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NEEM OIL EMULSION FORMULATION OVERVIEW AND FURTHER SCOPE OF IMPROVEMENTS/DEVELOPMEMT

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ABSTRACT

Azadirachtin is the most well-known and studied triterpenoid in neem oil, Azadirachtin is a natural product found in the seeds of the Neem tree (Azadirachta Indica), which protect crops from pests. due to effect on the environment use of some insecticides have been banned. As a result, a search has been going on for "Biorational pesticides" these are compositions which deter insects and minimal harmful effect on environment. Neem oil formulations are formulated using different ingredients to form Emulsion, it is hydrophobic in nature; in order to emulsify it in water for application purposes, it is formulated with surfactants/Emulsifying agents.

KEY WORDS

Neem Oil; Azadirachtin; Biopesticide; Emulsion

INTRODUCTION:

Neem oil is the triglyceride constituent normally found in the neem seeds. Azadirachtin is the most well-known and studied triterpenoid in neem oil. The azadirachtin content of neem oil varies from 300ppm to over 2500ppm depending on the extraction technology and quality of the neem seeds crushed.

Figure no.1.Images of Neem Seeds, leafs and oil

Azadirachtin is a natural product found in the seeds of the Neem tree (Azadirachta Indica). which protect crops from pests. The Neem tree is found in India, Pakistan, Banfladesh, Burma, Thailand, Malaysia and Africa. For many years now, several powerful and effective insecticides have been used to protect food and fiber crops. Most recently due to effect on the environment use of some insecticides have been banned. As a result,

a search has been going on for "Biorational pesticides" these are compositions which deter insects and minimal harmful effect on environment.

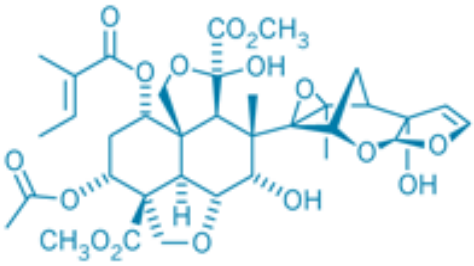

Figure No.2.Structureof Azadirachtin

IUPAC Name : Dimethyl (2aR,3S,4S,R,S,7aS,8S,10R,10aS,10bR)-10-(acetyloxy)-3,5-dihydroxy-4 [(1S,2S,6S,8S,9R,11S)-2-hydroxy-11-methyl-5,7,10 trioxatetracyclo[6.3.1.02,6. 09,11]dodec-3-en-9-yl]-4-methyl-8-{[(2E)-2-methylbut-2-enoyl]oxy}octahydro-1H-furo[3',4':4,4a] naphtho[1,8-bc]furan-5,10a(8H)-dicarboxylate

Molecular Formula: $C_{35}H_{44}O_{16}$

Molecular Weight: 720

Terpenoids: Also called isoprenoids, are a large and diverse class of naturally occurring organic chemicals similar to terpenes, derived from five-carbon isoprene units assembled and modified in thousands of ways. Most are multicyclic structures that differ from one another not only in functional groups but also in their basic carbon skeletons. These lipids can be found in all classes of living things and are the largest group of natural products. About 60% of known natural products are terpenoids.

Plant terpenoids are used extensively for their aromatic qualities and play a role in traditional herbal remedies. Terpenoids contribute to the scent of eucalyptus, the flavors of cinnamon, cloves, and ginger, the yellow color in sunflowers, and the red color in tomatoes. Well-known terpenoids include citral, menthol, camphor, salvinorin A in the plant Salvia divinorum, the cannabinoids found in cannabis, ginkgolide and bilobalide found in Ginkgo biloba, and the curcuminoids found in turmeric and mustard seed.

Azadirachtin is the most well-known and studied triterpenoid in neem oil. The azadirachtin content of neem oil varies from 300ppm to over 2500ppm depending on the extraction technology and quality of the neem seeds crushed. Nimbin is another triterpenoid which has been credited with some of neem oil's properties as an antiseptic, antifungal, antipyretic and antihistamine. Neem oil also contains several sterols, including (campesterol, beta-sitosterol, stigmasterol).

Mode of action/Mechanisms of Action: Azadirachtin found to have anti-feedant(deters insects from feeding on plants)/ phagorepellent and growth regulation potency against several pests. It is structurally similar to insect hormones called “ecdysones,” which control the process of metamorphosis as the insects pass from larva to pupa to adult. Metamorphosis requires the careful synchrony of many hormones and other physiological changes to be successful, and azadirachtin seems to be an “ecdysone blocker.” It blocks the insect’s production and release of these vital hormones. Insects then will not molt, thus breaking their life cycle. Azadirachtin may also serve as a feeding deterrent for some insects. Depending on the stage of life-cycle, insect death may not occur for several days. However, upon ingestion of minute quantities, insects become quiescent and stop feeding. Residual insecticidal activity is evident for 7 to 10 days or longer, depending on insect and application rate. Azadirachtin is used to control whiteflies, aphids, thrips, fungus gnats, caterpillars, beetles, mushroom flies, mealybugs, leafminers, gypsy moths and others on food, greenhouse crops, ornamentals and turf.

Neem oil is usually comprised of a mixture of components. Azadirachtin is the most active component and is used for for repelling and killing pests. After the extraction of azadirachtin, the portion left over is called clarified hydrophobic neem oil. As reported by Current Science, it works as an effective non-toxic insect control agent to agriculture.

NEEM OIL PREPARATION

Forming neem seed particles

The step of forming neem seed particles involves comminuting or otherwise size-reducing, typically to form particles ranging in size from about 350 microns to about 2 millimeters. The regular grind is preferred because extraction is easily carried out on this particle size

Extraction

Extraction is preferably carried out using ethanol at a temperature ranging from about 75°C to about 85°C and optimally at 80°C. The extraction is carried out to obtain a solution comprising about 10000ppm Azadirachtin which is the solubility limit for azadirachtin in ethanol. Very preferably extraction is carried out to obtain a solution containing from about 40% to about 45% Neem oil.

The Extraction is readily carried out by passing a batch of the extracting agent which has been heated to the aforementioned temprature through the particles of neem seeds. The evaporation of the extract from the particles is readily carried out for example using vacuum filtration or centrifugation or other common separating method.

The Extraction is preferbly carried out by a process involving multiples passes of the extracting agent through the particles.

NEEM OIL EMULSION FORMULATION PREPARATION

It is highly preferred to include an emulsifying agent in the composition so that the Azadirachtin and neem oil and any other ingredients are kept uniformly distributed in the composition. the percentage of the composition which is emulsifier normally depends on the emulsifier which is used. Typically, the emulsifying agent is use in an amount ranging from about 0.2% to about 30% of the composition. An emulsifier also known as a surfactant from surface active material or emulgent is a substance which stabilizes an emulsion.

I. Classification of the emulsifying agents By Source

1. **Natural Polysaccharides**
   a) Acacia
   b) Tragacanth
   c) Starch
   d) Pectin
   e) Carrageenan

The main problem with these agents is their natural variability between batches and microbial contamination.

2. **Semi-synthetic polysaccharides**

a) Methylcellulose (MC)
b) Carboxymethylcellulose (CMC)
c) Hydroxypropylmethylcellulose (HPMC)

3. **Synthetic hydrocolloids**

a) Carbopol
b) Polyvinyl alcohol (PVA).
c) Polyvinyl pyrolidone (PVP)

II. Classification of the emulsifying agents by nature of the polar group

According to the nature of the polar group, Emulsifying agents/surfactants can be classified into nonionics and ionic, which may be of anionic, cationic, and amphoteric or zwitterionic nature.

1. **Anionic surfactants**

These are organic salts which, in water, have a surface-active anion

a) Alkali metal and ammonium soaps (salts of long chain fatty acids) such as sodium stearate and potassium oleate (o/w).
b) Soaps of divalent and trivalent metals such as calcium oleate (w/o).
c) Amine and ammonium soaps such as triethanolamine oleate (o/w).
d) Alkyl sulphates such as Sodium lauryl sulphate (SLS) (o/w).

Disadvantages:

a) Incompatible with some organic and inorganic cations and with large organic cations such as cetrimide.
b) They are irritant internally so widely used in external preparations as o/w emulsifying agents.
c) pH sensitivity: They must be in their ionized form to be effective and emulsions made with anionic surfactants are generally stable at more alkaline pH.

2. **Cationic surfactants:**

a) These are usually quaternary ammonium compounds which have a surface-active cation.
b) Examples include cetrimide and benzalkonium chloride.
c) They are used in the preparation of o/w emulsions for external use and must be in their ionized form to be effective.
d) The cationic surfactants also have antimicrobial activity.

Disadvantages:

a) They are sensitive to anionic surfactants and drugs.
b) Emulsions formed by a cationic surfactant are generally stable at acidic pH.
c) They are more Toxic than other surfactants.

3. Non-Ionic surfactants

a) They are synthetic materials and make up the largest group of surfactants.
b) The non-ionic surfactants are compatible with both anionic and cationic substances and are highly resistant to pH change.
c) They are used to produce either o/w or w/o emulsions for both external and internal use.
d) The type of emulsion formed depends on the balance between hydrophilic and lipophilic groups which is given by the HLB (hydrophilic-lipophilic balance) number.
e) Examples of the main types include
   - **Esters**: such as glycol esters, glycerol esters, macrogol esters, sorbitan esters (spans) and polysorbates (tweens).
   - **Amides**: such as alknolamides.
   - **Ethers**: such as Macrogol ethers and Poloxamers.

LIST OF CURRENT MARKETED FORMULATIONS

The first commercial product of neem, Margosan-O@ (W. R. Grace & Co., Cambridge, MA, U.S.A.) wasregistered in the U.S.A. in 1985.

1. Margosan-O@ (W. R. Grace & Co., Cambridge, MA, U.S.A.) Azatin (Agridyne Technologies, Salt Lake City, UT, U.S.A.);
2. Bioneem and Neemesis (Ringer Corp.,Minneapolis, MN, U.S.A.);
3. Safer's EN1 (Safer Ltd,Victoria, B.C., Canada, now incorporated into RingerCorp.);
4. Wellgro and RD-Repelin (ITC Ltd, Andhra Pradesh, India);
5. Neemguard (Gharda Chemicals,Bombay, India);
6. Neemark (West Coast Herbochem,Bombay, India)
7. Neemazal (Trifolio M GmBH, D-6335 Lahnau 2, Germany).

LIST OF EQUIPMENTS/INSTRUMENTS USED FOR PREPARATION AND CHARACTERIZATION OF EMULSION

1. High pressure homogenizer.
2. High shear homogenizer
3. pH meter
4. Globle size analyzer (Horiba/Malvern)
5. Zeta seizer(Malvern)
6. Manufacturing vessels
7. Circulating bath (Cooling and Heating)
8. HPLC/UPLC

DISCUSSION

Based on literature and analyzing of current marketed formulations a novel stable Neem oil formulation to be developed conducting experimental work. In which identification of sources(vendors) for raw material and screening/pre-formulation studies to be conducted further. Formulation will be developed using empirical approach/ more systematic approach.

CONCLUSION

After review of literature and based on earlier emulsion development experience further scope identified for development of novel stable emulsion using suitable emulsifying agent as compare to existing formulations, control of evaporation rate of Neem oil using polymers for prolonged/sustained release, cost effective formulation can be developed increasing dilution ratio for final use.

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