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Review On: Oral Liquid Formulation in Cancer Therapy

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ABSTRACT:
The main aim of this study is that oral liquid formulation such as nanoemulsion, nanosuspension, solutions and injections is very important for cancer treatment. Oral cancer is an aggressive tumour that invades the local tissue and can cause metastasis and high mortality. Conventional treatment strategies, e.g., surgery, chemotherapy, and radiation therapy alone or in combinations, possess negligible issues, and significant side and adverse effects for the clinical applications. Currently, targeting drug delivery is emerging as an effective approach for the oral delivery of different therapeutics. Herein we provide a state-of-the-art review of the current progress of targeted drug delivery for oral cancer therapy. Variously oral delivery systems including polymeric/inorganic nanoparticles, liposomes, cyclodextrins, nanolipids, and hydrogels-based forms are emphasized and discussed, and biomimetic systems for oral delivery like therapeutic vitamin, exosomes, proteins, and virus-like particles are also described with emphasis on the cancer treatment. A future perspective is also provided to highlight the existing challenges and possible resolution toward clinical translation of current oral cancer therapies.

KEYWORDS:-Nanosuspension, Nanoemulsion, Oral cancer, Paclitaxel, Plumbagin, Itraconazole, PDT (Photodynamic Therapy).

I. INTRODUCTION:-

Cancer is an illness that can lead to death aberrant development and spread uncontrollably cells [(1)]Although many There are still difficulties in developing anticancer medications because of their use in cancer treatment their low bioavailability, insolubility non-water, and high-cost Toxicity and non-specific targeting lead to causing harm to healthy cells. Tumours of the lips, hard palate, upper and lower alveolar ridges, anterior two-thirds of the tongue, sublingual, buccal mucosa, posterior deltoid muscle of molars, and oral cavity are all examples of oral cancer. [(5)]More than 90% of oral malignancies are squamous cellcarcinomas. Oral squamous cell carcinoma is cancer that develops from the mucosal epithelium. Traditional oral cancer treatment options primarily involve surgery, chemotherapy, and radiation therapy, either alone or in combination. While these modalities have made tremendous advances in mouth cancer treatment, they are not without flaws and severe side and unfavourable effects Chemotherapy. for example, can induce nausea, vomiting, hair loss, infections, and diarrhoea in patients, while radiation therapy can cause transient or permanent damage to healthy tissues, hurting their well-being and quality of life significantly. [(2)]

Anticancer medicines (e.g., 5-fluorouracil, paclitaxel, cisplatin, and docetaxel) are used alone or in combination in current therapies and have been used in chrono-chemotherapy for the treatment of oral cancer[(3)]. However, as intravenously supplied with non-specific tissue distribution within the body, they are very poisonous to normal cells, readily causing greater harm to healthy tissues with significant adverse reactions. Low solubility, permeability, and absorption of these anticancer medicines in body fluids are also mentioned as oral chemotherapy limits. As a result, developing new therapy regimens or modifying existing techniques is critical for improving human health and survival against oral cancer and tissues.

The transparent/translucent multi-phase colloidal systems are made up of two immiscible phases (the dispersed internal phase (droplets) and the continuous exterior phase), both of which are solely kinetically related and stable and used to treat a variety of diseases and were dubbed nanoemulsions. Nanoemulsions range approximately between 10 and 500 nm either in oil/water and water/oil forms. Natural, semi-synthetic, and synthetic oils were used for the formation of nanoemulsions. Oil, surfactant, and

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cosurfactant are the main components of nanoemulsions. Nanoemulsions efficiency is based on the smaller size of droplets, increased surface area, low overall surface tensionsystem, and the droplets' low interfacial tension[4]

ADVANTAGES OF NANOEMULSION OVER CONVENTIONAL DOSAGE FORM:-

1) Traditional topical dose forms like ointment and gels are inferior to nanoemulsion-based delivery technologies. Nanoemulsions are made up of safe, well-known components that are mixed in a novel way to produce a stable emulsion.
2) The use of nanoemulsions boosts By solubility of medicines with low water solubility entrapment in the nanoemulsion drop Nanoemulsions aid in the delivery of agents to the desired location.
3) Nanoemulsions are efficient against bacteria, fungi, and viruses on their own. These droplets collect in the air.
4) They interact directly with and in the epidermis and dermis. Disrupt organisms at the injection site.
5) In topical distribution, nanoemulsions may provide the same benefits as liposomes, such as decreased side effects and increased physical stability, but at a considerably cheaper cost. because of the relative ease of scale-up and nanoemulsion-based formulations manufacturing.[12]

ADVANTAGES OF NANOEMULSION:-

1. It can be used to replace liposomes.[12,13]
2. It increases medication bioavailability. [14]
3. It is naturally non-toxic and non-irritating.
4. Physical stability has improved.
5. Nanoemulsions have small droplets with a larger surface area, allowing for higher absorption.
6. It's available in a variety of forms, including foams, creams, liquids, and sprays.
7. Cell culture technology improves the uptake of oil-soluble nutrients.
8. It aids in the solubilization of lipophilic drugs.
9. Helpful for disguising unpleasant tastes.
10. The quantity of energy required is reduced.

NOVEL PREPARATION METHODS OF NANOEMULSION:-

Drugs, bioactive materials, and bioactive proteins may be synthesised into nanoemulsions to represent an efficient treatment, given that they have good bioavailability and enhanced therapeutic response. To make a stable nanoemulsion, the right ingredients must be used are composition, controlled component addition, and application. The ability of the shear to efficiently rupture the droplets is a critical criterion. [6]High-pressure homogenization (high-pressure homogenizer, at a pressure of 50-100 MPa), microfluidization, and ultrasonication (ultrasound) are some of the nanoemulsion preparation processes. spontaneous emulsification, phase inversion approach, generators Hydrogel process with solvent evaporation approach. [7] Among them: The ultrasonic emulsification method also decreases the droplet size to a manageable level. Biodegradable polymers, principally, were used to prepare a significant level.cyclooxygenase-2 inhibiting perfluoropoly (ethylene glycol) ether theranostic nanoemulsions to increase water solubility. Celecoxib was used to get an increased tumors inhibitory effect.PluronicP105 with cremophor EL.[8]

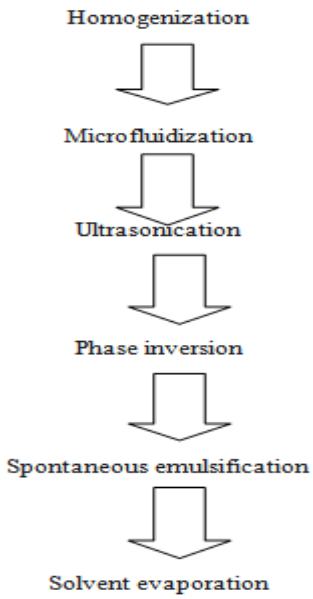

Fig 1:- Novel preparation methods for nanoemulsion

COMPONENTS OF NANOEMULSION: -

An emulsion system is one in which the dispersed internal phase (droplets) and the continuous exterior phase are both presents. Normally, they are in an oil-in-water environment. water-in-oil formations, where the core can be either oil or water, respectively. Surfactants are commonly used to make nanoemulsions. that the Food and Drug Administration considers safe for

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human consumption Drug Enforcement Administration The kind and concentration of surfactants are used in the aqueous phase to provide improved stability against coalescence. Various oils (natural, semi-synthetic, and synthetic) In nanoemulsion formulations, synthetic materials are employed. Nanoemulsions' ability to dissolve vast amounts of poorly soluble medications, as well as their mutual compatibility and ability to preserve the environment they are ideal for protecting pharmaceuticals against hydrolysis and enzymatic degradationdrug delivery vehicle.[9]

PHARMACEUTICAL APPLICATIONS OF NANOEMULSION IN CANCER THERAPY:

1. Oral drug delivery:-

Oral medicine delivery could be revolutionized thanks to nanoemulsion. It has overcome several flaws in older systems. Drug solubility, absorption rate, andConcerns about focused medicine administration were always present. when creating oral dose forms Drug in nanoemulsion. The delivery system has developed a single-step solution for all of these issues In terms of drug solubility, hydrophilic and lipophilic medicines can both be dissolved in O/W or a W/O nanoemulsion, which enables better dissolving due to the incredibly small particle size. units that are both hydrophilic and lipophilic Furthermore, these small particles can easily pass through the epithelial layer, resulting in a high rate of medication absorption. Scientists can fix and regulate little particles more easily. dosage optimization to avoid dose-related toxicity. As a result, nanoemulsion has opened up new possibilities. enables scientists to more precisely create poorly soluble and bioavailable medications that could not be produced using traditional methods. Nanoemulsions have both hydrophilic and lipophilic components, allowing for distinct targeting moieties and medicines from different classes to be used. [10]

These nano-emulsified medicines may even infiltrate the cytoplasm, providing a more targeted pharmacodynamic effect within the cell (cancer treatment). As a result, it could be an ideal delivery method for medications like steroids. Proteins, hormones, diuretics, and antibiotics are just a few examples. Oils are absorbed effectively in the GIT by a variety of lipid absorption mechanisms. As a result, one of the most effective techniques to enhance Protein medicines is absorbed by loading them inside the body. the oils such that medication absorption can considerably increase along with the oil droplets.

Itraconazole (ITZ), a poorly water-soluble medication, has recently been studied to improve in vitro dissolution and in vivo absorption. Nanoemulsion templates were used to create new pectin-based nanoparticles. A high-pressure homogenization process was used to create nanoemulsion templates. As an emulsifier, pectin (high-methoxyl pectin HMP) is used. As an oil phase, chloroform is used. In vivo absorption research in Pectin-based nanoparticles was shown to work in fasting rats. The quality of nanoemulsion templates might be improved.ITZ has a 1.3-fold better absorption rate than the Commercial ITZ product. These results indicated that HMP-based nanoparticles have the potential to be a successful formulation. because of their high AUC of 0–24 hours and C max.[11]

2) Improved lipophilic drugs delivery:-

The lipophilic molecule may be solubilized by the oil phase of the emulsion systems.

Therefore, compared to an aqueous solution, the solubility of lipophilic medicines can be greatly increased in an emulsion system, resulting in reduced administration quantities. Additionally, lipophilic medications are kept out of direct contact with bodily tissues and fluids because they are integrated into the innermost oil phase. By exposing the tissues to lower drug concentrations or by avoiding a tissue-irritating medium, lipid emulsions can reduce the discomfort brought on by intravenously delivered medications.Propofol, diazepam, methohexital, clarithromycin, etomidate, and a new cytotoxic drug have all been used to demonstrate this.

3) Photodynamic therapy of cancer(PDT):-

The idea behind photodynamic therapy (PDT) for cancer is that specific photosensitizers can be found in the neoplastic tissue and then activated with the right wavelength (energy) of light to produce active molecular species that are toxic to cells and tissues like free radicals and singlet oxygen (1 O2). A potential benefit of the binary therapy 57-59 PDT is its innate dual selectivity. By increasing the photosensitizer's concentration in the target tissue, selectivity is first made possible. Secondly, the irradiation can be restricted to a certain volume. In brief, various PDT therapies have reported two different vehicles for photosensitizers, a Cremophor oil emulsion and DPPC liposomal vesicles**.** [18]

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Nanosuspension As Oral Dosage Form:-

A nanosuspension is a colloidal dispersion of drug particles that is submicron in size. A pharmaceutical nanosuspension is defined as very finely colloid, biphasic, dispersed, and solid drug particles in an aqueous vehicle, with a size of less than 1 m, no matrix material, stabilised by surfactants and polymers, and prepared by suitable methods for drug delivery applications via oral, topical, parenteral, ocular, and pulmonary routes[15]Solid particles in nanosuspensions typically have a particle size distribution of less than one micron, with an average particle size ranging between 200 and 600 nanometers[16]. A nanosuspension not only overcomes the problem of poor solubility and bioavailability, but it also changes the medication's pharmacokinetics, improving drug safety and efficacy.

For substances with a high log P value, high melting point, and high dosage, the nanosuspension formulation technique is ideal. The ability to address the nature of the deficiency associated with this class of medications by using nanotechnology to create poorly water-soluble pharmaceuticals as nanosuspension.Nanosuspension has been shown to improve absorption and bioavailability, potentially lowering the dose of traditional oral dosing forms. Reduction of drug particle size as a result of the increase in surface area.

ADVANTAGES OF NANOSUSPENSION:-[17]

1. Improve medication solubility and bioavailability.
2. Suitable for hydrophilic medicines
3. Higher drug loading is possible
4. It's possible to reduce the dose.
5. Improve medication physical and chemical stability
6. Allows for passive drug targeting.

Benefits And Drawbacks Of Nanosuspension Preparation Techniques:-

1. Product stability
2. Low energy consumption
3. Low equipment costs
4. Easy scaling up.

Table: Available marketed anticancer drugs in the form of Nanosuspension and Nanoemulsion with their route of administration[19]

Anticancer drugs in nanosuspension form	Anticancer drugs in nanoemulsion form
Thymectacin(parental intravenous)	Piplartine
Paclitaxel(parenteral intravenous)	Doxorubicin
Celecoxib(parental intravenous)	Imatinib
Busulfan(intrathecal)	Plumbagin
Oridonin(Intravenous)	Flutamide
Silybin Oral, IV	Curcumin

II. CONCLUSION:

From this study, it is concluded that oral liquid formulation such as nanosuspension and nanoemulsion is most important in cancer therapy as compared to other conventional dosage forms. Nanoemulsions are helpful in malignant growth treatment as they show a high stacking limit, little molecule size, great actual dependability also, protected poisonousness, and more prominent zeta potential. They have perfect future applications as they can be directed through different courses and have more prominent helpful soundness, increasingly slow supported drug discharge. They have generally shown that they are more adequate in the counteraction and treatment of cancer development.

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