringenin loaded nanoparticles. MTT-based colorimetric assay shown that higher cytotoxic efficacy of naringenin loaded nanoparticle than the free Naringenin in HeLa cells. Further NARNPs treatment significantly raised of intracellular ROS level (p<0.05) and decreased GSH level when compare to free naringenin. It has been noticeable that there was remarked alteration of mitochondrial potential.

16. Purusotam Basnet et al 2011 32 Reviewed mainly on the anti inflammatory potential of curcumin and recent development in dosage form and nanoparticulate system with possibilities of therapeutic application of curcumin for the prevention and/or treatment of cancer.

17. Tuğba gulsun et al 2009 33 Narrated that nanocrystal technology for oral delivery of poorly water soluble drugs . Report of this review said that how to improve the solubility of drug by making the nanocrystal and how to stable the prepared nanocrystal by adding the suitable stabilizer and different technique employed to fabricate nanocrystal formulation of powder like homogenization, co-precipitation spray drying and milling. There are numerous advantage of nanocrystal formulation such as enhance oral bioavailability, improved dose proportionality, reduced food interaction and suitable for all route of administration. In addition that Nanocrystal technology is cheap and easy to apply; thus, it appears that this technology will be substantially useful for the manufacture of poorly water-soluble drug products for oral delivery.
18. **Suvadra das et al 2011** 34 developed a nanoparticle that prevents paracetamol-induced hepatotoxicity. Study report shows the Smnps were prepared by nanoprecipitation in polyvinyl alcohol stabilizer and polymer is Eudragit RS 100. The process optimization provides entrapment efficacy was 67.39%, particle size was about 120.37nm. sm release from nanoformulation was considerably sustained in all the preparation. Thus Smnps were strongly protective against paracetamol induced liver cell. Smnps recorded none of the animal died even in high dose of Paracetamol. In addition to that it preventing progress of Paracetamol induced hepatic damage and Smnps significantly improve the glutathione regeneration to the level of 11.3 µmol/g in Hepato cell.

19. **Tzu-Hui Wu et al 2008** 35 prepared quercetin nanoparticles by nanoprecipitation method and their physicochemical characterization evaluated by various method like differential scanning calorimetry (DSC), X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FT-IR) and dissolution study. It was observed that particle size of < 85nm, polydispersity index was < 0.3 and encapsulation efficiency were <90%. Result of XRD and DSC of quercetin shows crystal of the drug it might converted in to amorphous state. FTIR demonstrated that QU formed a intermolecular hydrogen bounding with carrier. The *invitro* releasing study of QUEN ws 74-fold higher as compared with the pure drug. In addition the antioxidant study of QUEN was more effective than pure QU on DPPH scavenging, anti-superoxide formation, superoxide anion scavenging and anti lipid peroxidation.

20. **Teresita Guarudia et al 2001** 36 investigated the anti-inflammatory activities of three flavonoids (Rutin, Quercetin and hesperidin). Result shows that considerably inhibit the acute and chronic phases but rutin was more active in the chronic phase as compare others.

21. **Lei Gao et al 2012** 37 reviewed nanocrystal formulation: *Invivo* performances. The result was proved that drug nanocrystal could be used as a versatile formulation to alter and improve the pharmacokinetic, pharmacodynamic and molecular level targeting properties of poorly soluble drugs.
22. **Laid Selloum et al**\(^{38}\) Demonstrated that the anti-inflammatory effect of rutin on rat paw oedema model. This study result reviled that the maximal swelling in placebo group was observed at 5 hours, after carrageenan injection. Oral administration of rutin suppress the paw volume with in 2 hours. In addition to that rutin remarkably reduced (p<0.05) and dose dependant manner the polymorphonuclear neutrophils chemotaxis to fMet-Leu-Phe, was partially inhibited by rutin up to 25µM. This study revealed that rutin possesses anti-inflammatory properties.

23. **Moorthi Chidamram et al 2012**\(^{39}\) Demonstrated that application of Plackett-Burman Factorial design in the development of curcumin loaded Eudragit E 100 nanoparticle. Plackett-Burman design was implemented to influence of eight independent variable on three dependent variables. 12 experimental trails involving 8 independent variable at higher and lower levels were generated by design expert .out of 12 trail 4\(^{th}\) and 9\(^{th}\) trails were within the acceptable limits.

24. **C.Moorthi et al 2012**\(^{40}\) Designed a dual loaded polymeric nanosuspension: Incorporating analytical hierarchy process and data envelopment analysis in the selection of a suitable method. The study indicated that nanoprecipitation was identified as best method and same method applied to prepare the dual loaded polymeric nanosuspension containing curcumin and bio-enhancer. The obtained nanosuspension were average particle size was 116.4 nm with polydispersity index of 0.177 and zeta potential of 38.8mV.the study was concludes that the integration of analytical hierarchy process and data envelopment analysis has play a important role in selection a suitable method for the preparation of nanosuspension.

25. **Young –Soo Lee et al 2011**\(^{41}\) studied synergistic antibacterial effect between silibinin and antibiotics in oral pathogen.result shows MIC values ranging from 0.1to 3.2 and 0.2 to 6.4 µg/ml. MIC\(_{50}\) value was 0.025-0.8 µg/ml.

26. **Xiangrong Song et al 2008**\(^{42}\) Formulated a dual quercetin –vincristine(drug) loaded PLGA nanoparticles: Systemic study of particle size and drug entrapment efficiency. Result was submicron size (139.5±4.3nm) with low polydispersity
index $0.095 \pm 0.031$. Nanoparticles observed by TEM showed extremely spherical shape.

27. **Wu HT et al 2007**\(^{43}\) Carried out the physicochemical characterization of nanoparticles using different methods like transmission electron microscopy (TEM), differential scanning calorimetry (DSC), powder X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FT-IR) and dissolution study. Particle size determination, encapsulation efficiency, drug release and SEM studies have also been used for characterization of nanoparticles.

28. **Urmila J. Joshi et al**\(^{44}\) Studied the anti-inflammatory, antioxidant and anticancer activity of quercetin and its analogues. The study result indicated that the structural modifications result in significant reduction in the anti-inflammatory activity and antioxidant activity of these compounds. The anticancer activity of Quercetin–Cl is comparable to quercetin in HepG2 cell lines and to a lesser extent in the other cell lines.

29. **Jun He et al 2007**\(^{45}\) Prepared and studied the pharmacokinetics and body distribution of silymarin-loaded solid lipid nanoparticles after oral administration. The *in vitro* release experiment showed that a prolongation drug release can be achieved from the SM-SLNs produced by cold homogenization. Result of relative bioavailability of the cold SM-SLNs was 2.79-fold compare with plain SM suspension. In addition except for kidney, the AUC of cold SM-SLNs was higher in all test organ than that of the SM suspension including Liver. Hence it might used for the oral drug targeting system for SM to the liver.

30. **Dong Y et al 2013**\(^{46}\) developed a dual loaded novel bioadhesive drug delivery system, poly(d,l-lactide-co-glycolide)/montmorillonite. The results of this study were found to be of spherical shape with a mean size of around 310 nm and polydispersity of less than 0.150. Adding MMT component to the matrix material appears to have little influence on the particles size and the drug encapsulation efficiency. The drug release pattern was found biphasic with an initial burst followed by a slow, sustained release, which was not remarkably affected by the MMT component. Cellular uptake of the fluorescent coumarin 6-loaded PLGA/MMT nanoparticles showed that MMT enhanced the cellular
uptake efficiency of the pure PLGA nanoparticles by 57-177% for Caco-2 cells and 11-55% for HT-29 cells, which was dependent on the amount of MMT and the particle concentration in incubation. Such a novel formulation is expected to possess extended residence time in the gastrointestinal (GI) tract, which promotes oral delivery of paclitaxel.