LITERATURE REVIEW

1. Jyoti Wadhva et. al (2011) studied that taste is mainly a function of taste buds in the mouth. In the formulation for pediatric & geriatric, bed ridden & non-cooperative patients the main challenge to the compounding pharmacist is to mask the taste of obnoxious and bitter drugs, result is patient not receiving the optimal therapeutic value of their medication. Taste masking is the main factor in the development of the dosage form. It opens the doors for new inventions and patents. Many techniques have been developed which not only improve the taste of molecule but also the formulation and performance of the molecule. The main objective of present review is to explore different method, technologies and evaluations to mask the obnoxious taste of drugs, so that patients can use these drugs without hesitation of taste.

2. Gupta A. K. et. al (2010) studied that organoleptic properties are important considerations for development of a solid oral dosage form that can influence consumer preference and compliance. In the case of bitter drugs, taste is one of the most important parameter governing patient compliance1 and oral administration of bitter drugs with an acceptable degree of palatability is a key issue for health care providers especially for pediatric and geriatric2. Chewing large pieces of gum or tablet is difficult for elderly patient and sometimes experiences the bitter or unpleasant taste of drug if the taste masking coatings rupture during mastication. Bitter sensation is the result of signal transduction from the receptor organs containing very sensitive nerve endings, which produce and transmit electrical impulses3. Masking the bitter taste of drugs by either decreasing its oral solubility on ingestion or decreasing the amount of drug particles exposed to taste buds thereby reducing the perception of bitter taste.

3. Mohapatra A. et. al (2008) worked on dionvenience of administration and patient compliance are gaining significant importance in the design of dosage forms. Metformin hydrochloride is an orally administered antihyperglycemic agent, used in the management of non-insulin-dependant (type-2) diabetes mellitus. Difficulty in swallowing (dysphagia) is common among all age groups, especially in elderly and pediatrics. Unfortunately, a high percentage of patients suffering from type-2 diabetes are elderly people showing dysphagia. Persons suffering from dysphagia may get
choked when they consume liquid formulation, thus to alleviate such problem liquid formulation of high viscosity was prepared.

4. **Alka Lohani et. al (2007)** developed ciprofloxacin hydrochloride soft gel using sodium alginate as a gelling agent and sodium citrate as a source of cation. Gels are formed by aggregation of polymers with minimum two components; the gelling agent and the fluid component. Short term stability study carried out for four weeks at different temperatures (0°C and room temperature) showed no considerable changes in performance characteristics of developed optimized formulation.

5. **M. C. Gohel et. al (2009)** developed soft paracetamol gel using gellan gum as a gelling agent and sodium citrate as a source of cation. All the gels possessed acceptable sensory characteristics when evaluated by human volunteers. Short term stability study carried out for four weeks at different temperatures revealed no considerable changes in performance characteristics of developed optimized formulation.

6. **Deborah Evangeline.D et. al (2011)** prepared medicated jelly with Ajowan extract was formulated using polymers like sodium alginate and tragacanth. The jellies were evaluated for their physiochemical parameters like pH, spreadability and stability studies. The antimicrobial activities of the gels were also carried out. Formulations using sodium alginate shows desired properties and significant antimicrobial activity.

7. **Vishnu Vardhan Reddy Beeram et. al (2010)** developed an elegant, stable and most paediatric acceptable medicated jelly of Cefixime for oral administration. Cefixime is an orally administered antibacterial agent in most of the paediatrics. It is having good oral absorptivity and bio availability. But most of the paediatric cefixime formulations are available in syrups, reconstituted powders form, but they are having most of the problems like stability and disliking children’s to take that dosages.

8. **C. D. Nieuwoudt et. al (2004)** studied oral antibiotic choices to treat infections in horses are limited. In many cases, such as peritonitis, osteomyelitis, or pleuropneumonia, to name a few, long-term therapy may be necessary. In instances where owners need to administer the antibiotic doses, the IV or IM route may be
difficult or dangerous, and the oral route is preferable. Enrofloxacin is not only another alternative to the few antibiotics currently available to give orally to treat infections in horses [1,2], but also offers a broad spectrum of activity [3-5]. The commercial enrofloxacin tablets, approved for use in dogs, are cumbersome to crush, and the volume of the cattle injection is large, resulting in loss of some of the dose when administered. We developed an oral flavored gel formulation from the cattle injection that significantly eased administration of the dose.

9. Singh B.N. et. al (2005) evaluated the effects of various divalent cations on the encapsulation efficiency of gellan gum and to probe the underlying mechanisms responsible for drug-loading efficiency. Spherical beads containing azathioprine were prepared from deacetylated gellan gum by ionotropic gelation method. One molar solution of various divalent chlorides (MgCl(2), BaCl(2), CaCl(2), CuCl(2) and ZnCl(2)) and two additional concentrations of CaCl(2) (2.5 M and 5.0 M) were used as ionotropic media. Drug solubility was also determined in these ionotropic media and statistically evaluated using ANOVA. Solubility in various divalent chloride solutions (1.0 M) suggests that azathioprine forms complex with Ca(2+), Zn(2+) and Cu(2+), while there might be a formation of poorly water-soluble chelates with Mg(2+) and Ba(2+) as solubility in these media were less than in deionized water. The encapsulation efficiency of gellan gum was much higher in the presence of transition elements (Cu(2+) and Zn(2+)) when compared to alkaline earth metal ions (Ca(2+), Mg(2+) and Ba(2+)). Higher concentrations of Ca(2+) decreased the encapsulation efficiency of gellan gum in a nearly proportional manner. The correlation between encapsulation efficiency and pH of the ionotropic media was negative and significant (r=-0.9574, p<0.05), although the solubility of azathioprine seems to be independent of the pH of the ionotropic medium. Overall, the results suggest that drug encapsulation efficiency of deacetylated gellan gum is largely affected by the concentration and nature of various divalent cations (e.g. atomic number, valency or electro-positivity, coordination property, etc.) and pH of the ionotropic medium.

10. Shishu et. al (2005) worked on taste masked microspheres of ornidazole were prepared using amino alkyl methacrylate copolymers (Eudragit E-100) by solvent evaporation technique. Taste assessment of these microspheres was done by both
spectrophotometric taste evaluation technique and panel testing. Compressed tablets of
taste masked ornidazole microspheres which rapidly disintegrated in the oral cavity
were prepared using microcrystalline cellulose as directly compressible filler and
sodium starch glycolate as a super-disintegrant. These were subsequently evaluated for
various pharmacopoeial tests, drug release, and disintegration time in the oral cavity.
Sensory taste evaluation was carried by panel testing in 20 healthy human volunteers.
Results indicate successful formulation of oral fast disintegrating tablets which
disintegrated in the oral cavity in about 30 s and possessed good taste.

11. Vikesh Shukla et. al (2010) worked on periodontal diseases are the conditions that
affect the supporting structure of teeth leading to the formation of pocket due to which
tooth loss occurs, for which site specific injectable drug delivery systems are gaining
importance. In the present study six batches of Ornidazole gels were prepared using
natural biodegradable polymers Chitosan, Xanthum gum and Locust bean gum in
variable concentrations. The formulated gels were characterized for surface pH,
viscosity, bioadhesion strength, in vitro drug release studies and antimicrobial
susceptibility test. The results revealed that the surface pH was within the range of
neutral pH. The bioadhesion strength was maximum for F3 formulation (3% chitosan);
viscosity values were ranging from 1400 to 1975 dyne/cm2. Best formulation in terms
of cumulative percent drug release along with bioadhesion was formulation F3 with
79.23% drug release for 7 days and fulfilled many requirements of once a week
delivery system, easy to fabricate, cost effective patient compliance is also very high.
Zone of inhibition was also satisfactory for all the formulations.

12. Karan Malik et. al (2011) studied Ofloxacin is a synthetic chemotherapeutic antibiotic
used for treatment of a variety of bacterial infections, but therapy suffers from low patients’
compliance due to its unpleasant taste. This study was aimed to develop taste masked
microspheres of ofloxacin using Eudragit and to prepare orodispersible tablets of the
formulated microspheres using natural superdisintegrant. Taste masking Eudragit E100
microspheres were prepared by solvent evaporation technique with an entrapment
efficiency ranging from 69.54 ± 1.98 to 86.52 ± 2.25%. DSC revealed no interaction
between the drug and polymer. Microspheres prepared at a drug/polymer ratio of 1:4 and
Drug loaded microspheres were formulated as orodispersible tablets using locust bean gum as a natural superdisintegrant offering the advantages of biocompatibility and biodegradability. The wetting time, water absorption ratio and in-vitro disintegration time of the tablets were found to range between 19 ± 2 to 10 ± 3 seconds, 59.11 ± 0.65 to 85.76 ± 0.96 and 22 ± 2 to 10 ± 2 seconds, respectively. The in-vitro ofloxacin release was about 97.25% within 2h. The results obtained from the study suggested the use of eudragit polymer for preparing ofloxacin loaded microspheres with an aim to mask the bitter taste of the drug and furthermore orodispersible tablets could be formulated using locust bean gum as a natural superdisintegrant.

13. Stein GE et. al (2011) studied the relative bioavailability and pharmacokinetics of ofloxacin tablets and a reference oral solution of ofloxacin were compared in 32 normal male subjects using a randomized two-way crossover design. After an overnight fast, subjects were randomized to receive a single 200 mg or 300 mg dose of ofloxacin (tablet or solution) and blood samples were obtained prior to and 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 16, 24, 36, 48, 72, 96, and 120 hours after the dose. After a 5-day wash-out period, subjects were administered the same dose but of the other formulation, and blood samples were collected in an identical manner. Plasma concentrations of ofloxacin were determined by high-pressure liquid chromatography. The results showed that ofloxacin tablets were more slowly absorbed when compared to the solution and mean peak plasma concentrations were obtained in about 1.5 hours for the tablet preparation. Maximum plasma concentrations were higher after administration of the solution (Cmax = 2.24 micrograms/ml, 200 mg; Cmax = 3.25 micrograms/ml, 300 mg) compared to the tablet (Cmax = 1.74 micrograms/ml, 200 mg; 2.61 micrograms/ml, 300 mg).

14. Bhusari K. P. et. al (2009) studied two simple, sensitive, accurate and economical spectrophotometric methods were developed for the estimation of ofloxacin and ornidazole simultaneously in tablet dosage form. First method is based on the simultaneous equations and second method is based on Q-analysis (absorbance ratio method). Ofloxacin and ornidazole shows absorbance maxima at 294 nm and 317 nm in
N/2 acetic acid, respectively. The linearity was obtained in the concentration range of 2-10 μg/ml for ofloxacin and 2-30 μg/ml for ornidazole. In the first method, the concentrations of the drugs were determined by using simultaneous equations; and in the second method, the concentrations of the drugs were determined by using ratio of absorbance at isoabsorptive point and at the _max of the one drug. The results of analysis have been validated statistically and by recovery studies.

15. Somashekar Shyale et. al (2009) studied Ofloxacin is widely used antibacterial drug recommended in the treatment of chronic bronchitis, respiratory/ENT infections, nonspecific urethritis, gonorrhoea, a typical pneumonia, leprosy, cervicitis. One of the major drawbacks of this drug is its bitter taste which may give rise to patient noncompliance when formulated as conventional dosage forms. To conclude, efficient taste masking was achieved for the bitter drug ofloxacin using the technique of granulation. Patient compliant dosage forms i.e. oral liquid suspension and rapidly disintegrating tablets that had good taste were successfully formulated. These studies suggest that these patient friendly taste masked dosage forms may be useful for children and elderly patients.

16. Sharma J. B. et. al (2007) compared the efficacy and cost effectiveness of ofloxacin, ornidazole, serratiopeptidase and Saccharomyces Boulardii combination with traditional doxycycline and metronidazole combination with serratiopeptidase in the outpatient management of pelvic inflammatory disease. A total of one hundred and ninety three women presenting with symptoms of pelvic inflammatory disease (PID) confirmed to be a case of PID on clinical examination were randomized to one of the two treatments. No investigations were performed to cut the cost and to avoid loss of follow up. A total of 98 women (Group I) were prescribed ofloxacin (400mg), ornidazole (500mg), Serratiopeptidase (10mg), Lactic acid bacillus 60 million spores and Saccharomyces Boulardii 2 million spores once a day for 10 days while a total of ninety five women (group II) were given a 10 day course of doxycycline (100 mg BD) with metronidazole (400mg TDS) along with 10mg of serratiopeptidase once daily. All women were seen after 2 weeks for relief of symptoms and possible side effects. The results were then analyzed. It was found that although the efficacy of both drug
regimens was similar. The incidence of gastrointestinal side-effects mainly were less in group I. This was probably due to the addition of probiotic Saccharomyces Boulardii and lactic acid bacillus. The once daily administration led to better compliance in the first group.

17. Mattias Paulsson et. al (1999) studied gels have been successfully used to increase the mucosal contact time and hence the bioavailability of nasal and ophthalmic formulations. The use of in situ gelling polymers requires a rapid sol–gel transition that produces a strong gel for an optimal contact time. In this study, the rheological behaviour of deacetylated gellan gum (Gelrite®) was analysed in order to better understand the reasons for the good performance in humans. Thermal scans were used to study gel formation and other changes in the structure of the samples when the macromolecular and ionic contents were altered. The effect the different ions in tear fluid (Na, K, Ca) had on the gel strength and the consequences of dilution due to the ocular protective mechanisms were examined. Na was found to be the most important gel-promoting ion in vivo. It was also found that gels are formed in tear fluid even when the concentration of Gelrite® is only 0.1%. Samples with concentrations of Gelrite® of 0.5–1% do not require more ions than 10–25% of those in tear fluid to form gels. These two findings can partly explain the good performance of Gelrite® in vivo. Gels with a high elastic modulus can thus be formed even though dilution of instilled drops takes place.

18. Vijay Sharma et. al (2010) reviewed that acceptability of any drug dosage form mainly depends over its taste i.e. mouth feel. Drug molecule interacts with taste receptor on the tongue to give bitter, sweet or other taste sensation, when they dissolve in saliva. This sensation of taste is the result of signal transduction from the receptor organs for taste, commonly known as taste buds. Now a days most of the potent drugs that may be cardiac, analgesics, anti inflammatory, anti tubercular, antihelmentics, antibacterial, anticoagulants, anti epileptics, antimalarial, anti neoplastics, anti thyroids, antiprotozoal, diuretics, histamine receptor antagonists, nutritional agents, opioids analgesics, oral vaccines and sex hormones, most of them are bitter in taste. So it
becomes necessary to develop such a dosage for that must be acceptable in taste to patient especially in case of children or geriatrics.

19. **Inderbir Singh et. al (2009)** reviewed that ion exchange resins are water insoluble cross-linked polymers containing a salt-forming group at repeating positions on the polymer chain. They can be classified as cationic or anionic exchange resins depending upon the nature of the exchangeable ion of the resin as a cation or anion, respectively. The degree of cross-linking and particle size of the resin substantially modify its properties and applications. Ion exchange resins can be use to overcome various pharmaceutical formulation problems including bitter taste, poor stability, deliquescence, and poor dissolution of the drugs. Resins have also been used as superdisintegrants in tablet formulations because of their swelling properties. Modified release of drugs from resinate (drug – resin complexes) is another potential application of ion exchange resins. Because of the versatile utility of ion exchange resins, they are being used for various drug delivery and therapeutic applications.

20. **Rashmi Dahima et. al (2010)** formulated a rapid-disintegrating tablet of the metoclopramide hydrochloride. Taste masking was done by complexing the drug with ion exchange resin, Indion 204 and Indion 214, in different ratios. The complex loading process was optimized for the concentration of resin, swelling time, stirring time, pH, and temperature for maximum drug loading. Drug-resin complexes (DRC) were tested for flow properties, drug content, in-vitro release in simulated salivary fluid, and in simulated gastric fluid (SGF), taste evaluation by the panel method. Taste evaluation of DRC revealed considerable taste masking with the degree of bitterness below threshold value (40 μg/ml) in 0 to 5 min. Complex of both Indion 204 and Indion 214 masked the taste, but on the basis of the comparative study, resin 214 was selected for taste masking property. Disintegrant croscarmellose (5% wt/wt) gave the minimum disintegration time in comparison to crosspovidone and sodium starch glycolate.

21. **Chaul Soon Yong et. al (2001)** studied liquid suppository systems composed of poloxamers and bioadhesive polymers were easy to administer to the anus and mucoadhesive to the rectal tissues without leakage after the dose. However, a liquid
suppository system containing diclofenac sodium could not be developed using bioadhesive polymers, since the drug was precipitated in this preparation. To develop a liquid suppository system using sodium chloride instead of bioadhesive polymers, the physicochemical properties such as gelation temperature, gel strength and bioadhesive force of various formulations composed of diclofenac sodium, poloxamers and sodium chloride were investigated. The mixtures of P 407 (15%) and P 188 (15–20%) existed as a liquid at room temperature, but gelled at physiological temperature. Diclofenac sodium significantly increased the gelation temperature and weakened the gel strength and bioadhesive force, while sodium chloride did the opposite. Furthermore, the poloxamer gels with less than 1.0% of sodium chloride, in which the drug was not precipitated, were inserted into the rectum of rabbits without difficulty and leakage, and retained in the rectum of rats for at least 6 h. Our results suggested that a thermosensitive liquid suppository system with sodium chloride and poloxamers was a more physically stable and convenient rectal dosageform for diclofenacsodium.

22. Wataru Kubo et. al (2003) evaluated the potential for the oral sustained delivery of paracetamol of two formulations with in situ gelling properties. Oral administration of aqueous solutions of either gellan gum (1.0%, w/v) or sodium alginate (1.5%, w/v) containing calcium ions in complexed form resulted in the formation of gel depots in rabbit and rat stomachs as a consequence of the release of the calcium ions in the acidic environment. In vitro studies demonstrated diffusion-controlled release of paracetamol from the gels over a period of 6 h. The bioavailability of paracetamol from the gels formed in situ in the stomachs of rabbits following oral administration of the liquid formulations was similar to that of a commercially available suspension containing an identical dose of paracetamol.

23. Jian-Hwa Guo et. al (1998) studied the polymers such as hydroxypropylcellulose, hydroxyethylcellulose, sodium carboxymethyl cellulose, hydroxypropyl methylcellulose, polyvinylpyrrolidone, pectin, carrageenan and guar gum have wide application in the pharmaceutical industry, and many techniques in polymer characterization are performed with the polymer molecules in aqueous solution; this is because the thermodynamic properties of polymer solutions can be readily measured
and the results interpreted in terms of the size and structure of the macromolecules, thus enabling characterization of the polymer. The authors address some important properties and practical applications of water-soluble polymers.

24. Roger E. Stier (2010) reviewed there are numerous pharmaceutical and OTC preparations that contain actives, which are bitter in taste. With respect to OTC preparations, such as cough and cold syrups, the bitterness of the preparation leads to lack of patient compliance. Currently, companies are developing dissolvable films as alternative dosing mechanisms for drug actives for patients who are unable to use the traditional dosing method: tablets. In order to ensure patient compliance and to allow dissolvable films to become a viable delivery system, bitterness masking becomes essential. This paper discusses the research done at Noville to achieve pleasant tasting pharmaceuticals in which bitter actives have been successfully masked. Noville is a flavor and fragrance house dedicated to the research into the masking of various unpleasant tastes together with the development of base formulations and flavors to complement the active ingredients.

25. Piyush Gupta et. al (2002) reviewed the recent advances in semisolid dosage forms for dermatological application. Several studies have demonstrated the utility of semisolid bases for systemic drug delivery by dermatological application. Studies about the effect of formulation excipients on the rheology of semisolids have contributed significantly toward their characterization. The development of computer-assisted instruments also has contributed substantially to their characterization and thereby to improving their quality. Moreover, some of the guidelines established by regulatory agencies, especially by FDA, are major steps toward the standardization of these dosage forms.

26. Kuchekar B.S. et. al (2003) concluded taste masking of bitter drugs is common in pharmaceutical industries to develop a desired palatable and to enhance the aspect of action as well as bioavailability of drug. so all the above approaches not only being used to mask the bitter taste of drug as well as to enhance the solubility, onset of action as well as bioavailability of drug either by one of the above mentioned technique.
27. **Jigar Shah (2007)** reviewed the large variety of applications as well as the steadily increasing number of research workers engaged in studies of Gellan gum due to their unique properties, have made significant contributions to many types of formulations and suggest that the potential of Gellan gum as novel and versatile will be even more significant in future.

28. **Dipjyoty et. al (2010)** prepared fruit-based gels with gellan gum as the gelling agent. Textural attributes of the gellan gum gels, formed with different concentrations of the gum (0.5–3.0%) and sugar and/or pineapple juice, were determined employing the methods of large-deformation uniaxial compression and stress relaxation. Fracture stress/energy markedly increases with an increase in the concentration of gellan gum while fracture strain exhibits a marginal effect. The change in these compressive textural parameters is more pronounced for sugar added samples compared with gels without sugar. Marked decay in stress relaxation curves was observed; the extent of relaxation decreases marginally with an increase in gum content up to 2% but shows much lesser values beyond 2% addition. The sugar added samples exhibit lesser relaxation characteristics but higher relaxation times indicating elastic characteristics compared with samples without sugar. Use of gellan gum provides an innovative method for developing fruit juice based gels as a convenience food because of attractive transparent appearance and textural attributes.

29. **Vikas Anand et. al (2001)** reviewed ion-exchangeresins (IER), or ionic polymer networks, have received considerable attention from pharmaceutical scientists because of their versatile properties as drug-delivery vehicles. In the past few years, IER have been extensively studied in the development of novel drug-delivery systems (DDSs) and other biomedical applications. Some of the DDSs containing IER have been introduced into the market.

30. **Monk J. P. et. al (1987)** reviewed Ofloxacin is one of a new generation of fluorinated quinolones structurally related to nalidixic acid. It is an orally administered broad spectrum antibacterial drug active against most Gram-negative bacteria, many Gram-positive bacteria and some anaerobes. Ciprofloxacin is the only
other quinolone with superior in vitro antibacterial activity. However, the pharmacokinetic profile of ofloxacin is superior to that of ciprofloxacin, with more rapid absorption and a peak serum concentration several times higher. Moreover, ofloxacin achieves high concentrations in most tissues and body fluids. The results of clinical trials with ofloxacin have confirmed the potential for use in a wide range of infections, which was indicated by its in vitro antibacterial and pharmacokinetic profiles. It has proven effective against a high percentage of infections caused by Gram-negative organisms, slightly less effective against Gram-positive infections, and effective against some anaerobic infections. Clinical efficacy has also been confirmed in a variety of systemic infections as well as in acute and chronic urinary tract infections, and ofloxacin has generally appeared to be at least as effective as alternative orally administered antibacterial drugs. Ofloxacin is well tolerated and, although experience with the drug in clinical practice to date is limited, bacterial resistance does not appear to develop readily. Thus, ofloxacin is an orally active drug which offers a valuable alternative to other broad spectrum antibacterial drugs.