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Hand Sanitizer Using Natural Ingredients: A Review

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Abstract: *Current Covid-19 widespread caused by the SARS-COV-2 virus has created a crucial importance of hand hygiene as hands act as a transmission media of transmitting various microorganisms. For disinfecting hands, usage of sanitization tools has increased on a large scale. Many spirit industries have pitched-in to produce alcohol based hand sanitizers due to increasing coronavirus threat and shortage of sanitization materials available in the market. But several studies show the harmful impact of alcohol based hand sanitizers on human health. Here, we report on the hand sanitizers, toxic ingredients based spirit hand sanitizers, and all-natural elements based spirit hand sanitizers. Also our present study focuses on hand sanitizers that use pure organic components like Aloe Vera, Glycerin, Neem oil and Lavender Essential oil.*

Keywords: *Hand Sanitizer, Ethanol, Aloe Vera, Lavender essential oil.*

1. INTRODUCTION

Hand sanitizer, also called hand antiseptic, handrub, or hand rub, agent applied to the hands for the purpose of removing common pathogens (disease-causing organisms). Their use is recommended when soap and water are not available for hand washing or when repeated hand washing compromises the natural skin barrier.[1] A novel human coronavirus that is now named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (formerly called HCoV-19) emerged in Wuhan, China, in late 2019 and is now causing a pandemic.[2] The emergence of the COVID-19 (Coronavirus Disease-2019) pandemic has risen to be a significant global public health concern and led to extensive use of hand disinfectants given its contagious nature. [3] Coronavirus disease 2019 (COVID-19), the highly contagious infectious disease is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[4] The recent study reveals that transmission of SARS-CoV-2 is possible in the form of aerosol and fomite, and the virus can remain viable and infectious in aerosols for hours and on surfaces up to days, depending on the inoculum shed.[5] Hence, it is crucial to interrupt the transmission chain of the virus through contact isolation and strict infection control tools.[6] However, it was noticed that the demand of hand sanitizers has increased manifold since the inception of COVID 19. The alcohol (ethanol or isopropanol) based hand sanitizers were recommended by scientists, doctors and health agencies across the world. However, the alcohol content in the majority of commercial hand sanitizers remained 60–65 % contrary to studies, which suggests greater effectivity at concentration of 75–80 %. Moreover, excess occurrence of chemicals like triclosan, phthalates, benzalkonium, and synthetic fragrances in hand sanitizer's formulations also have huge health and environment issues over prolonged usage. Therefore substituting these toxic chemicals additives and synthetic fragrances in hand sanitizer formulations with natural and sustainable ingredients with evident safety and efficacy data is highly commendable. [7]

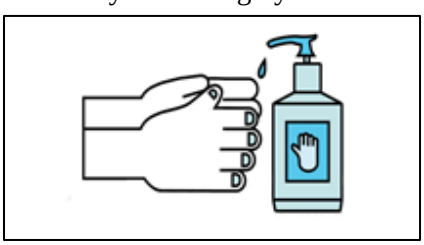

Figure1.1. *Usage of hand sanitizer*

2. HAND SANITIZERS

Maintaining hand hygiene has been established as crucial for reducing the colonization and incidence of infectious diseases in all populations. [8] Using hand sanitizer is a better way to stop the spread of infections of bacteria & viruses. Hand sanitizers as a disinfectant are in more use today because of its ease of availability, lack of water and time, and their proven efficacy in lowering microbial load. According to the World Health Organization (WHO), "an alcohol-containing preparation (liquid, gel, or foam) designed for application to the hands to inactivate microorganisms and/or temporarily suppress their growth. Such preparations may contain one or more types of alcohol, other active ingredients with excipients, and humectants.[9] The alcohol-based hand rubs (ABHRs) are the most effective and convenient infection preventive measure[10]

2.1. History and Improvisation in Making of Hand Sanitizer

In 1966, hand sanitizers came into existence in healthcare facilities and were popularized significantly in early 1990s.[11] alcohol has been in use as an antiseptic since the late-1800s at least, the exact origins of hand sanitizer are up for debate. One version of the story points to Lupe Hernandez, a nursing student in Bakersfield, California in 1966, as the inventor of hand sanitizer after combining alcohol and gel for use by doctors in situations where they don't have time to access soap and warm water before treating patients. However, a recent investigation by the Smithsonian Institution historian Joyce Bedi was unable to turn up any trace of Hernandez, or any evidence of a U.S. patent for hand sanitizer under that name from the 1960s.[12] There's also Sterillium, which the German company Hartmann claims was "the world's first marketable alcohol-based hand disinfectant" when it hit European shelves in 1965. It's made with glycerin and 75% alcohol. Still, others trace modern hand sanitizer back to Goldie and Jerry Lippman, the married couple that developed a waterless hand cleaner in 1946 for rubber plant workers who previously used harsh chemicals like kerosene and benzene to remove graphite and carbon black from their hands at the end of their shifts. The product, which they called Gojo (a portmanteau of their names) is a mix of petroleum jelly, mineral oil and less than 5% alcohol that's still used today by auto mechanics and other workers to clean off substances like grease and oil. The Lippman's mixed their first batches of Gojo in a washing machine in the basement of Goldie's parents' Akron, Ohio home, where the couple was living at the time, according to The New Yorker. They put the resulting product in pickle jars and sold it out of the trunk of their car. Over the ensuing decades, Gojo continued selling their products as industrial cleaners. Then, in 1988, the company invented the hand gel Purell, which consists of 70% ethyl alcohol as its primary ingredient, along with propylene glycol. While Purell is now the world's best-selling hand sanitizer, it took some time for stores to carry the product that most everyday customers weren't really asking for. As such, Gojo did not release Purell onto the consumer market until 1997.That same year, Vi-Jon Industries followed Gojo's lead by introducing GermX, which is now the second best-selling hand sanitizer in America, after Purell, according to Nielsen.[13]

2.2. Types of Hand Sanitizers

Hand sanitizers mainely can be classified as alcohol-based or alcohol-free. Alcohol-based sanitizers comprise between 60 and 95 percent alcohol in the form of ethanol, isopropa-nol, or n-propanol. Alcohol has a tendency to disseminate proteins and counteract certain microorganisms at this concentration.[14] Alcohol-free products have a property of disinfectants, such as benzalkonium chloride (BAC), or on antimicrobial agents, such as triclosan, which is immediate and purposeful. Several sanitizers comprise emollients (e.g., glycerin) that pacify the skin, thickening agents, and provides aroma.[15]

2.3. Indications & Increasing Demand of Sanitizers

Natural ingredient Alcohol-based sanitizers are very effective at quickly destroying a variety of pathogens and that too without the need for water, plumbing, and drying facilities.[16] According to the World Health Organization (WHO), alcohols have an excellent activity against gram-positive bacteria, gram-negative bacteria, enveloped viruses, non-enveloped viruses, mycobacteria, and even fungi. [17]Numerous studies have also documented the in-vivo antimicrobial activity of alcohols and the effectiveness in removing clinical strains of Acinetobacter baumannii, methicillin-resistant Staphylococcus aureus, Escherichia coli, Enterococcus faecalis, Pseudomonas aeruginosa, and Candida albicans from profoundly contaminated hands of human.[18] When the COVID-19 pandemic

spread worldwide, the use of alcohol-based hand rubs (ABHRs) increased exponentially, causing a lack of sanitizers available in the market. To respond to the severe shortage in hand sanitizers, pharmaceutical companies and cosmetic industries, breweries, and perfumeries have started, in an unprecedented move, to produce hand sanitizers. [19] Consumer habits and patterns are rapidly reshaping under the COVID-19 crisis and the unprecedented demand for hand sanitizers is likely to remain as the "new normal" for an extended period of time. [20]

3. Toxic ingredients based spirit hand sanitizers v/s All natural ingredient based spirit hand sanitizers

Alcohol-based hand sanitizers (ABHS) are an alterna-tive to handwashing with soap that does not require water. They have been found to improve hand hygiene compliance, and to significantly reduce the rate of infection, in health care settings. Several laboratory studies have demonstrated that ABHS can reduce bacterial test organisms such as Escherichia coli, Staphylococcus aureus, and Serratia marcescens by greater magnitudes than soap and water.[21] Alcohol-based hand sanitizers rapidly kill viruses that are commonly associated with respiratory and gastrointestinal (GI) infections. [22] Hand washing facilities like soap, water, and sink are not readily available at work or public places. [23] ECDC notes that alcohol-based disinfectants have been shown to significantly reduce infectivity of enveloped viruses such as SARS-CoV-2 in concentrations of 70%-80% with one-minute exposure time.[24] These days, alcohol-based hand sanitizers are increasingly being used instead of soap and water for hand hygiene in healthcare settings. Their ease of use, increased availability, and proven effectiveness are some of the reasons why alcohol-based hand sanitizers are gaining popularity.[25]

Alcohol-based hand sanitizer is a liquid, gel, or foam that contains ethanol or isopropanol used to disinfect hands. Hand hygiene is an important component of response to the emergence of SARS-CoV-2.[26] Alcohol-based hand sanitizers used in health care settings should contain 60%–95% alcohol (≥60% ethanol or ≥70% isopropanol) [27] Studied ozonated water compared with propanol-based hand rubs and found ozone to be inferior to propan-1-ol 60% hand rub for hand asepsis. However, Breideblik et al recommend ozonated water as an alternative that is viable especially for people with skin problems which alcohol-based products may adversely affect 19[28] Hand rubs are generally less irritating to hands and are effective in the absence of a sink. CDC does not have a recommended alternative to hand rub products with greater than 60% ethanol or 70% isopropanol as active ingredients. Benzalkonium chloride along with both ethanol and isopropanol is deemed eligible by FDA for use in the formulation of hand rubs for use in healthcare settings. However, available evidence indicates that benzalkonium chloride has less reliable activity against certain bacteria and viruses than either of the alcohols. BMJ Best practice prefers CDC and WHO guidance, and cites the need to wash hands often with soap and water for at least 20 seconds, or with an alcohol-based hand sanitiser that contains at least 60% alcohol. [29]

3.1. Role of Alcohol Based Hand Rubs and Toxic Ingredients

Note that disinfectant effectiveness in alcohol-based hand rubs depends on:type of alcohol; concentrations; quantity applied on hands; and time of exposure. Isopropanol, ethanol, n-propanol or combinations of these alcohols are most commonly used in hand rubs. As distinct from other antiseptics, these alcohols do not have the potential for acquired bacterial resistance and none are effective against bacterial spores. When used at the same concentration, ethanol seems to have a lower bactericidal activity than propanols. However, ethanol has superior virucidal activity than propanols against non-enveloped viruses. Also, skin tolerance is better with ethanol compared to n-propanol or isopropanol.[30] Many studies showed that ABHSs in the dosage forms of gels and foams are more widely accepted by consumers, compared to liquid, especially in terms of handleability and low risk of spillage, although the latter left a high clean feeling and took a shorter time to dry.[31] Moreover, gel-based formulations reduce the evaporation rate of alcohol and help alcohol to spread and penetrate through contaminating organ-isms.[32] Thus, they can be considered the best products both in terms of users compliance and stability. Gels can be obtained by incorporating different types of viscosity enhancer excipients that were listed, during the COVID-19 emergency, for the preparations of hydroalco-holic gels, by the Italian Society of Compounding Pharmacists (SIFAP); this list includes car-bomer, hydroxypropyl cellulose (HPC), hydroxypropyl methylcellulose (HPMC), sodium

carboxymethyl cellulose (CMC), hydroxyethyl cellulose (HEC). Xanthan gum (XG), not included in this list, is a viscosity enhancer that has received great attention from both researchers and manufacturers due to its nontoxicity, biocompatibility, biodegradability, and acceptable cost, which permit its use in various applications [33].

3.2. Effects Due to Toxic Ingredients and How to Prevent

Indeed, it is a thickening agent, becoming more commonly used in cosmetic and pharmaceutical industries. However, frequent application of hand hygiene products can be the cause of skin reaction and irritant contact dermatitis (ICD) [34] That are actually really common [35] and result in skin irritation, skin dryness, enlargement of pores, thus making sensitive skin more susceptible to infection [36].The adverse effects caused by sanitizers can be easily prevented by selecting products that have a good balance between effectiveness, safety, and compatibility with all skin types [37]. For example, the prevention of ICD is possible by selection of a low-irritating hand rub, which contains emollients [38].Glycerin is the most common humectant used in hand sanitizers and other cosmetic products; the studies in [39] showed that incorporation of glycerin in hand rubs promotes hand hydration to an extent that is directly proportional to its concentration in the formulation. The major issue concerning the use of glycerol is the fact that it can lower the bactericidal activity of ABHRs when used at a concentration of 1.45% (v/v), as shown in a study by Suchomel et al. [40]. Thus, although the WHO ethanol-based hand rub (EBHR) formulation contains 1.45% glycerol, reducing glycerol content to concentrations of 0.50−0.73% has been proposed as the best compromise in maintaining antimicrobial activity while still offering the needed skin protection [41].

3.3. Natural Ingredient Based Spirit Hand Sanitizers

Recently, the increasing consumer interest in natural products has suggested adding Aloe vera (Aloe barbadensis Mill.) gel as an emollient in hand sanitizers in which the moisturizing effects of cosmetic formulations containing different concentrations of lyophilized Aloe vera gel were studied, showed that formulations with higher concentrations (0.25% w/w and 0.5% w/w) increased the water content of the stratum corneum after a single application. The same study stated, furthermore, that Aloe vera extract improves skin moisture by a humectant mechanism. Moreover, Aloe vera has antimicrobial properties so it may increase the activity of sanitizers [42], Aloe vera is an herbaceous perennial plant that belongs to the Aloaceae family and has been used for many centuries for its curative and therapeutic properties [43].A study by DalBele et al. [44], until now, no study has demonstrated this synergistic action. Similar to Aloe vera, Calendula officinalis (L.) extract also has antifungal, anti-inflammatory, and antibacterial properties that might make it useful in healing wounds, soothing eczema, and relieving diaper rash, and it is also used as an antiseptic [45]. In fact, through web research findings, Calendula officinalis extract and oil have been shown to be used more commonly as excipients in hand sanitizer formulations. Fragrances are another component that is usually added to alcohol-based hand sani-tizers in order to adjust the smell produced by alcohol or other components. According to the WHO, alcohol-based hand-rub preparations with strong fragrances may be poorly tolerated by those HCWs with respiratory allergies. In fact, the most common causes of contact allergies are fragrances and preservatives, with emulsifiers being less common [46]. Consequently, consideration should be given to selecting a product with mild or no added fragrances. A valid alternative to fragrances can be adding essential oils to ABHRs because in addition to being generally considered as safe at low concentrations, indeed they are used as food additives, they also carry out antimicrobial and antioxidant action [47].

3.4. Reason why People Demand Natural Ingredient Based Spirit Sanitizers and not Toxic Ingredients Based Spirit Hand Sanitizer

The aim of this work was to produce and evaluate two different gel formulations of ABHS which, due to the addition of natural emollients and essential oils, could have antimicrobial action and, at the same time, result in acceptable long-term usage in terms of impact on the skin and hedonistic needs of consumers and compare them to WHO Formulation 1 published in Guide to Local Production of WHO-Recommended Handrub Formulations [48]. Research indicates that ethanol tends to be less irritating than n-propanol or isopropanol. Some studies have also posed the question of possible health effects related to unintentional alcoholization (via inhalation and dermal contact) from frequent professional usage of alcohol-based hand sanitizers.[49] It was noticed that the demand for hand

sanitizers has increased manifold since the inception of COVID 19.The alcohol (ethanol or isopropanol) based hand sanitizers were recommended by scientists, doctors and health agencies across the world. However, the alcohol content in majority of commercial hand sanitizers remained 60–65 % contrary to studies, which suggests greater effectivity at concentration of 75–80 % Moreover, excess occurrence of chemicals like triclosan, phthalates, benzalkonium, and synthetic fragrances in hand sanitizers formulations also have huge health and environment issues over prolonged usage (Dinwiddie et al. 2014; Pereira and Tagkopoulos 2019; Daverey and Dutta 2020). Therefore substituting these toxic chemicals additives and synthetic fragrances in hand sanitizer formulations with natural and sustainable ingredients with evident safety and efficiency data is highly commendable. Hence, we have developed an alcohol based hand sanitizer formulation with essential oil as natural ingredients. This hand sanitizer exhibits enhanced antimicrobial effectivity and offers additional benefit of free from toxic ingredients, which might be quite beneficial for health and environment as well.[50]

The natural ingredients like Aloe Vera, Glycerine, Neem oil, Lavender essential oil have been explained below.

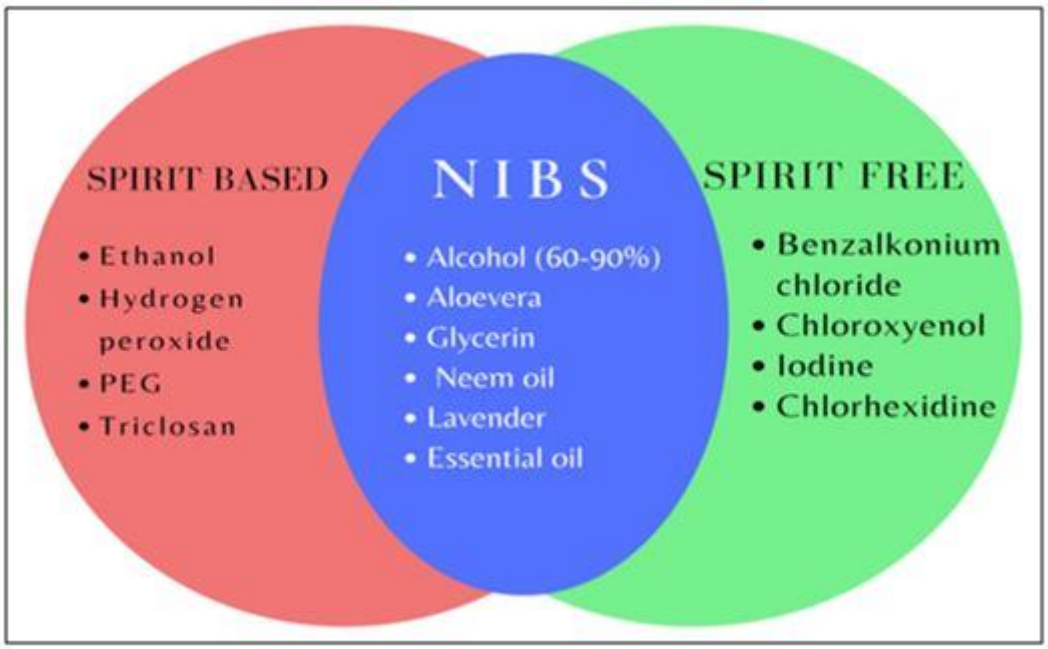

Figure3.1. *List of main compounds used in hand sanitizers(NIBS-Natural Ingredients Based Sanitizers)*

3.5. Aloevera

Many people admit to self-treating burns or cuts by applying the leaf of a potted Aloe Vera gel houseplant directly to their wounds. [51] Aloe Vera contains a majority of the necessary amino acids and vitamins that our skin needs to heal. The Aloe Vera gel itself forms glue-like substance on skin which acts as a natural “band aide”, sealing in the nutrients and allowing them to begin working immediately and keeping out any bacteria or agents that could cause healing to slow or cease completely. It mainly protects the wounds due to its moisturizing properties. Aloe Vera is used widely in Dermatology, as it acts as an astringent, moisturizer, humidifier and cleanser. It softens the skin, diminishes wrinkles and cures acne, herpes, red spots, psoriasis, eczema, mycosis, fever blisters, skin irritation and provides protection to the skin against pollution. Also, it is ideal for sunburns, fragile skin, and for removal and repair of dead skin and cells. Aloe Vera Juice contains 12 essential nutrients that inhibit inflammation with rare incidence of side effects. Also, the juice of Aloe Vera improves joint and muscle mobility and Acts as an Anti-inflammatory Agent. It has Antiviral and Anti-tumor Activity as Aloe Vera facilitates the stimulation of the immune system that in turn protects the body against viral and tumor related disorders. [52] In Vitro Properties of Aloe Vera says that some researchers claim that Aloe Vera has both antibacterial and anti-inflammatory properties. [53] It has been reported by several authors that different fractions of Aloe Vera as well as unfractionated

whole gel have antioxidant effects. Wound healing is a response to injured tissue that results in the restoration of tissue integrity. It was shown that aloe gel could improve wound healing after topical and systemic administration in several studies. [54] Aloe Vera extract is a natural effective ingredient for improving skin hydration, possibly through a humectant mechanism and it may be used in moisturizing cosmetic formulations and also as a complement in the treatment of dry skin. [55] The chemicals present in aloe are not nearly as effective in retaining moisture when they are separated in their natural mucilaginous form, and that the physical structure of the aloe itself is greatly responsible for its attributes as a humectant. [56] The base of all hand sanitizers is alcohol, added to vitamin E, Aloe Vera (or another softening ingredient), and glycerin.[57]

Benefits of Aloe Vera are explained in the Figure (3.5.1)

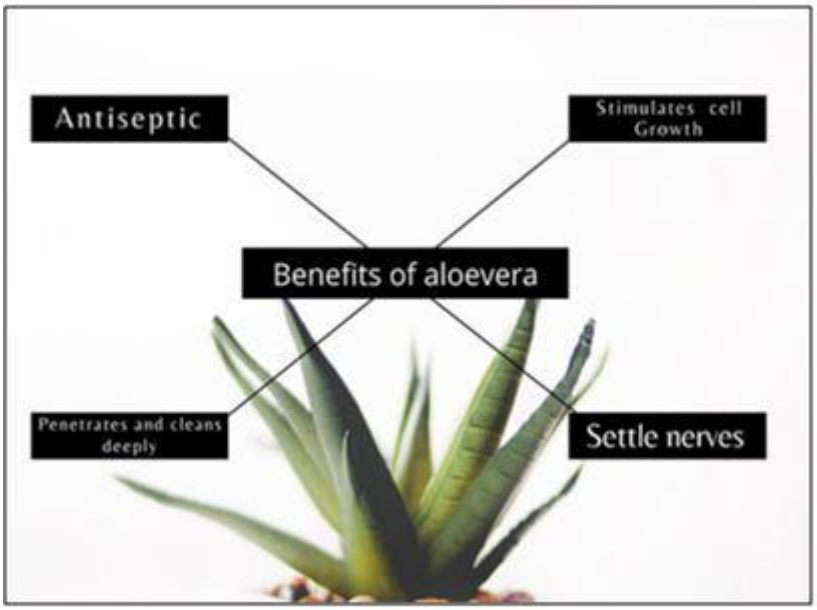

Figure3.5.1. *Benefits of Aloe Vera*

3.6. Glycerin

Glycerin functions as a denaturant, fragrance ingredient, hair conditioning agent, humectant, oral care agent, oral health-care drug, skin protectant, skin conditioning agent—humectant, and viscosity-decreasing agent.[58]Natural glycerin is obtained as a byproduct in the hydrolysis of fats and oils.[59] Glycerin is one of the most widely used ingredients in drugs and pharmaceuticals. It functions as a solvent, moistener, humectant, and bodying agent in tinctures, elixirs, ointments, and syrups. The ability to meet a nontoxicity requirement plus the availability of bonus properties in addition to those associated with its principal function in a product make glycerin a prized ingredient among chemists and formulators. In a hand cream, for example, glycerin may be incorporated as an ingredient because of its outstanding humectancy. Simultaneously, glycerin's emollient qualities may improve the efficacy of the formulation, its viscosity may give the product a very desirable body, and its antifreeze qualities may afford necessary protection in shipping and storage-all in addition to the main function of maintaining the moisture content of the product at the proper level. [60] ABHS also often contain humectants, like glycerin, which help prevent skin dryness, and emollients or moisturizers, like aloe vera, which help replace some of the water that is stripped off during use. [61]

3.7. Neem Oil

The Neem is a tropical evergreen tree native to Indian sub-continent. It has been used in Ayurvedic medicine for more than 4000 years due to its medicinal properties. Most of the plant parts such as fruits, seeds, leaves, bark and roots contain compounds with proven antiseptic, antiviral, antipyretic, anti-inflammatory, antiulcer and antifungal uses.[62,63] The antifungal, antibacterial, insecticidal and other versatile biological activities of these products are well established. [64]

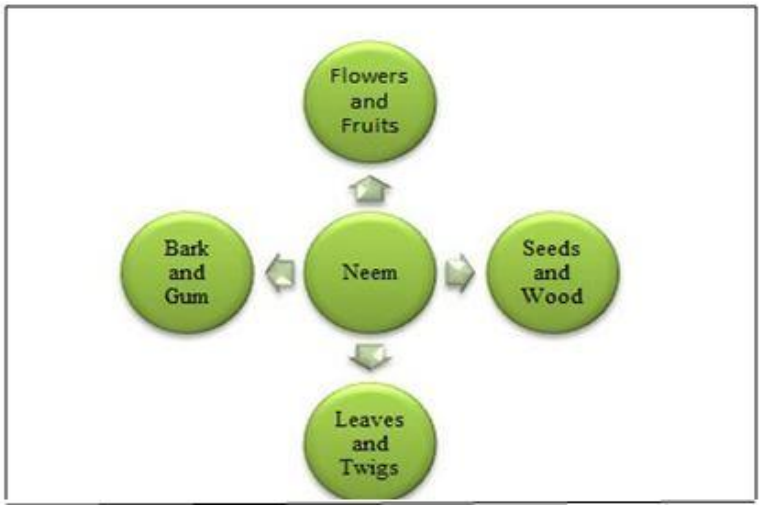

Figure3.7.1. *Different and useful parts of the neem tree*

Neem oil has the following uses:-

Medicinal:- Analgesic, Anticholinergic, Antihelminthic, Antihistaminic, Antiprotozoal, Antipyretic, Antiviral, Bactericidal, Contraceptives, Fungicides, Insecticides, Insect repellents, Veterinary medicines.

Technical: Cosmetics, Hair oils, Lubricants, Propellants, Shampoos, Soaps, Tooth pastes. [65]

Neem oil has been shown to possess activity by selectively activating the cell-mediated immune mechanisms to elicit an enhanced response to subsequent mitogenic or antigenic challenge. [66] Neem sanitizer due to its bitter taste cannot be used as hand sanitizer but can be used as floor cleaner, as disinfectant, toilet spray or to clean medical devices as it does not leave any color traces. Lemon-neem sanitizer can be used as hand sanitizers. As neem and lemon possess bioactive molecules it can also be used to formulate cream for wound healing and also for treating other skin diseases. [67]

3.8. Lavender Essential Oil

Lavender essential oil is popular as a complementary medicine in its own right and as an additive to many over the counter complementary medicine and cosmetic products. The oil is traditionally believed to have sedative, carminative, antidepressant and anti-inflammatory properties, in addition to its recognized antimicrobial effects. Indeed, lavender oil today is used predominantly in aromatherapy or massage, and many benefits are claimed for its use in this way, including relief of the symptoms of stress and depression, in improving 'mood' and relieving anxiety. [68] Lavender oil is known to relieve psychological problems and also helps in treating fungal infections, allergies, insomnia, etc. Lavender oil possesses certain properties like antibacterial, antifungal and antidepressant. Lavender oil is found to be useful in the treatment of acute as well as chronic pain.[69] The extracts and *Lavandula angustifolia* essential oil have various pharmacological effects described in the literature, such as anticonvulsant, anxiolytic, antioxidant, anticholinesterase, antimicrobial, and antifungal activities. Additionally, various constituents in the oil also have valuable pharmacological properties, such as anti-inflammatory, antioxidant, and antimicrobial. [70]

4. Conclusion

Hand sanitizer is an inseparable component of our life. It has become a necessity in our daily lives. There are mainly two types of spirit hand sanitizers available Toxic ingredients based and Natural Ingredients based. The effects and side effects of both are taken into consideration and are studied in detail. The formulation of all-natural ingredients based-spirit hand sanitizer can prove to be a boon to mankind.

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A review is never complete without the guidance of expertise in this field. I would take this moment to thank everyone who helped us in making this review. We would like to thank our guide for her immense support and advice throughout the writing process. She has been a major source of inspiration for us to be flexible in our approach and thinking of tackling issues. She ensured that we are always on the right track.

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