1. Introduction:

Mosquitoes are among the world's most extensively dispersed organisms due to their ability to adapt to a variety of environmental situations. The global temperature has risen by 1°C above preindustrial levels. If this trend continues, there is a high chance of widespread distribution of *Aedes albopictus* and *Ae. aegypti,* population even towards the poles (Ryan et al., 2019; Rocklöv and Dubrow, 2020; Colón-González et al., 2021). This will contribute towards increased disease morbidity and mortality as mosquitoes are vectors to various disease-causing pathogens, including arboviruses, protozoa, bacteria, and helminthes. Because of the haematophagous nature of female mosquitoes and the high transmission rate, about 2.5 billion individuals are in danger worldwide (Escalante et al., 2009; Kamau et al., 2012). In tropical and subtropical areas, a lack of effective medicine and immunization has rendered these diseases unavoidable. As a result, vector management is one of the most important strategies for preventing disease transmission. For this reason, insect vectors are currently managed with synthetic pesticides, which are both inexpensive and effective. However, its negative impacts, such as the development of multiple pesticide resistances, adverse environmental effects, and high toxicity to people and non-target animals, have raised serious concerns around the world. It is now well acknowledged that a considerable proportion of pesticides are carcinogenic; for example, 18% of all insecticides and 90% of all fungicides were shown to be carcinogenic. Pesticide risks are frequently classified according to whether they have short-term (diarrhoea, abdominal pain, headaches, nausea, vomiting, etc.) or long-term effects (skin diseases, cancer, depression, neurological deficits, diabetes, genetic disorders, or even death) (Tago et al., 2014). As a result, some governments have banned certain pesticides. For example, as of September 30th, 2018, around 50 distinct pesticides have been banned for manufacturing, formulation, use, import, and export, and the Indian government has cancelled registration for approximately 18 pesticides (Directorate of Plant Protection, Quarantine and Storage, 2019). As there are no substantial vaccines or medicines for these diseases, the failure of these synthetic insecticides may lead to the re-emergence or major outbreaks of vector-borne diseases in the near future (Rezza, 2012). Therefore, researchers have focused their efforts on developing an alternative method of vector control. Plant secondary metabolites are one such example that are examined for their insecticidal properties (Isman et al., 2014; Wang et al., 2019; Afzal et al., 2018). Their higher preference is mainly based on their characteristic features, such as being inexpensive, easily available, readily biodegradable, and highly diverse in their phytochemical content (Arnason et al., 2012; Pavela et al., 2019). Furthermore, unlike current control techniques, phytochemicals provide a wide range of active components, even within a single family such as Apiaceae (Spinozzi et al., 2021), which can supply a multitude of compounds with different modes of action and bioactivity. On the other hand, herbivore-plant interactions have led to the co-evolution of both organisms since time immemorial, consequently giving rise to highly diverse secondary metabolites that are specifically synthesized by plants to counter herbivores, especially insects (Isman et al., 2014).

The northern districts of West Bengal, India, are the focal point for mosquito-borne diseases. It harbours several species of mosquitoes, which are established vectors for many disease pathogens that cause malaria, dengue, filariasis, *etc*. (Kalra et al., 1997; NCVBDC, 2022). In order to combat these vectors, synthetic insecticides are the major arsenal used by the public health administrators in this region. But earlier studies have revealed that *Culex quinquefasciatus,* Say and *Aedes albopictus,* Skuse from Siliguri, Shivmandir area of Darjeeling district, have already developed insecticidal resistance against synthetic pyrethroids, organophosphates (including temephos), and organochlorines (Rai et al., 2019; Bharati et al., 2017).

1.1. Burden of mosquito-borne diseases:

Vector borne- diseases contributes 17% of the total infectious diseases in the world. Mosquitoes accounts for a major fraction of these diseases (WHO, 2020). There are over 3500 species of mosquitoes in the world 3/4th number of which consume blood (Breedlove and Arguin, 2007). The major mosquito vectors fall under three genus namely, *Anopheles, Aedes* and *Culex.* About 15 different species/subgroups has been reported from West Bengal alone that is responsible for spreading disease like Dengue, Malaria, Chikungunya, Lymphatic filariasis and Japanese encephalitis (Rudra and Mukhopadhyay, 2010; Gurav et al., 2016; Bharati and Saha 2019). These species either feeds on human or other warm blooded animals. They are mostly attracted towards their host via chemicals released by their host called kairomons. In case of human beings more than 300 different kairomons are known which is released through breath and sweat in the form of volatiles (Bernier et al., 2000).

Dengue has been one of the major widely spreading mosquito-borne diseases in the world with an infection rate of 96 million every year and a death rate of 40,000/year (WHO, 2020). Dengue is now prevalent in all the major continents to some island countries with a significant number of human settlements (Servadio et al., 2018). Worldwide trade in second hand tyres which mostly contains rainwater provides an opportunity for *Aedes sp*. mosquitoes to lay eggs. Though *Ae. aegypti* is known to be the major dengue vector causing severe epidemics reports of *Ae. albopictus* spreading/re-emergence of dengue outbreaks in *Ae. aegypti* free areas like Mauritius and Hawaii has been accounted (Effler et al., 2005; Ratsitorahina, et al., 2006; Xu et al., 2007; Leroy, et al., 2009; Issack, et al., 2010). India is also a dengue endemic region where Nagaland and Lakshadweep had 8 and 0 cases in 2019, respectively. But the number of case has significantly rose to 4943 and 445 in 2023, respectively. The most affected states are Uttar Pradesh, Maharashtra, West Bengal, Odisha, Rajasthan, Punjab and Haryana (NCVBDC, 2024). According to the Survey data of National Center for Vector-Borne Disease Control, West Bengal reported the highest number of dengue incidence of about 67271 in 2022 followed by 30683 cases in 2023 (report till 13.09.2023).

Malaria is one of the most challenging mosquito-borne disease due to a variety of vectors and disease causing pathogen that transmit this disease. Besides, insecticide resistance in malaria vectors and drug resistance in *Plasmodium sp*. further aggravates the situation. Global burden of malaria is 219 million cases per year and 4,00,000 deaths per year (WHO, 2020). In India, Odisha, Chhattisgarh, Jharkhand, Uttar Pradesh and West Bengal are some of the most malaria affected states of India. West Bengal reported 14,049 malaria cases with 07 deaths in 2020 while in 2022 this figure saw a sudden rise in the number of case of about 40,594 with a death toll of 3 people and a frequency of approximately 1 case per 286 blood samples examined (NCVBDC, 2024).

Lymphatc filariasis is a neglected tropical disease which is caused by the filarial worm *Wuchereria bancrofti, Brugia malayi* and also *Brugia timori.* It is mostly transmitted by *Cx. quinquefasciatus* and also by *Anopheles* and *Aedes* mosquitoes. Globally about 25 million males are affected with hydrocele and 15 million patients are affected with lymphoedema. According to WHO data, in 2021 more than 882 million people from 44 different countries are at risk of contracting this disease and requires immediate chemical therapy to eradicate it (WHO, 2023). In the Indian scenario, as of 2023, 6.19 lakh Lymphedema and 1.26 lakh hydrocele cases have been reported Odisha, Jharkhand, West Bengal, Uttar Pradesh and Telangana are some of the Indian states that has reported cases of Lymphedema and hydrocele cases in 2023. Around 473 million people are at the risk of contracting Lymphatic filariasis all around the world (Agarwal and Sashindran, 2006).

1.2. Richness of Phytochemicals and traditional medicine in Northern part of West Bengal:

The Indian part of Himalayan region has reported around 8000 vascular plant species. Nearly 21% of these vascular plants possess some medicinal values (Singh and Hazra, 1996). Joshi et al., 2016 has documented about 116 different medicinally important plant species from Himalayan region comprising Nepal, Bhutan and India. Out of these eight species *Artemisia japonica, Valeriana jatamansi, Artemisia nilagirica, Cinnamomum glaucescens, Aegle marmelos, Cinnamomum tamala*, *Juniperus macropoda* and *Curcuma longa* are known to possess insecticidal/mosquitocidal activity. In the West district of Sikkim, India around 54 different ethnomedically important plants were documented. Due to over exploitation and lack of awareness some among them are under IUCN red list (Tamang et al., 2017). Considering the climatic condition elevation and other edaphic factors Darjeeling hills are also highly rich in ethnomedicinal plants. The hills of Darjeeling, located in the Himalayan region, are the abode of several medicinal plants due to their exclusive climatic and unique edaphic conditions. About 218 different medicinal plants under 97 different families has been reported to be found here (Yonzone et al., 2012). Darjeeling inhabits different ethnic groups like Limbu, Lepcha, Bhutias who has their own mode of treatment and they are rich in their traditional knowledge.

The richness in ethno-medicinal plants in Darjeeling is so profound that about 74 different species were recorded for the treatment of 42 various ailments within an area of just 10 sq. km. (Subba et al., 2011). Another study recorded 78 different plant species from three sub-divisions of Darjeeling district namely Kurseong, Kalimpong and Darjeeling that displayed antimicrobial and antioxidant activities (Saha et al., 2011).

1.3. Brief history about use of insecticides both synthetic and botanicals against mosquitoes:

The precise timing of usage of botanical pesticides cannot be traced back; nevertheless, certain accounts imply that the earliest use of botanicals as insecticides occurred over three thousand years ago. Around 400 B.C., it was recorded in Persia that the powder of dried *Chrysanthemum cinerariaefolium* flowers, as well as various plant essential oils, were used as an antiparasitic therapy against ectoparasites (Pavela, 2016; El-Wakeil, 2013). This plant commonly called as Dalmatian pyrethrum and it was sold in powdered form as 'Persian powder' to the Europeans (Davies et al., 2007). It was used against bedbugs, flies, cockroaches and mosquitoes. Elderberry flower, tobacco were some of the plants that were used against insect pest in early days (Oberemok, 2015). In fact nicotine, derived from the tobacco plant, was the first commercially available pesticide (Sohail et al., 2012). Some early efforts included using plant-based poison baits and repellent plants in grain stores. Later, additional botanicals such as rotenone were used, but these were eventually superseded by synthetic pesticides after World War II.

Vector control Programmes can loosely be divided into Pre-World War II era and Post-World War II era after the discovery DDT. Before the ground-breaking discovery of the malarial vector by Sir Ronal Ross fever and malaria were associated with bad air and nearby dictches and swamps. So, during the late 1800s mechanical control and environmental control of vectors was the sole method of vector control. Clearing of marshes, subsoil drainage, bush and tree trimming, oiling of containers were some of the mechanical control measures practiced during those days (Wilson et al., 2020). In fact fines were imposed to people in Cuba if anybody failed to follow these protocols (Le Prince et al., 1916). Slowly this methods were replaced with chemical control of vectors.

Chemical control of vectors dates back to 1000BC when fumigation with inorganic sulphur was used as a vector control method. Use of Arsenic, lead arsenate and cryolite, borax are some of the other chemicals that were also used (Oberemok et al., 2015). Paris green was another chemical that was in use to control agricultural pests and also malarial vectors in the early 20th century (Majori, 2012). During the construction of Panama Canal Paris green and oil was used as larvicides to control *Anopheles albimanus, An. tarsimaculata* and *Ae. aegypti* (Le Prince et al., 1916). After the discovery of DDT in 1874 and its insecticidal properties in 1939 the whole scenario of vector control programme was changed for better or worse. Countries like USA, Indonesia, Italy, Brazil and Egypt started using DDT and continued using Paris green for controlling malarial and Dengue vectors (Shousha, 1948; Takken et al., 1990; Majori, 2012). Italy also introduced community education and participation in vector control programmes along with DDT aerial spray. Between 1933 and 1950 Tennessee, USA saw a significant drop in the population of *An. quadrimaculatus* and the malarial incidents after the implementation of larvicides and Indoor Residual Spray (IRS) using DDT. During World War II , 'Cactus' a military malaria control unit was formed to combat malarial infection in Solomon island using fumigation, topical repellent, oils and malaria prophylactic medicine, atabrine (Wilson et al., 2020) with high rate of success. During same time, similar result was achieved in Egypt by using pyrethrum, Paris green as larvicides through residual sprays in planes, automobiles trains and huts (Shousha, 1948). Later pyrethrum and paris green were replaced with DDT. Again in South East United States of America effective control of *Anopheles quadrimaculatus* through Indoor residual sprays of DDT, from 1947 to 1951, rendered the area a malaria free zone (Williams, 1963). All the previous efforts were made by individual nation in a smaller scale, however, a worldwide initiative was taken 1955 under the flagship of Malaria Elimination programme. This programme focused on the elimination of malaria vectors in multinational states through IRS, DDT and other insecticides with partial success (Nájera et al., 2011). During the 1950s to 1970s IRS with DDT was very effective in controlling mosquito population. Its effectiveness was recognised in Peruvian Andes where use of IRS-DDT controlled the mosquitoes effectively but when the spraying was halt resurgence in mosquito population was observed again (Davies et al., 1994). Presently insecticide treated mosquito nets are used as an effective measure to control mosquito borne diseases. After 2005, under the flagship project Malaria Elimination Programme and Pacific Programme for the Elimination of Lymphatic Filariasis, long lasting insecticide treated nets (LLITNs) in Papua New Guinea were introduced to control the population of *An. farauti, An. koliensis, An. puntulatus*. In India, Nepal and Bangladesh IRS-DDT are still being used in homes and animal shelter to control mosquito related problems (Rijal et al., 2019).

After realizing the ill effects of DDT organophosphates and carbamates were developed and used to control mosquitoes. Since Organophosphates and carbamates are similar in structure their target sites are similar. They bind to acetylecholine esterase irreversible and influences sympathetic and parasympathetic nervous system in non-target organism. Some of the common symptoms are nausea, hallucination, delirium, tremor, seizures etc. (Vale and Lotti, 2015).

In 1949, based on the pyrethroids the first synthetic pyrethrin, allethrin was synthesized. This set the basis for the first generation of pyrethroids or type I pyrethroids. Type I pyrethroids lack α-cyano group and are photosensitive to UV-radiation. Although their toxic effect is highly imporved as compared to the natural pyrethrum due to their photosentive nature their residual effect is very low. A second generation pyrethroid was synthesized with better activity and phtostability. Type II or second generation pyrethroids like cyfluthrin, deltamethrin, cypermethrin, lambda-cyhalothrin etc contain α-cyano group with increased insecticidal activity. However, apart from insecticidal resistance developed in mosquitoes pyrethrin Type I and Type II cause poisoning syndromes in non-target organisms T syndrome and choreoathetosis syndrome (CS) syndrome, respectively (Nasuti et al., 2003).

Presently in India both chemical and non-chemical mode of control is into play. Chemical control are into two different formulations Wettable powder and emulsifying concentrate. WP is used for IRS whereas EC is used for larval control. In WP fomulation synthetic insecticides like Malathion 25%, Deltamethrin 2.5%, alphacypermethrin 5% Cyfluthrin 10% Lambdacyhalothrin 10%, and DDT 50% are used. Synthetic pyrethroids are also used in ITNs and LLINs. IRS are applied for those mosquitoes that are endophagic but exophilic in nature while ITNs or LLINs best controls those mosquitoes that are exophagic and exophilic. Considering the longer residual effect of DDT 50% WP the Government of India has recommended 190 metric tonnes in two rounds of sprays with an additional 75 metric tonnes in the third round if required. Other recommended requirement of other insecticides per million population are as follows: 900 metric tonnes of Malathion 25% WP, 60metric tonnes of Deltamethrin; 18.75 metric tonnes of Cyfluthrin 10%; 18.75 metric tonnes of lambdacyhalothrin 10% and 37.5 metric tonnes of alphacypermethrin 5%. The duration of use of LLINs is about 3 years and the insecticide activity retains in the nets for approximately 20 washes.

For larval control biological agents like larvivorous fishes and bacterial formulations. Currently, *Gambusia affinis* and *Poecilia reticulata* are used as biocontrol agents whereas two formulations aqueous solution and wettable powder of bacteria namely *Bacillus thuringiensis* israelensis are used as non-chemical agents. In chemical control Temephos 50% EC and mosquito larvicidal oil are used (NCVBDC, 2022).

Neem and pyrethrum, among plant-based insecticides, have proven to be potential alternatives to synthetic insecticides. Azadirachtin inhibits the secretion of PTTH in insect pest juveniles, thereby impeding the insects' developmental process, whereas pyrethrin is known to block voltage gated sodium channels, causing neuron hyperactivity and knocking down adult flying insects (Pavela, 2016).

1.4. Aims and goals in popularizing botanicals:

Despite extensive research into the creation of effective, sustainable green pesticides, botanicals face a significant challenge in commercialization. This is attributable to three primary factors: sustainability, botanical standardisation, and regularisation (Isman 1997; El-Wakeil 2013). To begin, given the high demand for insecticides in agriculture and public health, large-scale production of plant biomass is required as a raw material. Plants such as neem and pyrethrum are grown on a large scale in many regions of the world, but other such plant sources will need a substantial period of time to attain this aim.

Second, the effectiveness of plant extracts or essential oils is affected by both seasonal and regional variations. Cultivators and extractors must consider these variables before commercialising their goods. As a result, developing a consistent operating protocol with suitable and exact analytical equipment and facilities is an absolute necessity. Thirdly, botanicals are subject to regulatory clearance. The market for botanical pesticides is small, but their regulatory costs are very high, reducing the profit margin of the finished good. There should be strict scrutiny in the regulation of botanical use, but government agencies should focus on providing maximum subsidies on the use of green pesticides until their market grows to a significant level, at which point the profit margin will be comparable to that of synthetic pesticides. This will inspire more industries to invest in botanical pesticides, lowering the total cost burden for manufacturers. Furthermore, encouraging research and development in the field of botanical pesticides might result in more effective and economical pest control options for vector control.

Lemon eucalyptus essential oil is another example of broadly commercialized product against mosquitoes where p-menthane-3,8-diol is the active ingredient approved by United States Environmental Protection Agency (USEPA) (Batish et al., 2008). Moreover, the mammalian toxicity of eucalyptus oil is relatively low as compared to the pyrethrin and technical grade pyrethrum (Regnault-Roger, 1997; Batish et al., 2008; Casida and Quistad, 1995).

2. Review of literature:

2.1. Extraction of Phytochemicals:

There are several methods by which phytochemicals can be extracted. With the help of present day technology phytochemicals are extracted utilizing sophisticated instruments as per the need of the extracts. By far the most ancient and common extraction technique is maceration. Almost every Indian household practices the process of maceration for the preparation of pickles. Popularity of maceration is easy to perform, requires less instrumentation, thus, cheap and requires no external heat, which ensures extraction of thermo-labile compounds in their natural intact form. But, it takes longer extraction time and has lower yield than any other methods. Due to this several other processes of extraction has been devised. One such process is called Soxhlet extraction.

2.1.1. Microwave Assisted Extraction (MAE):

It is a method of extraction where microwave radiation is used to extract compounds from organic matter. Microwaves are electromagnetic waves that uses dipolar rotation and ionic conduction to heat substances. In an electric field molecules, in sample as well as in solvent, with dipole moments try to align producing dipole rotation (Azwanida, 2015). This