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Efficacy of Phytochemicals Against Mosquito Larvae: An Update to Integrated Mosquito Management

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Abstract: Mosquitoes are considered a most common human enemy; causes mortality, morbidity, monetary and social disruption. It plays a significant role in endemic conditions for Malaria, Japanese encephalitis (JE), Dengue, Yellow fever, Chikungunya, and Filariasis etc. The prolonged use of synthetic insecticides raises the risk of unintended harmful or fatal consequences such as biological amplification, mosquito resistance development, and negative impacts on environmental quality and non-target species, including human health. So that there is urgent need to find natural and environmentally safe phytochemicals as an alternative to synthetic pesticides from indigenous plant sources that are accessible to the whole local community. Phytochemicals are botanicals that are naturally occurring pesticides produced from floral resources, and they are a viable alternative to synthetic insecticides in Integrated Mosquito Management (IMM). Plant based insecticides are less toxic, delay the development of resistance because of its structure and easily biodegradable. In this article, we have summarized the recent studies published in 2020 and 2021 on the biopesticide effect of botanicals with their suitable solvents which possess strong potential against mosquitoes larva. We also focused on their mode of action on the target population, variance in larvicidal efficacy among *Culex*, *Aedes*, and *Anopheles* mosquitoes, polarity of solvents employed during extraction, active component, and prospective improvements in biological control.

Keywords: Synthetic insecticides, Phytochemicals, Larvicidal, Secondary metabolites, LC_{50}, *Culex quinquefasciatus*, *Aedes aegypti*, *Anopheles stephensi*

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Introduction

Mosquitoes are considered as oldest human enemies and, play a significant role in the health hazards to society. They transmit many medically important pathogens and parasites such as bacteria, viruses, protozoans and roundworms (Sathishkumar and Manimegalai, 2008). They have the ideal ability to transfer the vector pathogens that affect millions of people worldwide, especially in developing countries due to their unhygienic and poorest conditions (WHO, 1992; James, 1992; Awad and Shimaila, 2003). World Health Organization (WHO) has declared that mosquito (Diptera: Culicidae) is a "Public enemy number one" as they act as a vector for fatal diseases like Malaria, Dengue, Chikungunya, Japanese Encephalitis (JE), Filariasis, Yellow fever, Lyme disease, Poly arthritis etc. globally including India (WHO, 1996; Gubler *et al*., 1998; Ghosh *et al*., 2012; Kalita *et al*., 2013; Dawet *et al.,* 2016). If we see the epidemiology of these diseases, it's a big source of malaria with an estimated 241 million new cases and 627,000 deaths worldwide in 2020 due to unfocused prevention strategies of malaria during the pandemic of COVID-19 (WHO, 2021). Another mosquito borne infection, dengue, covers 390 million people including 70% of the actual burden in Asia, including India, which has reported 32,796 cases upto November 30, 2020 (WHO, 2020). There are about 68,000 clinical cases of encephalitis, 13,600-20,400 deaths per year globally, and more than 3 billion people at risk of infection (WHO, 2020). JE cases have recently declined; it showed 44,000 new cases and 6,000 fatalities between 2008 to 2014, particularly in the states of Uttar Pradesh and Bihar, India. In 2016, encephalitis cases rise with over 125 children reported to have died in one hospital in Gorakhpur (Times of India, 2016). As of November 30, 2020, India has reported 32,287 suspected cases and 5,159 confirmed cases of chikungunya (WHO, 2020). There are also about 893 million people in 49 countries infected by filariasis, including 23 states known to be endemic to lymphatic filariasis in India (WHO, 2020).

Integrated mosquito management (IMM) is based on knowledge of mosquito biology, their life cycle, and vector phenomenon of mosquitos. There are about 3500 species of mosquitoes, classified into three subfamilies, named as Toxorhnychitinae, Anophelinae, and Culicinae (Reinert, 2000; Bayer Environmental Science, 2007). *Culex, Aedes*, and *Anopheles* genera constitute the major mosquito vectors, in which mostly hazardous mosquitoes are *Culex quinquefasciatus*, *Aedes aegypti*, and *Anopheles stephensi* which transmitted many endemic diseases in India including this lowland area recognized as a Poorvanchal (Redwane *et al*., 2002). This region provides a better breeding place for mosquitoes with the significant presence of poor drainage systems, an increasing rate of mosquitoes in fish ponds, especially in the rainy season, irrigation ditches, and rice fields containing stagnant water. Thus, it is essential to control mosquitoes to prevent vector borne diseases and their transmission. The approaches to disrupting disease transmission by above vectors are the killing of mosquitoes and preventing mosquito's bites (Malik *et al*., 2013; Kumar *et al*., 2012). Synthetic pesticides are used for public health sprays as chemicals with insecticidal properties such as organochlorines, organophosphorus, carbamates, pyrethroids, synthetic pyrethroid pyrroles, and phenyl pyrazole (Schofield, 1993; Pal, 1994). The excessive, unlimited, uninterrupted, indiscriminate, and continuous application of synthetic insecticides as principal agents results in the unwarranted toxic or lethal effects on non- target organisms, the development of resistance in mosquitoes, and more importantly, potential toxicity in the environment and adverse effects on human health, posing a great threat to life and the environment (Shrivastava *et al*., 2002; Kawada *et al*., 2009; Koures *et al*., 2012; Raveen *et al*., 2014; Rathy *et al*., 2014; Hemlatha *et al*., 2015; Roy *et al*., 2017). So, there is an urgent need for an alternative source to synthetic insecticides across the globe.

Phytochemicals from natural resources are emerging as a promising alternative to synthetic insecticides for insect management. They are effective, environment friendly, easily biodegradable and have less or no effect on non-target organisms. They are also often less expensive than synthetic insecticides (Govindarajan *et al*., 2011). Different chemical classes of phytochemicals are investigated for insect control potential and found promising, such as steroids, alkaloids, terpenes, and phenolic constituents (Nisha *et al*., 2009; Pavela 2015; Pavela and Benelli 2016; Pavela *et al*., 2017). Essential oils are complex mixtures of phytochemicals extracted from citronella plants (citronellal), neem (azadirachtin), lavender (linalool), and mentha (p-menthane) plants (Chaubey, 2019). Their biological effects might be the result of a synergistic effect involving all the molecules, or they could merely reflect the actions of the major molecules. However, the ability of phytochemicals to repel insects varies with age, species, plant source of extract, collection site and solvent used for extraction (Isman, 2015; Benelli 2015). Many investigations have shown the efficacy of different solvent extracts of plants and essential oils as mosquito larvicides, as repellents, ovideterrents and growth inhibitor without causing any harm to humans (Pavela 2015; Govindarajan *et al*., 2016a, b, c, d, e; da Silva *et al*., 2016; Pavela and Benelli, 2016; Benelli *et al*., 2018; Lalthazuali and Nisha, 2017). These bioactive chemicals may act as insecticides, repellents, antifeedants, moulting hormones, juvenile hormones mimics, growth inhibitors, anti-moulting hormones, as well as attractants. Plant based insecticides are less toxic, delay the development of resistance because their structures are easily biodegradable (Ignacimuthu, 2000). Approximately 2000 species of terrestrial plants are reported with their insecticidal properties including plant's secondary metabolites and their derivatives which provides substitute source for reducing the mosquito population (Feinstein, 1952; Shivkumar *et al*., 2013; Kumar *et al*., 2021). Recently, investigations have proved the effectiveness of phytochemical compounds such as saponine, steroids, isoflavonoids, essential oils, alkaloids, and tannins against mosquito larvae (Cavalcanti *et al*., 2004; Wiseman and Chapagain, 2005; Khanna and Konnabrian 2007; Chowdhury *et al.,* 2008; Joseph *et al*., 2008). It can be easily eradicated in their larval stages for mosquito control operations in comparison to adults.

We have summarized the major studies on phytochemicals that have been effective on larvae, adults or both types of mosquitoes. This review is focused on the basic methods of mosquito vector control, synthetic insecticides and their drawbacks, the role of phytochemicals with their sources and modes of action and the current situation of natural plant sources for reducing the risk of mosquito borne diseases under the umbrella of Integrated Mosquito Management (IMM).

Integrated Mosquito Management (IMM) – An inclusive control approach:

IMM involves a combination of techniques and systems for keeping up with low levels of mosquito vectors. It is a dynamic cycle for the administration of mosquito populations. The motivation behind IMM is to provide insurance against sicknesses spread by mosquitoes, keep up with a healthy environment through legitimate use and removal of pesticides and work on general satisfaction through reasonable and successful mosquito control procedures. The major approaches of integrated vector control for mosquitoes are anti-larval, anti-adult, protection against mosquito bites, and legislative controls. Control of mosquitoes at an immature stage is necessary and efficient in IMM (Elimam *et al*., 2009). Controlling mosquitoes at the larval stage is more efficient and target specific of all the avenues of IMM because the mosquitoes are relatively immobile during the immature stage; remaining the most concentrated than they are in the adult stage.

Mosquito larva control measures:

Mosquito vector control is the serious concern in developing countries like India due to the lack of general awareness, the development of resistance, and socio-economic reasons. Vector control, which includes both anti-larval and anti-adult measures, constitutes an important aspect of any mosquito control programme. In particular, larval habitats are small, widely dispersed and transient. So, larva control would seem to be an ideal approach to mosquito control as it eliminates mosquitoes before they reach the stage where they can transmit vector borne diseases. The major methods that may be implemented through source reduction, chemical larviciding, and biological control (Fig. 1) are described below:

Source Reduction:

The removal or permanent destruction of breeding grounds is referred to as "source reduction." Mosquito larvae habitats can be eradicated by filling water collecting depressions,

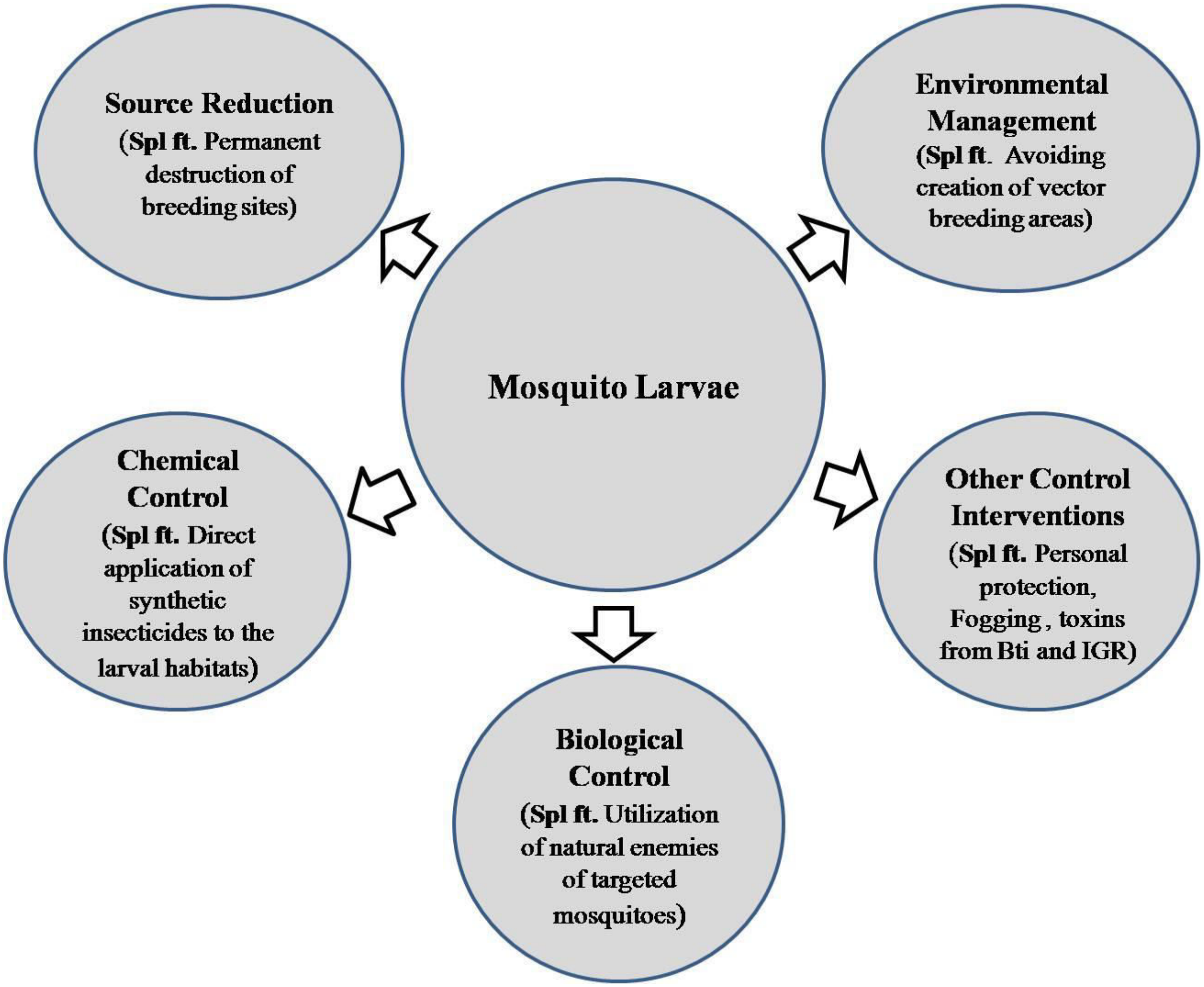

Fig. 1: Major methods of Mosquito's control. Spl ft.- special feature

swamps, or ditching marshy regions to remove stagnant water (Lawler and Lanzaro, 2005). Mosquitoes that breed in containers are more susceptible to sources because people can remove or cover stagnant water in cups, cans, and rain barrels around houses. Irrigation water–breeding mosquitoes can be reduced with careful water management.

Chemical application:

Some mosquito species are not controlled by habitat elimination alone but also need direct application of synthetic insecticides to the larval habitats. Chemical application methods include space spraying, larviciding, and targeted residual spraying. It can be planned fast, effectively, and generate outcomes at a cheap cost. Synthetic insecticides have a unique function in mosquito-borne illness control programs, particularly in the initial stages of intervention when other control strategies are still developing and playing effective roles in an integrated strategy (Chavasse and Yap, 1997).

Biological Control:

To accomplish efficient vector management, biological control strategies involve the use of natural enemies of targeted mosquitoes as well as biological toxins. It includes alternative control measures such as invertebrate predators, nematodes (e.g., *Romanomermis culicivorax*), larvivorous fish (e.g., *Gambusia affinis*), including some protozoa and fungi (e.g., *Lagenidium giganteum)* (Das and Amalraj, 1997). They are typically most feasible with easily identifiable breeding places.

Environmental management:

Environmental management is commonly used to lessen the burden of vector borne diseases over time. These include marsh alteration, house screening, filling, grading, and drainage of stagnant water places as well as vegetative plantings (Ault, 1994; Utzinger *et al*., 2001). These applications aim to minimize the quantity of a target vector by avoiding the establishment of vector breeding places, modifying natural habitats, or improving human habitation while minimizing negative environmental and social impacts.

Other vector control interventions:

Apart from all the above measures, fogging also, called area spray, is used mostly in emergency situations such as epidemics (Agosta, 2002). Though, in any malaria endemic area, mosquitoes are typically found in regions where pesticides are difficult to reach and here fogging become not much more beneficial. Fogging must be timed to coincide with peak adult mosquito activity. It will need to be done regularly to have an impact and this might become too expensive to sustain or result in insecticide misuse. The use of oils added to the water surface can be utilized to suffocate the larvae and pupae of mosquitoes. Toxins from the bacterium *Bacillus thuringiensis* var. *Israelensi* and insect growth regulators like methroprene are mosquito-specific and can be used as effectively as chemical insecticides (Barnard, 1999). We must also include personal protection measures against mosquitoes such as window screens, insecticide-treated bed nets (ITNs) and repellents (such as N, N diethyl-meta-toluamide), including wearing habits of light coloured and full-sleeved clothes.

Other measures like ovitraps, space spray, biological control agents, etc. are examples of little development for mosquito control encouraging when used on a limited scale (Raghavendra *et al*., 2011). Several biological agents recently introduced for vector control, such as insect growth regulators, biocontrol agents, and natural plant products, have yet to gain the needed scale of utility, including bacterial pesticides (Hardin and Jackson, 2009). Environmental management has shown sufficient promise for vector and disease control, but still needs advocacy for intersectoral coordination and can sometimes work very intensive. Recently, genetic engineering and sterile insect technology have been developed and are being considered for use in routine vector control. Standardized procedures and methods are available, but with biological, ethical considerations, and an understanding of a properly trained workforce for implementation is required. They are technically focused methods. In particular, plants are extracted as an alternative form of synthetic chemicals for combating mosquito resistance problems.

Synthetic pesticide control measures: historical prospective and drawbacks:

Throughout history, scientists have experimented with numerous strategies to address the threat of mosquito-borne diseases with synthetic insecticides serving as the primary instruments in mosquito control operations. However, the widespread and repeated use of synthetic organic insecticides such as organochlorines and organophosphates have disrupted biological control systems. This may result in target species' revival and resistance as well as the destruction of non-target beneficial fauna, raising environmental and human health concerns. Pesticide residues have been shown to biomagnify when they enter the ecosystem and circulate through the food web. The negative consequences of insecticide use have required research and development of environmentally safe, biodegradable, and indigenous mosquito control methods.

The first incidence of DDT resistance was discovered in *Aedes tritaeniorhynchus* and *Aedes solicitans* in 1947, not long after DDT was introduced for mosquito control in 1946 (Brown 1986). Since then, roughly half of more than 100 mosquito species have been reported as resistant to one or more insecticides (WHO, 1992). The principal categories of insecticides used for malaria control are organochlorines, organophosphates, carbamates, and pyrethroids, with the latter increasingly taking a larger share of the market for both indoor residual spraying and large-scale insecticide-impregnated bednet programmes (Zaim and Guillet, 2002). Unfortunately, resistance tends to follow changes in insecticides. Key vectors of malaria like *Anopheles culicifacies*, *Anopheles stephensi*, *Anopheles albimanus*, *Anopheles arabiensis,* and *Anopheles sacharovi* have been reported to exhibit organophosphate (OP) resistance, which can be either broad-spectrum or malathion-specific OP (Eshgy 1977; Hemingway and Georgeon, 1983; Hemingway 1983, Hemingway *et al.*, 1985; Herath *et al.*, 1986). In addition, *Anopheles albimanus*, *Anopheles stephensi* and *Anopheles gambiae* have shown resistance to pyrethroids, while resistance to carbamates has been noted in *Anopheles sacharovi* and *Anopheles albimanus* (Brogdon and Barber, 1990; Hemingway *et al*., 1992; Vatandoost *et al.*, 1996). All of the above mentioned studies and given the recent emphasis by the WHO, synthetic resistance has become the magnifier of mosquito-borne diseases worldwide, including developing countries like India. While synthetic pesticides are effective in combating mosquitoes, they cause many environmental problems, including pesticide resistance, pollution, and toxic side effects on humans. (Mecedo *et al*., 1997; Lixi *et al*., 2006). These problems, together with the insecticide residuals in the environment, pose us to seek attention towards alternative methods.

In past DDT sprays have had remarkable success in reducing disease-carrying organisms, but have led to the development of pesticide resistance. Organophosphates, carbamate, and synthetic pyrethroids were also introduced into indoor residue sprays with sufficient success to control resistance, but they subsequently developed extensive multi-insecticide resistance in vectors. As part of IMM, the search for novel bioactive compounds in plants was initiated after experiencing several issues through the injudicious and overuse of synthetic insecticides in nature from the mid 1970s to till date. Efforts have been made to determine plant derived phytochemicals' structures and their commercial production for mosquito control.

Role of Phytochemicals in IMM:

Phytochemicals are botanicals that can be clearly based on pesticides acquired from floral resources. Many herbal products have been investigated and utilised as biopesticides, even before the discovery of synthetic pesticides botanicals such as *Pyrethrum*, *Chrysanthemum, Derris*, *Nicotine*, *Quassia, Azadirachtin*, and *Turpentine,* etc. (Shalaan *et al*., 2005). Plants produce a variety of chemicals, many of which have medicinal and pesticide properties. More than 2,000 plant species are known to produce chemical factors and metabolites that are important for pest management programs. However, the discovery of synthetic insecticides, particularly organochlorines, such as DDT in 1939, diverted attention away from the use of phytochemicals in mosquito control (Shalaan *et al*., 2005). After experiencing a number of issues due to imprudent and overuse of synthetic insecticides in nature, a refocus on phytochemicals that are readily biodegradable and have no adverse effects on non-target organisms was welcomed. Phytochemicals account for up to 1% of the global pesticide market (Isman, 1997).

Phytochemicals are largely secondary metabolites that help plants endure herbivorous predators' continual selection pressures and other environmental conditions. It has various plant sources, such as alkaloids, steroids, terpenoids, essential oils, and phenolics, which have previously been recommended for their insecticidal properties (Shalaan *et al*., 2005). They have been extracted from the full plants or from various parts such as, roots, stems, bark, leaves, fruits, etc. In particular, members of the Solanaceae, Asteraceae, Zinniaceae, Laviatae, Milaceae, Oocystaceae, and Rutaceae families plants have different types of larvicidal, adulticidal or repellent activity against different mosquito species (Shalaan *et al*., 2005). A wide range of phytochemicals from herbs, shrubs, and large trees have been used to extract mosquito toxins.

Phytochemicals with mode and site of action for larvicidal activity:

Worldwide plants involve a rich, undiscovered pool of phytochemicals that might be utilized in place of synthetic insecticides in mosquito control. The mode and site of action of larvicidal phytochemicals, including essential oils, has received little attention. Kishore *et al*. (2011) surveyed the adequacy of phytochemicals against mosquito hatchlings as indicated by their substance nature and depicted the mosquito larvicidal probability of a few plant derived secondary materials, for example, alkanes, alkenes, alkynes, and basic aromatics, lactones, essential oils and unsaturated fats, terpenes, alkaloids, steroids, isoflavonoids, pterocarpans, and lignans. They additionally archived the disengagement of a few bioactive toxic standards from different plants and revealed their harmfulness against various mosquito species (Kishore *et al*., 2011). However, it is clear that they change the physiology of insects in a variety of ways by affecting biochemical processes in insects, especially disrupting the endocrine balance (Rattan, 2010). Monoterpenes, cinelole, eugenol, limonene, terpenolene, citronellol, citronellal, camphor, and thymol are incessant fixings in various essential oils that have mosquito repellent properties (Nerio *et al*., 2010). The repellent phytochemicals connect with the female mosquito's olfactory receptors, hindering the impression of smell thus keeping the mosquitoes from perceiving the host (Tripathi *et al*., 2009). It can also disrupt correspondence in mating conduct of bugs by impeding the capacity of antennal sensilla, and fruitless mating could prompt a sweetheart fertility and eventually bring down the number of inhabitants in the population of insect pests. However, botanicals primarily influence the midgut epithelium and optionally influence the gastric caeca and malpighian tubules of mosquito larvae (Rey *et al*., 1999; David *et al*., 2000). There has been report of hindering of acetyl cholinesterase (AChE) amalgamation by essential oils which assume part in cholinergic neural connections in insect and higher animals for nerve conduction (Fournier and Mutero, 1994). In the case of larvicidal activity, efficacy and insecticidal potency of phytochemicals seem to be dependent on relative absorption on the insect surface (Enan, 2001). However, it could be attributed to different species of mosquitoes or variation in composition of essential oils used (Lee *et al*., 2002; Pavela, 2005). The mixture of phytochemicals also ought to be considered as an elective insect spray possibility for mosquito control in rearing locals, particularly in situations where helplessness is diminishing.

Larvicidal potential of phytochemicals depends on mosquito type, plant components, and solvent polarity:

Plant species, plant parts used, maturity of plant parts, solvent employed during extraction, and accessible mosquito vector species can all influence the effectiveness of phytochemicals against larvae. Changes in the larvicidal efficiency of plant extracts also happened as a result of a plant's geographical origin. It has been demonstrated that the polarity of the solvents employed affects the extraction of active biochemicals from plants, with polar solvents extracting polar compounds and non-polar solvents extracting non-polar molecules. Changing in solvent types can have a big impact on the potency of extracted phytochemicals, and plant species have varied chemo-profiles.

The best way to check the toxicity effect of phytochemicals is to use lethal concentration 50 (LC_{50}). It is the concentration of a compound that kills 50% of the tested population. In this study, we have covered updated studies, especially those published in the years 2020 and 2021 in the COVID-19 era. Out of 25 studies, only 10 studies met the qualifying inclusion criteria, which are mentioned here in context of target mosquitoes, plant name with family and used part for extraction, solvents and the level of LC_{50} (Table 1).

Sogan *et al.* (2020) reported the lowest value of LC_{50} as 6.843 recorded for leaf of *Spergula arvensis* (family: Caryophyllaceae) in the solvent of methanol against the *Anopheles culicifacies* (principal vector of Malaria). On other hand, Shahat *et al.* (2020) have recorded the highest LC_{50} value of 683.28 in the same metholic solution of leaf extract of *Otostegia fruticosa* (family: Lamiaceae) aganisnt *Culex pipiens* (principal vector of West Nile virus). Different investigations additionally revealed the LC_{50} level of various parts of plants among dissolvables utilised for extraction based on polarity: aqueous, methanol, ethanol, chloroform, hexane, ethyl acetic acid, and petroleum ether derivation against different types of mosquito's larvae (Table 1).

Isolation of toxic larvicidal active phytochemicals and a futuristic approach:

More land is required to support development, agriculture, or urbanization as the world's human population continues to expand at a rate of 1.24% each year (Melorose *et al*., 2015). These human activities contribute to the opening up of possible mosquito breeding areas as well as the speciation of mosquito-borne disease vectors. Mosquito control has been fully reliant on synthetic organic compounds since the discovery of DDT. However, overuse of synthetic organic pesticides has resulted in environmental risks as well as the development of physiological resistance in important vector species during the last seven decades. Following repeated application, the overwhelming development of vector resistance to currently available synthetic pesticides continues to pose a significant threat to the transmission of diseases by vectors. This has forced the search again for the development of ecologically friendly, biodegradable, low-cost, indigenous vector control technologies that may be employed with little caution by individuals and communities in certain situations.

Although several plant derivatives have been found to exhibit mosquitocidal or repellant action against mosquito vectors, only a few plant products have proven useful in mosquito control. Even before the discovery of synthetic organic insecticides, some phytochemicals and their derivatives, such as nicotine derived from tobacco leaves, *Nicotiana tobaccum*, Anabasine and lupinine, the alkaloids extracted from Russian weed *Anabasis aphylla*, rotenone derived from *Derris eliptica*, and pyrethrums derived from *Chrysanthemum cinererifolium* flowers, were used as natural insecticides (Jacobson and Crosby, 1971; Campbell *et al*., 1993). As one strategy, phytochemicals with proven pesticide or repellent capability can play a substantial role in interrupting the spread of mosquito-borne diseases at the personal and community level. The biologically active phytochemicals have yet to be tested on a significant scale for managing insect pests and vectors. As a result, a "laboratory to grassland" transfer of tested bioactive chemicals and subsequent incorporation into IMM might counteract pesticide resistance, significantly lowering vector populations and the danger of vector-borne disease transmission. It necessitates the availability of scalable and long-term technology for both small and large-scale manufacturers. Nanotechnology, in particular, is actively transforming the manufacture of commercial pesticides. It has revolutionized the manufacturing of plant-based silver nanoparticles, which have been shown to be effective against even insecticide-resistant disease-transmitting vectors, particularly targeting immature stages at low dosages of 1-30 ppm (Benelli, 2016). The longevity of essential oil strength is increased by the production of plant-derived nanoparticles and non-encapsulation chemicals by the process of slow release for long-term protection against mosquito bites (Maia and Moore, 2011). Phytochemicals might also be utilized to control mosquito vectors by changing their behaviour and perhaps replacing pyrethroids in bed net impregnation (Deletre *et al*., 2015). However, the limitation of utilization of phytochemicals in IMM is poor characterization and inefficiency in

Table 1: Efficacy of botanical extracts among various solvents in term of LC_{50} against the major vector Mosquito's larvae

S. No.	Reference	Target Mosquitoes	Plants Scientific Name (family)	Plant Parts Used	LC_{50} (PPM)				
					Methanol	Ethanol	Chloroform	Ethyl acetate	Petroleum Ether
1	Dakum *et al*. (2021)	*Anapheles stephensi*	*Hyptis suaveolens* (Lamiaceae)	Leaf	316.22	-	-	-	-
2	Sogan *et al*. (2020)	*Anopheles culicifacies*	*Spergula arvensis* (Caryophyllaceae)	Leaf	6.843	-	-	-	-
3	Shinde and Goyal (2020)	*Aedes aegypti*	*Datura inoxia* (Solanaceae)	Seed	72.44	-	-	-	-
4	Paul *et al*. (2020)	*Aedes aegypti*	*Andrographis paniculata* (Acanthaceae)	Stem, Leaves, Roots	154.94	197	-	-	-
			Tinospora cordifolia (Menispermaceae)	Stem, Leaves	181.63	162.88	-	-	-
5	Egunjobi and Okoye (2020)	*Anopheles gambiae*	*Datura erecta* (Solanaceae)	Leaf	-	76.94	-	-	-
			Tridax procumbens (Asteraceae)		-	214.22	-	-	-
			Pennisetum purpureum (Poaceae)		-	213.41	-	-	-
6	Al-Mekhlafi *et al*. (2020)	*Culex pipiens*	*Matricaria chamomilla* (Asteraceae)	Flower	-	-	-	287.1	-
7	Ali and Venkatesolu (2020)	*Anopheles stephensi*	*Saussurea costus* (Asteraceae)	Leaf	18.96	-	57.37	73.35	17.72
		Aedes aegypti			26.52	-	75.84	113.49	23.49
		Culex quinquefasciatus			35.85	-	84.14	136.34	50.12
		Anopheles stephensi		Root	7.96	-	29. 84	39.45	14.26
		Aedes aegypti			10.79	-	49.56	86.95	22.42

		Culex quinquefasciatus			15.31		66.54	90.68	31.58
8	Raj and Shettu (2020)	*Aedes aegypti*	*Cymbopogon citratus* (Poaceae)	Leaf	**Aqueous**				**Hexane**
					299.98	164.31	256.59	244.24	196.37
			Syzygium aromaticum (Myrtaceae)		205.71	194.74	213.42	213.89	205.44
			Eucalyptus deglupta (Myrtaceae)		269.13	72.19	219.0	113.87	199.0
			Azadirechta indica (Meliaceae)		663.06	130.37	165.05	185.30	400.63
			Tagetes erecta (Asteraceae)		160.29	141.44	167.16	288.37	135.62
		Culex quinquefasciatus	*Cymbopogon citratus* (Poaceae)		270.37	140.27	233.08	220.99	184.46
			Syzygium aromaticum (Myrtaceae)		184.14	177.94	188.11	186.05	200.65
			Eucalyptus deglupta (Myrtaceae)		119.77	63.54	213.73	109.07	186.76
			Azadirechta indica (Meliaceae)		424.56	118.24	143.61	151.37	370.9
			Tagetes erecta (Asteraceae)		138.40	119.54	137.21	234.85	117.14
9	Shahat *et al.* (2020)	*Culex pipiens*	*Otostegia fruticosa* (Lamiaceae)	Leaf	683.28	-	261.13 (chlorobenzene)	585.48	129.92
10	Karthi *et al.* (2020)	*Aedes aegypti*	*Rhizophora mucronata* (Rhizophoraceae)	Leaf			**Acetone**		**Petro-benz**
					154	-	113	305	502
		Anopheles stephensi			415	-	378	427	504
		Culex quinquefasciatus			295	-	129	378	584

defining the structure of active toxic components as major reasons for the failure of bioactive toxic phytochemicals to migrate from the laboratory to the field.

The following stages might be recommended for any study design using phytochemicals to follow a futuristic strategy for the long-term objective of producing a green biopesticide: (i) screening of floral biodiversity for crude plant extracts with larvicidal efficacy against mosquitos, (ii) preparation of plant solvent extracts ranging from non-polar to polar compounds, as well as the identification of the most efficient solvent extract with their lethal dose, (iii) phytochemical examination of the solid residue and structure determination using appropriate techniques such as column and thin layer chromatography, nuclear magnetic resonance (NMR), and gas chromatography and mass spectrometry (GC-MS), (iv) study of the effect of the active substances on non-target organisms, and finally (v) to check the active principle in the field before being recommended for use in a vector control programme and commercial manufacture.

Conclusion

The rapid increase in the human population, the increasing rate of global warming, synthetic pesticide resistance in mosquitoes and lack of awareness among people, together with environmental change and the adoptability of vector mosquitoes are responsible for the results of an increase in the mosquito's population and mosquito-borne diseases. Excessive indiscriminate and continuous use of synthetic pesticides has resulted in the progress of resistance species of mosquito and adverse effects on the environment and human health. Synthetic insecticides also negatively influence the soil, water, air, and food, contaminating the food we eat and the environment we live in. To prevent all of the negative consequences, we must develop more effective techniques to eliminate these vectors from our ecosystem.

Traditionally, plant based products have been used in human communities for managing insect pests. Several secondary metabolites present in plants serve as a defense mechanism against insect attacks. A wide range of plant species from various geographical locations have been shown to contain phytochemicals capable of inducing a variety of acute and chronic harmful effects on mosquitoes. They have also been proven to cause a major deleterious impact on mosquito fertility and hatching, as well as larvicidal effects.

Several difficulties to be explored and addressed include residual effectiveness, preservation of non-target species, and uniformity of testing techniques. The recent studies included in this review suggest that plant botanicals and their components are extensively used as culinary herbs and spices, as well as pharmaceuticals. It will help to prevent the disposal of thousands of tonnes of pesticides into the environment and provide a safe environment to live in. Combined action of phytochemicals might be more promising for reducing the negative impacts and the development of mosquito resistant species.

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