



Production of first- and second-generation ethanol for use in alcohol-based hand sanitizers and disinfectants in India

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Abstract

Emergence of “severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)” causing “COVID-19” or “coronavirus disease 19” as pandemic has got worldwide attention towards hygiene as the first line of defense for the infection control. It is first line of defense not only from COVID-19 but also from other infectious diseases caused by deadly pathogens such as cholera, hepatitis, tuberculosis, polio, etc. Absence of any particular vaccine or treatment let World Health Organization (WHO) recommend to the public to maintain social distancing along with regularly washing their hands with soap, sanitize their hands (where washing is not possible), and disinfect their belongings and buildings to avoid the infection. Out of various formulations available in the market, WHO has recommended alcohol-based hand sanitizers, which mainly comprise of ethanol, isopropyl alcohols, and hydrogen peroxides in different combinations due to their high potential to kill the broad range of pathogens including bacterial, viral, fungal, helminthes, etc. Therefore, alcohol-based sanitizers are in high demand since centuries to prevent infection from pathogenic diseases. Ethanol is the most common and popular alcohol in terms of vanishing wide range of pathogens, convenient to use and its production. Ethanol is produced worldwide and is used in various sectors, e.g., beauty and cosmetics, food and beverages, and as the most demanding gasoline additive. The present review is focused on the ethanol production in India, its diversified applications emphasizing hand sanitizers with discussions on formulation of sanitizer and disinfectants, and viability of lignocellulosic and food grain-based ethanol. The review article also emphasizes on the technological details of 1G and 2G ethanol production, their associated challenges, and inputs for the improved ethanol yields so as to strengthen the supply chain of ethanol in India, and making “Atmanirbhar Bharat” (Self-reliant India) campaign of Indian government successfully viable.

Keywords Sanitizer · Disinfectant · Ethanol · Lignocellulosic biomass · Infectious disease

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1 Introduction

Hygiene is an important practice to keep human as well as its belonged living organisms healthy on the earth to avoid pathogenic diseases for centuries. Regularly emerging pathogens belonging to bacterial, viral, protozoan, or other phyla of animal or plant kingdom responsible for the diseases like cholera, chickenpox, measles, polio, hepatitis, and tuberculosis have posed severe challenges to the community health worldwide for a long time. Recently encountered pathogen “severe acute respiratory syndrome coronavirus 2” (SARS-CoV-2) has caused worldwide pandemic coronavirus disease 2019 (COVID-19) [1]. It is a well-known deadly virus with total number of infections and deaths as 136,136,860 and 2,941,349, respectively, worldwide and 13,358,805 and 169,305, respectively in India as on April 11, 2021 [1, 2].

Though the emergence of several effective vaccines for this newly emerged disease made some relief in the society, but

there are still the preventative guidelines need to be followed to control the outbreak of deadly disease, which are social distancing, and hygiene through cleanliness via regularly washing hands or their sanitization, and disinfection of buildings in public areas, e.g., hospitals, railway station, airport, banks, schools, and colleges, as recommended by the “World Health Organization” (WHO) [3]. Thus, the use of sanitizers and disinfectants for sanitizing the hands or human belongings and disinfecting the buildings, respectively, is the primary preventive measure of avoiding this deadly disease, COVID-19. Therefore, during this pandemic, the demand for sanitizers and disinfectants has increased drastically, which led to the need of safe and promising formulations to be available in the market. Other than “COVID-19,” WHO has always advised to maintain hand hygiene by washing with soap as well as by using sanitizer as a first line of defense against other infectious diseases [4]. WHO has recommended regularly cleaning the hands and belongings with an efficient sanitizer with an accurate formulation (discussed later in Section 4.1) [4]. Out of a variety of commercialized formulations, the most popular and demanding formulations are alcohol-based sanitizers and disinfectants; ethyl alcohol or ethanol being the simplest and widely accepted ingredient of a promising product. In fact, ethanol is found to be more effective against viruses than other alcohols such as propanol [5]. About 42.6% (w/w) ethanol is reported to be effective against SARS and middle east respiratory syndrome, coronavirus, ebolavirus, influenza-A-virus (H3N2, H3N8, H1N1), influenza-B-virus, human immunodeficiency virus, vaccinia virus, hepatitis B virus, pseudo rabies virus, toga virus, Newcastle-disease-virus, bovine viral diarrhea virus, zika virus, herpes simplex viruses type 1 and 2 type, and respiratory syncytial virus in 30 s, whereas 73.6% (w/w) is effective against hepatitis C in 15 and 30 s [6, 7]. The brewing and distilleries in Canada have taken necessary actions to produce high quality of hand sanitizers to mitigate viral transmission for combating the spread of coronavirus during COVID-19 outbreak [8].

Ethanol is widely produced through biochemical (via fermentation) as well as thermochemical (via gasification) routes for its applications in diversified areas, e.g., cosmetics, food and beverages, pharmaceutical and transportation sector as a promising biofuel. Currently, the major producers of bioethanol are the United States of America (U.S.A) and Brazil utilizing food crops, corn and sugarcane juice, respectively as feedstock via biochemical route, and produced about 15.8 and 8.6 billion gallons of ethanol, respectively in 2019, which contributes about 89% of the world’s total ethanol production [9].

In this paper, we review the current status of ethanol production in India, its diversified applications with special emphasis on hand sanitizers and disinfectants, their formulations, viability of ethanol produced from biomass refinery for development of hand sanitizers, industrial scenario, and health issues of ethanol-based sanitizers.

2 Current status of ethanol production in India

Bioethanol has been recognized as one of the key ingredients of cosmetics and beauty products, pharmaceutical, food and beverages, and as an oxygenated additive of gasoline. The increasing demand for ethanol to be used in various sectors with major emphasis for gasoline blending led to the installation of several ethanol distilleries in the country with most of the plants using molasses as feedstock and produced about 2.7 billion liters of ethanol in 2018 [10]. The estimated ethanol production from molasses, damaged food grains and sugarcane juice was recorded as 2.2 billion liters, 167.5 and 20 million liters, respectively in 2019 (https://apps.fas.usda.gov/newgainapi/api/report/downloadreportbyfilename?filename=Biofuels%20Annual_New%20Delhi_India_8-9-2019.pdf). The ethanol produced in India is primarily consumed by the liquor industry followed by chemical industry, and other sectors [10]. A variety of feedstocks, e.g., sugarcane molasses (SCM), sugarcane juice, and food grains, are used as feedstock for producing ethanol known as first-generation (1G) ethanol (discussed later in Section 5). Currently, 330 distilleries are operating in the country with an average annual production of 4.8 billion liters of ethanol. Being the 2nd most populated country in the world (16% of total population), India is largely dependent on the ethanol import to fulfill even daily requirements. U.S.A is the largest ethanol exporter for 6 consecutive years followed by Pakistan, UAE, South Africa, and UK, whereas China, Netherland, and South Korea are the intermittent exporters (https://apps.fas.usda.gov/newgainapi/api/report/downloadreportbyfilename?filename=Biofuels%20Annual_New%20Delhi_India_8-9-2019.pdf). The annual ethanol consumption rate during last 5 years (2015–2019) was higher (14%) than the annual production rate of ethanol (8%). Total consumption of ethanol was recorded as 3.1 and 3.8 billion liters during 2018 and 2019, respectively. As a result, overall ethanol import rate was kept high in 2019 with 750 million liters, which was the maximum in the decade.

Keeping the status of ethanol production vs. consumption in the last year in view, the Indian government notified a new scheme in March, 2019 for giving financial help worth about USD 3.72 billion to sugar mills, and about USD 0.75 billion to molasses-based ethanol distilleries for enhanced ethanol production (www.india.gov.in). Lack of sufficient supply of 1G ethanol due to the dependence on food crops and their by-products, and to meet daily requirements to the continuously increasing population, a wide research is taking place for second-generation (2G) ethanol production from lignocellulosic biomass (LCB), i.e., a non-food feedstock (discussed later in Section 5.2) [11, 12]. First of all, Biochemical Engineering Research Centre, IIT Delhi established an integrated bioprocess facility for producing 50 l bioethanol per day using rice straw as a feedstock with a yield of 181.5 kg

ethanol per ton of biomass with a cost of approx. USD 0.54 per liter [13]. India's first 2G ethanol demonstration plant using multi-feedstock, i.e., wheat straw, rice straw, bagasse, cotton stalk, bamboo, etc. with feeding capacity of 10 tons per day, was installed at India Glycols Ltd., Kashipur, Uttarakhand, in 2016. An active work is being conducted on 2G ethanol production with installation of a pilot plant at the National Institute for Interdisciplinary Science and Technology (NIIST) campus with a feeding capacity of 50 kg per day [10]. In spite of the abundant reserves of LCB in the country, technology of 2G ethanol production is still under development without any commercial production due to the high cost of biomass processing and technology along with complicated controlling factors of the process (discussed later in Section 5). Therefore, more research efforts are needed for the commercial success of 2G ethanol in India. Government of India on February 28, 2019, launched "Pradhan Mantri JI-VAN (Jaiv Indhan - Vatavaran Anukool Fasal Awashesh Nivaran) Yojana" to invest about USD 2.81 billion in 2G ethanol production technology in India with targeted funding for 12 commercial scale (worth USD 2.4 billion) and 10 demonstration scale (worth USD 0.2 billion) projects to be administered by Centre for High Technology including financial help of USD 26 million from 2018–2019 to 2023–2024 (www.india.gov.in).

3 Ethanol use in diversified sectors in India

There is a continuous rise in global ethanol production due to its remarkable applications in transportation fuels, pharmaceuticals, food and beverages, household products (paints, detergents, inks, and coatings), and cosmetics and beauty products. The global industrial demand of ethanol was 116.9 billion liters in 2019, and it is projected to grow at a compound annual growth rate (CAGR) of 2.5% to reach 135.5 billion liters by 2025 (<https://www.expertmarketresearch.com/reports/industrial-ethanol-market>). The Indian ethanol market was USD 2.50 billion in 2018, which is expected to increase to USD 7.38 billion by 2024 at a CAGR of 14.5% due to its increasing use in the diversified applications (<https://www.techscienceresearch.com/report/india-ethanol-market/3860.html>). "Gasohol," formed by the blending of ethanol with gasoline in different ratios, is used as an automotive fuel to increase the engine efficiency, fulfill the globally rising energy demand and reduce the emission of greenhouse gases (GHGs). The oxygen content of petrol and diesel has increased after ethanol blending which improves their combustion efficiency. This biofuel is recorded as eco-friendly and more sustainable as compared to methyl tertiary butyl ether (MTBE) and ethyl tertiary butyl ether (ETBE). One of the successful achievements in the implementation of bioethanol in automotive fuel is introduction of the flexi-fuel

vehicles in Brazil, which can run both on petrol and *E100*, i.e., bioethanol. Government of India has reported the successful trials on pilot projects for ethanol blending with fuel in India, and implemented the selling of petroleum fuel blended with 5% ethanol in nine states and four union territories from January 2003 [14]. Indian government has mandated the ethanol blending in gasoline by 10% for reducing the import of oil, and Bureau of Indian Standards (BIS) has finalized the specification of ethanol-blended gasoline to 20% for vehicular fuel [15]. Several scientific studies have proved the significant decrease in emission of toxic substances and GHGs from ethanol-petrol blends and ethanol-diesel blends [16–22].

In pharmaceutical industries, ethanol is used in film-coating process for tablets production and as solvent to solubilize the preservatives like injections [23–25]. Different organic solvents such as ethanol, acetone and isopropanol have been utilized in the formulation of tablets and capsules during wet granulation process and film-coating process [26–28]. Ethanol (95%, v/v) is widely used as a carrier for a wide spectrum of medicines like iodine solutions, decongestants cough [29]. The pharmaceutical organic solvent market is expected to grow at a CAGR of 4.4% from 2020 to 2030, and ethanol is used for high-quality tablet coatings, OTC drugs, and syrups. After considering the environmental issues caused by the use of toxic chemicals used in drug formulations, the United States Environmental Protection Agency (USEPA) has focused on need of greener chemical processes in the pharmaceutical solvents sector (<https://www.futuremarketinsights.com/reports/pharmaceutical-solvents-market>). Ethanol is used in hand sanitizers in combination with isopropanol and benzyl chloride to combat pandemic diseases like COVID-19 as approved by Food and Drug Administration (FDA), U.S.A [8].

In food industries, ethanol is the primary ingredient of various alcoholic beverages such as beer, wine and spirits (vodka, grappa, gin, whiskey, tequila, caipirinha), fruit juices, salads, candies, burger rolls, sweet milk rolls, and fermented foods like yogurt and bread [29–32]. The composition of ink-jet cartridge has ethanol (at least 70% by weight), a colorant, a conductive agent, and a binder [33]. A liquid hand dishwashing detergent containing ethanol/benzyl alcohol was patented by Tajmamet and his research team, and this product was commercialized by the Procter & Gamble Company, Cincinnati, OH (U.S.A) [34]. Phenoxyethanol has broad-spectrum of antimicrobial activity, and hence, it has been widely used as a preservative in cosmetic and skin-care products. It is also used in the fragrance mixtures in perfumes and deodorants [35]. Ethanol is used as a preferred solvent for extraction of fatty acids in bilayer oil paint models [36].

4 Sanitizer and disinfectant formulations and their use

The effectiveness of hand sanitizer is variable, and utilized for the infection control against a broad range of pathogens in different areas dealing with public, for example, schools, hospitals, healthcare clinics, supermarkets, etc. Hand sanitizers as well as disinfectants exist with various compositions as discussed ahead.

4.1 Use of ethanol in hand sanitizer

Though a number of hand sanitizers are available in the market with various compositions, but basically sanitizers fall into two categories, alcohol-based hand sanitizers (ABHS) and non-alcohol-based hand sanitizers (NABHS). A sanitizer of any of these categories comprises active and inactive ingredients [5]. Table 1 summarizes the composition of various sanitizers available in the market. The primary active ingredient of ABHS is alcohol, which can include 60–95% (v/v) ethanol, isopropyl alcohol, *n*-propanol, providone-iodine (PVP-I), chlorhexidine, or their combinations [1, 13, 37]. Alcohols help in preventing pathogen's infection by killing microbial cells via penetration and disruption of cell membrane, denaturation of proteins, and inhibiting or uncoupling of mRNA and protein synthesis via interrupting structure or functions of ribosomes and RNA polymerase [38]. Alcohols act against enveloped viruses; thus, their anti-viral activity is specific for the viral envelopes (adenoviruses, noroviruses, and rotaviruses) which are specifically made up of lipids, and perform all life functions inside the host cells; however, exact anti-viral mechanism of alcohols is not well-known [5, 39]. Furthermore, the effectiveness of ethanol with addition of acids increases against those viruses, which are resistant to only ethanol preparation [6]. However, this synergy of ethanol and acid is found to be ineffective against non-enveloped viruses. PVP-I or iodopovidone is a complex of povidone (polyvinyl pyrrolidone), hydrogen iodide, and elemental iodine, completely soluble in cold and lukewarm water, and some of the short-chain alcohols (e.g., ethyl alcohol, isopropyl alcohol), polyethylene glycol, glycerol, etc. and displays microbicidal activity against broad range of pathogens including bacteria, viruses, fungi, and protozoa [40]. The mode of action of PVP-I against microbial cells is the iodination of lipids and oxidation of cellular compounds by free iodine liberated from the complex and results into cell death. Chlorhexidine also known as chlorhexidine gluconate (CHG) or chlorhexidine acetate is a biguanide compound, and is commonly used as an antiseptic for surgery, and disinfectant to sterilize the surgical instruments [41]. It is effective against broad range of microorganisms, but not spores.

The mode of action of chlorhexidine includes the release of positively charged chlorhexidine cation from the compound by dissociation of chlorhexidine salts, which binds to the negatively charged bacterial cell walls causing bacteriostatic effect, i.e., stops the cell's multiplication instead of killing at low concentrations, whereas at high concentrations, causes cell death by precipitation or coagulation of proteins and nucleic acids via disrupting cytoplasmic and inner membrane of the cell [42, 43]. The inactive components of an ABHS include humectants (such as glycerin for liquid rubs) aid in the prevention of skin dehydration; excipients assist in increasing the biocidal activity of sanitizer by stabilizing the product and extending the time of evaporation of alcohol, propylene glycol and essential oils from plants, etc. [5, 44]. Furthermore, the primary active ingredient of NABHS is benzalkonium chloride, a quaternary ammonium, a commonly used disinfectant [5, 44]. It is considered to be generally less irritating than alcohol, however can cause contact dermatitis [45]. ABHS are used worldwide due to better efficacy of reducing pathogenic transmission and lower cost than NABHS (https://www.cadth.ca/sites/default/files/external_rr_l2_l2_5_process.pdf). Formulations of ABHS recommended by WHO are Formulation I comprising of ethanol 80% (v/v), glycerol 1.45% (v/v), and hydrogen peroxide (H₂O₂) 0.125% (v/v), and Formulation II consisting of isopropyl alcohol 75% (v/v), glycerol 1.45% (v/v), and hydrogen peroxide 0.125% (v/v) (<https://www.who.int/whosis/whostat/2009/en/>).

4.2 Use of ethanol in disinfectants

The protection of living beings and their belongings is carried out by hand sanitizer or simply sanitizer, which are mild in composition as discussed above; however, for very large surfaces and objects (specifically non-living) are sanitized or disinfected with the help of disinfectants, which are generally concentrated in formulation as compared to the sanitizers. A disinfectant is a chemical agent, which acts against broad range of microorganisms with necessary criteria of stability, very low cost, non-toxic and non-corrosive character, non-allergenic, and residual effect [46]. Disinfectants are a part of the regular use to clean floors in building premises of healthcare centers such as hospitals, kitchens and bathrooms of houses, schools and other public places; however, they are not able to kill all the microorganisms particularly bacterial spores but can still inactivate or kill a large variety of pathogens, thus provide a large-scale protection. The mode of function of disinfectants to destroy the microorganisms is by rupturing their cell wall by damaging the proteins and interrupting their metabolism. Disinfectant formulations are registered with the Environmental Protection Agency (EPA). Most EPA-registered disinfectants label the claim of their effect in killing or inactivating pathogens in 10 min [47]. However, effectiveness of these disinfectants against variety

Table 1 Formulation of commercialized hand sanitizers available in the Indian market

Product	Formulation	Company	Website
Sofia-Man® CHG	80% (v/v) ethanol, 0.50% (w/v) chlorhexidine gluconate solution, diisopropyl adipate, PEG-6 caprylic/capric glycerides, dexpantenol, bisabolol, allantoin	B. Braun	https://www.bbraun.co.in/en.html
Dettol®	Alcohol denatured, water, peg/ppg-17/6 copolymer, propylene, glycol, acrylates/c10-30, alkyl acrylate cross polymer, tetrahydroxy propyl ethylene diamine, aloe barbadensis gel, fragrance, limonene	Dettol	https://www.dettol.co.in/en/
Purell®	70% v/v ethyl alcohol, isopropyl alcohol, aminomethyl propanol	Gojo Industries	www.gojo.com
Lifebuoy Hand Sanitizer Lemon Fresh	95% v/v ethyl alcohol, IP 55% w/w, 10% w/w isopropyl alcohol, 0.05% w/w tocopheryl acetate ip	Lifebuoy	https://www.lifebuoy.co.za/
Sterillium hand sanitizer	45.0 g propan-2-ol, 30.0 g propan-1-ol, 0.2 g mecetrionum ethyl sulfate, 85% glycerol, tetradecan-1-ol, 85% patent blue V, purified water	Sterillium®	https://www.sterillium.info/en/
Savlon Hand HEXA _{pro}	0.5% (w/v) chlorhexidine gluconate, 70% ethanol, excipients	Savlon ⁺	https://www.savlon.in/
Avicel Instant hand sanitizer	70% isopropanol, aqua, aloe vera, vitamin E, glycerine	Avicel®-DuPont Pharma Solutions	www.pharma.dupont.com
VITRO Hand Disinfectant	70% (approx) alcohol, Mentha oil, aloe vera juice, glycerine, CIM-1166, Aqua	Vitro Naturals	https://www.vitronaturals.com/
Handrub	45% (w/w) isopropanol, 30% (w/w) 1-propanol, 0.2% (w/w) ethyl-hexadecyl-dimethyl-ammonium-ethyl sulfate, moisturizer, emollient	3M	https://www.3mindia.in/3M/en_IN/company-in/

of bacteria, yeasts, and viruses can be observed in 30–60 s [48]. As in sanitizers, active ingredients are also aided in disinfectants for the supportive functions such as **surfactants** for consistent wetting on the surface aid in easy cleaning, e.g., **dodecanoic acid** (coconut soap) in solution of alcohol. There is a broad range of disinfectants used in different areas with different purposes such as air disinfectants (chemicals suspended in the air, e.g., **propylene glycol**, **triethylene glycol**); alcohols (e.g., ethanol, IPA); aldehydes (e.g., **formaldehyde**, **glutaraldehyde**); oxidizing agents (e.g., **electrolyzed water**, **hydrogen peroxide**); peroxy and peroxo acids (e.g., **peroxyformic acid**, **peracetic acid**); phenolics (e.g., **phenol**, **chloroxylenol**); quaternary ammonium compounds (e.g., **benzalkonium chloride**); inorganic compounds (e.g., **sodium hypochlorite**, **potassium hydroxide**), and non-chemical (e.g., **ultraviolet germicidal irradiation**). Out of these, alcohol-based disinfectants are the most commonly used due to the effectiveness and low cost. Table 2 summarizes the composition of various disinfectants available in the Indian market. Most of the alcohol-based products are formulated with low concentrations of other supportive agents, for example, chlorhexidine, which aids in improving efficiency of sanitizers by decreasing its evaporation time from the surface [49].

However, effectiveness of alcohols against the microbial cells is only in the presence of water; for instance, absolute alcohol (100%) is not considered effective against microorganisms as it can denature proteins only of external membrane. Alcohols can only diffuse through the cell membrane with the help of water, i.e., their solution in **distilled water**, e.g., a solution of 70% ethanol or **IPA** in water is effectual against a wide range of pathogens [50]. Among alcohols, IPA kills bacteria effectively but is less active against hydrophilic viruses (e.g., poliovirus), which are destroyed by ethyl alcohol efficiently [49]. High-concentration mixtures of ethanol and IPA, for example, 80% ethanol and 5% IPA, can efficiently inactivate the lipid-enveloped viruses, e.g., **HIV**, **hepatitis B**, and **hepatitis C**. Furthermore, an efficacy of 29.4% (v/v) ethanol along with dodecanoic acid acts against a broad range of pathogens.

5 Technological details for ethanol production

5.1 First-generation ethanol

1G ethanol is produced primarily from food crops and by-products of their processing such as sugarcane (juice, molasses), grains (maize, wheat), and tuber crops (potato, sugar beet). However, 1G ethanol is categorized based on sugary and starchy feedstocks as discussed ahead, and process of

1G ethanol production from sugary as well as starchy feedstocks is presented in Fig. 1.

5.1.1 Sugary feedstocks

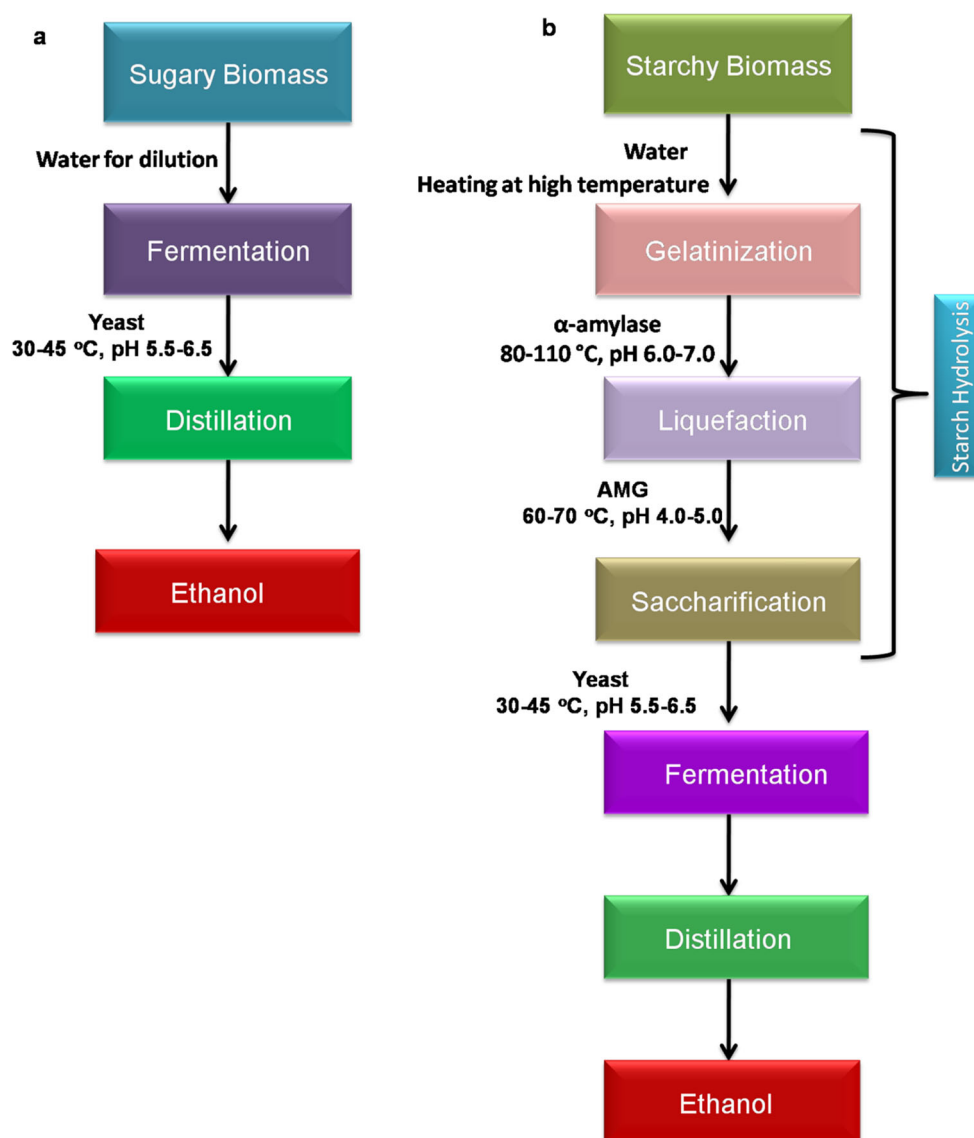
The sugary feedstocks are those which contain simple sugars or monosaccharides (glucose or fructose) or disaccharides (sucrose or saccharose), which can be extracted with water by simple technology, and fermented directly using a potential microbial strain (e.g., *Saccharomyces cerevisiae*) without any additional processing (Fig. 1a). Fermenting strain converts sucrose (one of the important disaccharides contained in 1G feedstocks) into monomeric units, glucose, and fructose that are reducing sugars with the help of enzyme invertase. Sugar crops are primarily cultivated for sugar production, and secondarily for alcohol production, though it largely depends on the availability versus demand profile of sugar and ethanol [51]. The two main sugar crops grown commercially for sugar production are sugarcane and sugar beet, which have a contribution of 80 and 20%, respectively, in the sugar market [52]. According to the Food and Agriculture Organization (FAO) of the United Nations, sugarcane is utilized for sugar production by 71 countries, sugar beet is utilized by 43 countries, and on the other hand, 9 countries utilize both the crops for sugar production. The primary and traditional source of ethanol worldwide is sugarcane of which juice and molasses are utilized for this purpose. It is an abundant and sustainable resource in sugar and fuel industry, largely grown in the tropical and subtropical countries with worldwide production about 1.91 billion tons. According to FAO, 2019 Brazil contributes about 39% (746.8 million tons) of the total sugarcane production followed by 20% from India (376.9 million tons) and 6% from China (108 million tons) and Thailand (104 million tons).

Sugarcane molasses (SCM) is the most traditional feedstock for ethanol production in Brazil and India, which is a dark brown liquid obtained as a by-product during sugar-refining process. A good amount of sugar (50–60%) remains in SCM affecting the revenue of the process adversely, which necessitates its sugar content to be converted into ethanol to take full advantage of sugarcane [53, 54]. SCM is comprised of 80–85° brix, 44–60% total sugars, 31–34% sucrose, 16–17% reducing sugars, 12.69% ash (wet weight), amino acids, and minerals e.g., 300–12000 ppm potassium, 150–2000 ppm calcium, and 80–3900 ppm magnesium with pH of 5–5.8 [54]. High sugar content of SCM has made them as primary source of 1G bioethanol production in countries such as India, China, and Brazil. India is one of the largest producers of SCM with an average production of 12.3 million tons during 2015–2018 (4.6 million tons in 2018) with about 38–48% (w/v) of fermentable sugars, which could lead to 200–290 l of ethanol (95% v/v) from 1 ton of molasses [55]. A study was reported for fermentation of SCM containing 390 g/l total sugars with

Table 2 Formulation of commercialized surface disinfectants available in the Indian market

Product	Formulation	Company	Website
Lizol disinfectant surface and floor cleaner	80% benzalkonium chloride solution, lauryl alcohol ethoxylate, sodium bicarbonate, cocoamidopropyl betaine, tetra sodium EDTA, butylated hydroxy toluene alkyl (67% C12, 25% C14, 7% C16, 1% C8-C10-C18), dimethyl benzyl ammonium chlorides (0.0860%), alkyl (50% C14, 40% C12, 10% C16) dimethyl benzyl ammonium chlorides (0.0216%)	Reckitt Benckiser (India) Pvt. Ltd.	https://www.rb.com/
Bacillol 25	450 mg/g propan-1-ol, 250 mg/g propan-2-ol, 47 mg/g ethanol	Raman & Weil Pvt. Ltd.	http://ramanweil.com/
Stardrops disinfectant spray	< 5% non-ionic surfactants, disinfectants, pine oil, 1.0 g benzalkonium chloride	Star Brands	starbrandsgroup.com
DR. PAX Double power multipurpose disinfectant	8.0% benzalkonium chloride I.P., 40% alkyl dimethyl benzyl ammonium chloride, lemon oil, purified water	Pax Group of Companies	https://paxgroup.com/
BodyGuard Multipurpose alcohol based disinfectant spray	70% v/v denatured ethanol, purified water, extracts; 0.30 mg <i>Vetiveriazanioides</i> , 0.30 mg <i>coriandrum sativum</i> , 0.25 mg <i>cyperusscariosus</i> , 0.10 mg <i>hedygium spicatum</i> , 0.05 mg <i>azadirachta indica</i>	Sirona	www.sironaindia.com
Lifebuoy Germ Killer	70% w/w ethanol, isopropyl alcohol, niacinamide, aloe vera	Lifebuoy	https://www.lifebuoy.co.za/
Bacto V Disinfectant Spray	70% (w/w) denatured ethanol-benzalkonium chloride, 100% w/w propellant	CavinKare	https://cavinkare.com/
Savlon Disinfectant Spray	95% v/v ethanol ip 62.00% w/w equivalent to 84.24% v/v absolute alcohol denatured with isopropyl alcohol, 3.1% w/w excipients, propellant	Savlon ⁺	https://www.savlon.in/

Fig. 1 Process of 1G ethanol production **a** from sugary feedstocks and **b** from starchy feedstocks; AMG: Amyloglucosidase



optimum urea (nitrogen source) and inoculum (*S. cerevisiae*) dosage at 4 and 0.5 g/l, respectively, at 35 °C resulting into an ethanol concentration of 87 g/l with a fermentation efficiency of 85.12% [56]. Maiti, Rathore, Srivastava, Shekhawat, and Srivastava [57] investigated another study of fermentation of SCM containing initial total sugars of 216 g/l using 10% (v/v) inoculum size (*Zymomonas mobilis* 2427) at 31 °C, and reported maximum ethanol yield of 59.59 g/l after 44 h. More recently, Wu, Chen, Cao, Lu, Huang, Lu, Chen, Chen, Guan, and Wei [53] studied the SCM fermentation with 70°C Brix value using industrially engineered strain *S. cerevisiae* MF01-PHO4 with 2×10^8 cells/ml, 0.2% (w/w) urea, and 0.02% (w/w) phosphoric acid at 30 °C, and reported a maximum ethanol yield of 114.71 g/l after 24 h [53]. Another sugar-rich feedstock which has been well studied for 1G ethanol production is sweet sorghum, which provides high ethanol yield per hectare (ha) of cultivation. The yield of sugary rich

stalk of sweet sorghum is 3–7 ton/ha, which is mainly utilized for fermentation (1G ethanol) out of the whole plant. Brix and sugar contents of sweet sorghum juice are in the range of 16–21 and 15–22%, respectively, depending on the variety, and exhibits potential of up to 10,600 l of ethanol/ha of sweet sorghum [58–60]. Brix content and biomass yield of sweet sorghum are less than sugarcane but water and fertilizer requirements for its cultivation are 1/3rd of sugarcane [61]. Juice extracted from sweet sorghum stalk comprising of sucrose, glucose, and fructose is screened to remove any particulate matter with subsequent sterilization, and is submitted for fermentation using suitable strain, e.g., *S. cerevisiae*. Ratnavathi, Suresh, Kumar, Pallavi, Komala, and Seetharama [60] reported 90 g/l ethanol through the fermentation of sweet sorghum juice containing 200 g/l sugars using 2% (v/v) cells of *S. cerevisiae* at 30 °C in 60 h. There is another study of fermentation of sweet sorghum juice

containing 191 g/l sugars using 1×10^8 /ml cells of *S. cerevisiae* at 30 °C resulting into ethanol concentration and yield as 82 g/l and 0.42 g/g total sugars consumed, respectively, which corresponds to 82.2% of the theoretical yield [58]. Fernandes, Braga, Fischer, Parrella, de Resende, and Cardoso [62] studied fermentation of juices of sweet sorghum with sugar concentration of 158.2 g/l using 30 g/l cells of *S. cerevisiae* Y940 at 35 °C resulting into ethanol concentration of 72.3 g/l and ethanol yield of 0.46 g/g total sugars consumed in 8 h. Apart from juice, other parts of 1G feedstocks e.g., sweet sorghum stem comprising of lignocellulosic composition, are utilized for 2G ethanol production as discussed later.

5.1.2 Starchy feedstocks

Starch-based feedstocks are comprised of storage polysaccharides in the form of starch, which in turn is formed of two chains of glucose, straight-chained amylose (α -1,4) and branched amylopectin (α -1,4; branching at α -1,6) forming 34–38 and 70–85% of total starch, respectively. The conversion of this complex polysaccharide requires hydrolysis of starch into fermentable sugars via (i) heating step, i.e., gelatinization comprising of heating the substrate in raw, powered form or chips along with water to enhance the enzyme accessibility towards it, (ii) liquefaction using α -amylase at high temperature, which hydrolyzes the α -1,4 linkage of starch causing the release of maltose, dextrin, maltopentoses, and maltotriose, and (iii) complete hydrolysis using amyloglucosidase (AMG), which breaks down the α -1,4 as well as α -1,6 linkages of starch resulting into the release of glucose along with other free soluble sugars if any, followed by the fermentation using selected microbial strain (Fig. 1b) [63]. However, gelatinization step is not necessary as reported by some researchers that it does not impact much on the hydrolysis rate of starch [64].

A variety of starch-containing feedstocks, e.g., corn, wheat, other grains, cassava, and sweet potato, are available, which are conventionally used in 1G ethanol production. The most important and leading starchy food crop used as ethanol feedstock is corn. The world's leading producer of ethanol, U.S.A produces 95% of its total ethanol using corn as the feedstock, and produced about 15.8 million gallons of ethanol during 2016, which was 54.3% of overall global ethanol production (29.1 million gal) (www.statista.com). Annual production of corn was about 1.04 billion ton during 2016–2017, U.S.A being the leading producer of corn contributed 37%, i.e., more than one-third of the world's production followed by China (21.2%) and Brazil (8.3%) [65]. The world's ethanol production from corn was almost doubled during 2007–2016. Corn is widely popular and highly successful crop worldwide with 72% starch, 9.5% fiber, 9.5% protein, and 4.3% oils, and is not only used as food, livestock feed, and feedstock for

ethanol production but also for various industrial products [66, 67].

Wheat is the second most widely used food grain utilized for ethanol production after corn. Annual production of wheat was 737.83 million metric tons in 2017 with European Union as the leading producer providing an average production of 150 million tons annually; however, individual countries, which are the leading producer of wheat, are China (130 million tons), India (90 million tons), and Russia (70 million tons) [65]. The average yield of wheat is about 3.4 tons/ha, which is almost half of that of corn (5.7 tons/ha). About 3% of total ethanol produced in U.S.A is from wheat after corn [65].

Other starch-containing food crops are tuber crops; for instance, cassava is the 5th most significant starch-containing food crop in the world with 70–90% starch content grown in the tropical and subtropical regions [68]. The annual production of cassava is approximately 250 million tons with the largest production in the African region providing 50% of the world's production, and Nigeria is the leading producer country with the annual production of more than 50 million tons [69]. Apart from its use in food and feed industry, cassava is widely used for ethanol production in countries like China, Thailand, and Vietnam in the form of dried chips, which are stored for longer use in the plant [70]. In a study, hydrolysis of cassava starch with enzyme derived from bacteria *Laceyell asacchari* LP175 supplemented with commercial glucoamylase was investigated at 50 °C for 12 h resulting into sugar concentration of 157 g/l with 66% hydrolysis rate, and subsequent fermentation of obtained sugars using *S. cerevisiae* M30 at 50 °C for 6 h followed by fermentation with *K. marxianus* DMKU-KS07 at 42 °C for 18 h resulting into 90.9 g/l ethanol concentration, which corresponds to 88% of theoretical yield and ethanol productivity of 3.79 g/l/h [71]. In another study, hydrolysis of cassava starch to glucose was done by using cultures of Loog-Pang (Thai rice cake inoculum) immobilized on thin shell silk cocoon at 35 °C for 120 h resulted into glucose concentration of 145.5 g/l with subsequent fermentation using 5% (v/v) cells of *S. cerevisiae* M30 at 33 °C for 72 h, and reported ethanol concentration of 71.2 g/l [72].

Sweet potato is another starch-enriched food crop with about 24.6–83.7% starch content along with 3.6–29.6% simple sugars, e.g., glucose, fructose, and sucrose providing it a sweet taste [73]. It is a promising feedstock for ethanol production, grown as a perennial crop in the tropical and subtropical regions and as an annual crop in the temperate regions. It is the world's 7th most significant food crop with the major use in the energy sector and as a phytochemical source of nutrition [74]. The annual production of sweet potato is about 2–15 ton/ha. Asia and Africa provide more than 90% sweet potato production in the world. China is the largest producer of sweet potato contributing 67% of the world's production followed by Indonesia, Vietnam, India, and so on [75, 76].

Due to high starch content (24.6–83.7%), significant content of simple sugars (3.6–29.6%), and good agricultural yield (2–15 ton/ha), sweet potato is mainly cultivated not for food but for energy sector particularly for ethanol production. Some of the industrial varieties of sweet potato possess the potential of ethanol yield as 4500–6500 l/ha [72, 77]. Preparation of sweet potato prior to bioprocessing into ethanol includes first chopping into small chips followed by crushing into powdered form by milling. Zhang, Zhao, Gan, Jin, Gao, Chen, Guan, and Wang [77] reported fermentation of raw sweet potato via liquefaction using α -amylase (Liquozyme Supra, Novozymes China) with loading of 0.12 KNU (Kilo Novo alpha-amylase Unit)/g substrate at 85 °C, pH 5.3, 20 min, saccharification with glucoamylase (*Aspergillus niger*) loading of 1.6 AGU (Amyloglucosidase unit)/g substrate for 3 h at 60 °C, and fermentation of obtained 28% (w/v) carbohydrates in substrate using 7% (v/v) cells of *S. cerevisiae* CCTCC M206111 at 30 °C, which resulted into the maximum ethanol concentration, yield, and productivity as 128.51 g/l, 91.4%, and 4.76 g/l/h, respectively, after 27 h. In a similar study, ethanol production was studied from sweet potato containing 75% (w/v) total sugars via liquefaction using 5.4 μ l of α -amylase (Liquozyme® SC, Novozymes) at 86 °C, saccharification using 5.4 μ l AMG (Spirizyme® Fuel, Novozymes) at 60 °C, and fermentation using 1×10^8 /ml cells of *S. cerevisiae* at 30 °C, resulted into ethanol concentration, yield, productivity, and fermentation efficiency of 45 g/l, 386.7 g/kg dry substrate, 3.2 g/l/h, and 84%, respectively, in 16 h [78]. In another study, pretreatment of liquid mash of sweet potato with cellulase enzyme was investigated with loading of 8 U/g dry substrate at 50 °C for 1 h resulting into reduced viscosity up to 81%, with subsequent liquefaction with 20 U/g dry substrate of α -amylase (from *Bacillus licheniformis*) at 95 °C for 0.5 h, and simultaneous saccharification and fermentation (SSF) by adding 200 U/g dry substrate of glucoamylase (*Aspergillus niger*) at 60 °C and 2 g/l yeast cells (*S. cerevisiae*) at 30 °C, and reported an ethanol concentration of 155 g/l from 284.2 g/l initial saccharides with an ethanol yield of 87.8% in 45 h [79].

5.2 Second-generation feedstocks

2G ethanol is produced from non-food LCB, and emerging area of research due to unsustainability of 1G ethanol owing to its sugar- and starch-based feedstocks, which are basically food crops or their derivatives causing increased global crisis of food scarcity [80, 81]. On the other hand, LCB is a sustainable feedstock due to its abundant availability, therefore a promising feedstock for large-scale and environment-friendly ethanol production. LCB have potential to be available as a major feedstock for the bioenergy sector [82, 83]. A total of 442 billion liters of bioethanol can be produced annually by utilizing LCB, and this number can rise to 491 billion

liters (approximately 16 times higher than the global production) after utilizing all crop residues and wasted crops [84, 85].

In India, states with highest biomass availability per unit area are as follows: Uttar Pradesh, Punjab, Haryana, Maharashtra, West Bengal, and Tamil Nadu. Annual agro-residue production is estimated to be 103 million tons of dry matter, whereas average forest residues production rate for temperate northern countries is about 12%. Biofuel policies of nations like U.S.A and EU have encouraged the growth of 2G ethanol at the global level causing enhanced contribution of inexpensive feedstocks towards growth of global market of ethanol [86]. The major LCB-based ethanol plants are located in Kansas, Texas, Illinois, Iowa, North Dakota and British Columbia, Minnesota and Nebraska, and Saskatchewan and Alberta. A novel environment-friendly process has been developed by Tel Aviv University, Israel, for local production of ethanol and hand sanitizers from paper and plant waste (<https://phys.org/news/2020-07-low-cost-sanitizer.html>). 2G ethanol plants located in India along with their capacity are summarized in Table 3.

The main components of lignocelluloses used for the bio-conversion into ethanol are polysaccharides; cellulose (30–50%), and hemicellulose (20–40%), which are hydrolyzed into their respective monomeric sugars that are glucose and xylose (along with arabinose, mannose, galactose, etc.), respectively [85, 87]. The presence of recalcitrant lignin (10–20%) in biomass hinders the accessibility of polymeric sugars for microbial utilization, which necessitates the prerequisite steps for 2G ethanol production that are pretreatment and enzymatic hydrolysis before fermentation [8, 85, 86]. Fermentation of monomeric sugars released after enzymatic hydrolysis is the key step using a suitable competent strain under favorable conditions. Although there is vast potential of 2G ethanol as the best alternative of 1G ethanol, which could resolve the issues related to imbalance in ethanol demand and production as well as food scarcity, however 2G ethanol production is a very expensive process due to which it is still under development to be commercialized successfully. One of the major steps which contribute the high cost to the process is pretreatment of biomass, which is carried out to make the cellulose and hemicellulose accessible to hydrolytic enzymes, and is proceeded through various physical, thermochemical, biological/enzymatic, or combined methods [8, 88, 89]. Furthermore, another major step contributing higher cost to the process is hydrolysis of accessed cellulose and hemicellulose, which is accomplished by chemical agents (specifically mineral acids) or enzymes [12, 85]. However, due to hazardous, toxic, and corrosive nature of mineral acids, requirement of expensive and sensitive equipment makes them economically as well as environmentally undesirable.

On the other hand, hydrolytic enzymes, available for specific polysaccharides and their components; cellulases, and hemicellulases are conveniently used for saccharification of

Table 3 List of 2G ethanol plants located in India along with their capacity

Name of the plant	Status	Capacity	Reference
Enfinity – Praj, Pune	Active	1 million liters per annum	https://praj.net/business-lines/bio-energy/2nd-generation-ethanol/
DBT-JCT, Kashipur (Uttarakhand)	Active	75,000 liters per annum	https://www.biofuelsdigest.com/bdigest/2016/04/21/indian-cellulosic-ethanol-technology-set-for-debut-at-demonstration-scale-in-uttarakhand/
IOCL, Panipat (Maharashtra)	Under construction	33.5 Kilo tons per annum	http://environmentclearance.nic.in/writereaddata/EC/2806201917BAL97UFR.pdf
MRPL, Harihar (Karnataka)	Under construction	60,000 LPD	https://bioenergyinternational.com/biofuels-oils/mrpl-planning-to-build-cellulosic-ethanol-plant-in-karnataka#:~:text=In%20India%2C%20Mangalore%20Refinery%20and,Davanagere%20district%20of%20Karnataka%20State
HPCL, Bathinda (Punjab)	Under construction	100 KL PD	http://www.ppcb.gov.in/Attachments/Proceedings%20of%20Public%20Hearings/HPCLExecutiveSummaryEng.pdf

these polymeric sugars into respective monomers on account of their working under mild conditions, harmless, and non-corrosive nature [8]. In spite of efficient hydrolysis of biomass, expensive hydrolytic enzymes make the process very costly, which needs to be reduced by means of using crude enzyme preparations, lower enzyme loading, fed-batch fermentation, etc. Other major factors responsible for the high cost of process include pH and temperature sensitivity of hydrolytic enzyme and microbial strain, feedback inhibition by substrates/metabolites/products leading to the lower product yield, which require highly sensitive and well-equipped reactors and chemicals for pH and temperature maintenance as well as selection of appropriate operative strategy for 2G ethanol process. Various operating strategies include (i) separate hydrolysis and fermentation (SHF); (ii) simultaneous saccharification and fermentation (SSF); (iii) simultaneous saccharification and co-fermentation (SSCF); (iv) semi- or pre-simultaneous saccharification and fermentation (SSSF or PSSF); (v) simultaneous saccharification filtration and fermentation (SSFF); and (vi) direct microbial conversion (DMC)/consolidated bioprocessing (CBP) in a single vessel or within a single microbial strain (genetically modified) to make the process cost-effective [90].

The widely used and promising LCBs well studied for 2G ethanol production are sugarcane tops and bagasse, rice straw, wheat straw, other cereal residues, residues of other crops such as cotton and chilli cultivation, forest residues such as bamboo, rye, pine needles, banana stem, sunflower stalk, stem of sweet sorghum, and weeds like *Saccharum spontaneum*, *Eichornia crassipes*, *Prosopis juliflora*, and *Lantana camara* with ethanol generating potential of 5.42 billion liters of ethanol considering 50% conversion rate [10, 91–96]. Sugarcane top is the most abundant agro-residue with annual production of 79.4 million mega ton (MMT), and is always burnt in the field itself [10]. Sugarcane bagasse (SCB) is also generated in good quantities with annual production as 1.88 Gt in sugar industry but it is utilized for electricity co-generation in sugar mills, and paper making in pulp and paper industry. SCB has been widely studied for 2G ethanol production: for instance, Chandel, Antunes, Silva, and da Silva [97] reported ethanol production from liquid ammonia pretreated (20%, v/v ammonia at 70 °C for 24 h) SCB via enzymatic saccharification using cellulase (Celluclast 1.5 l) and β -glucosidase (Novozyme 188) with loadings of 15 FPU/g dry biomass and 17.5 U/g dry biomass at 50 °C for 24 h and subsequent fermentation with *Pichia stipitis* (1 g/l, dry wt.) at 30 °C for 96 h, which resulted into reducing sugar concentration and yield of 28.43 g/l and 570 g/kg pretreated biomass (PB), respectively, and maximum ethanol concentration and yield of 10.31 g/l and yield of 0.387 g/g sugars consumed with 75.88% of fermentation efficiency. In a similar study, sodium hydroxide pretreated SCB (1.8%, w/v NaOH at 110 °C for 60 min) fermented via pre-hydrolysis using 10 FPU (filter paper

unit)/g substrate cellulase loading (Cellic CTec2, Novozymes) at 50 °C in 12 h, and fermentation using 1 g/l (dry wt.) of *S. cerevisiae* Y-2034 at 37 °C, and obtained maximum ethanol concentration of 31.25 g/l in 72 h [98].

Next surplus biomass available for the 2G ethanol belongs to the cereal crops, e.g., rice straw, wheat straw, and other cereal straws with annual production of 8.5, 9.1, and 6 MMT, respectively, although as a major share of it is consumed as fodder [10]. Uttar Pradesh generates highest wheat straw (33%) followed by Punjab, Haryana, Madhya Pradesh, and Bihar contributing more than 85% of total wheat straw production in India [94]. These agro-residual biomasses possess a vast potential of being converted into ethanol as investigated through various studies. For example, Arora, Behera, Sharma, Singh, Yadav, and Kumar [99] reported an ethanol production from alkali pretreated rice straw (0.5% (w/v) NaOH at 121 °C, 15 psi for 1 h) via saccharification with cellulase (*A. niger*) at a loading of 80 U/g PB at 45 °C for 24 h, and subsequent fermentation with *K. marxianus* NIRE-K3 at 45 °C resulting into glucose and xylose release as 10.47 and 1.85 g/l, respectively, and ethanol concentration, yield, and productivity as 3.98 g/l, 0.38 g/g of glucose, and 0.22 g/l/h, respectively, with 74.5% fermentation efficiency. In another study, bioconversion of wheat straw (pretreated by 0.9%, w/w H₂SO₄, and steam explosion at 180 °C for 10 min) to ethanol via SSF was studied using 15 FPU/g dry biomass of cellulase (Celluclast 1.5 l), 12.6 IU/g dry biomass of β -glucosidase (Novozyme 188), and 0.2 g/l cells of *K. marxianus* CECT 10875 at 42 °C for 72 h resulting into maximum sugar yield of 300 g/kg raw straw and ethanol yield of 110.5 g/kg raw straw [100]. Cotton, chilli, pulses, and oil-seeds produce a good quantity of biomass as they are not utilized in any other potential application and could be used for ethanol production. Bamboo plant and its processing waste are also abundantly available in India with annual production of 4 and 3.3 MMT, respectively [10]. A schematic representation of production of hand sanitizers from lignocellulosic-based ethanol and their application in combating hospital and community acquired infectious diseases is given in Fig. 2.

6 Industrial scenario of ethanol-based sanitizers in India

There is an exponential growth in the ethanol-based hand sanitizer market in the past few years. The outbreak of global coronavirus in 2019 has led to increase the demand of hand sanitizers by 1400% all across the globe during December 2019 to February 2020. As per the report published by Fior Markets, the global market of hand sanitizers is expected to increase at a CAGR of 7.5%, i.e., from 1.2 billion USD in 2019 to 2.14 billion USD by 2027 (<https://www.globenewswire.com/news-release/2020/03/26/2007160/0/en/>

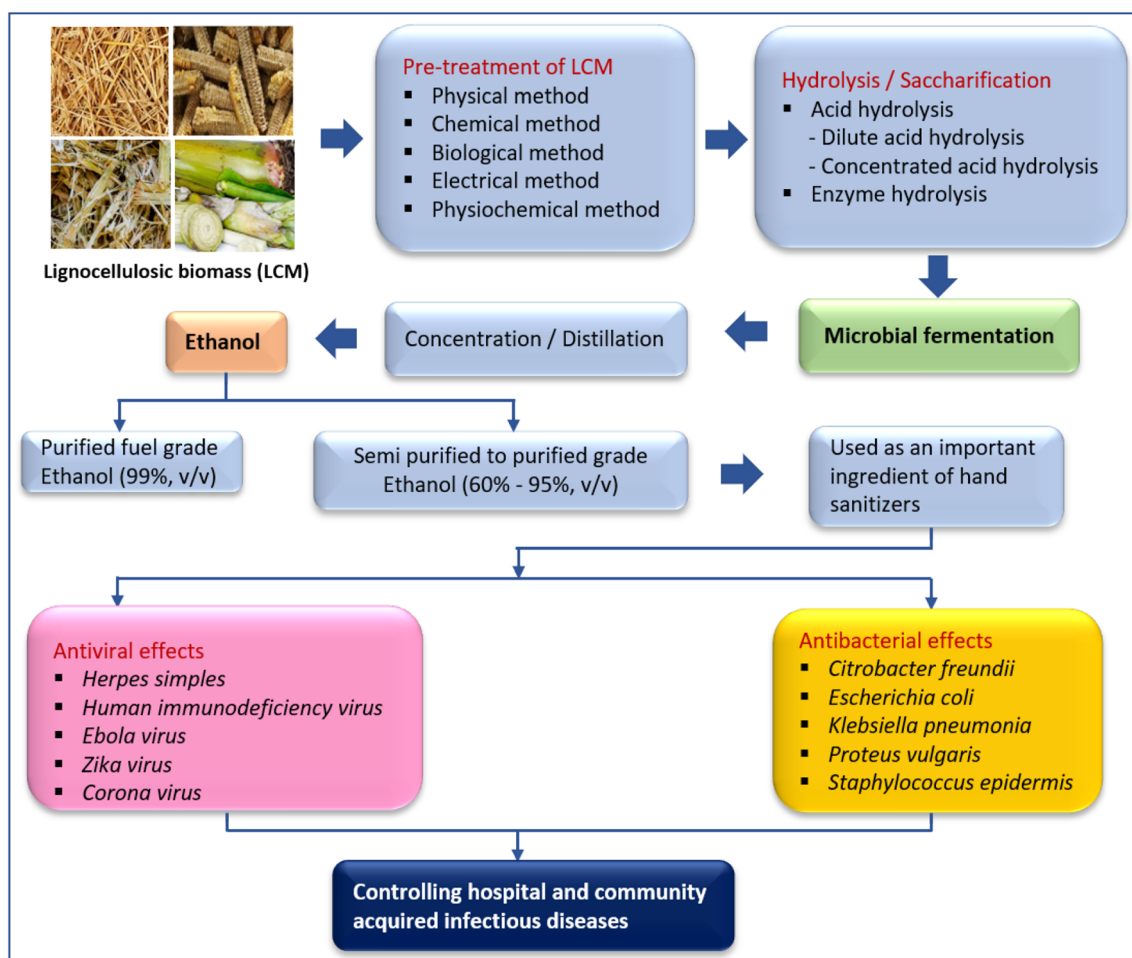


Fig. 2 Production of ethanol-based hand sanitizers by utilizing various lignocellulosic wastes

[Global-Hand-Sanitizer-Market-Is-Expected-to-Reach-USD-2-14-Billion-by-2027-Fior-Markets.html](https://www.marketresearch.com/ChemAnalyst-v4204/India-Ethanol-Plant-Capacity-Production-13320153/)).

The demand of hand sanitizers broke records in India since COVID-19 hit the country, which resulted in abrupt rise in ethanol demand. Therefore, there is a rise in ethanol production by several sugar mills conforming to the guidelines from All India Distiller Association (AIDA), and Indian Sugar Mills Association (ISMA) (<https://www.marketresearch.com/ChemAnalyst-v4204/India-Ethanol-Plant-Capacity-Production-13320153/>).

6.1 Impact of 2G ethanol-based sanitizer industries on economy

India is a developing agricultural country, where abundance of agricultural raw materials, i.e., waste starchy materials (i.e., barley, corn, rice, wheat processing waste), sucrose-containing feedstocks (i.e., sugarbeets, fruits, sugarcane), and lignocellulosic feedstocks (i.e., grasses, wood, corncob, rice straw, rice husk, wheat straw, switchgrass) are produced annually, and most of them remain unutilized and lead to the environmental pollution. From the past few years, the utilization of low-cost agricultural feedstocks (mainly LCB)

has captured scientific attention for the production of 2G ethanol. The integrated technologies that involve the cost-effective production of bioethanol include SHF, SSF/SSCF, and CBP, which have already been discussed in Section 5.2 [101]. Such lignocellulosic feedstocks also provide tremendous opportunities in the healthcare sector for the production of disinfectants and hand sanitizers. The current synthesis of ethanol for sanitizers is carried out by utilizing only molasses, and sugar mills, and it makes the market less competitive. The agricultural residues or lignocellulosic feedstocks also provide an opportunity for cost-effective production of sanitizers. A strong collaboration between government agencies, scientific institutions, universities, and agricultural and finance ministries may help to overcome this issue. The global demand of ethanol has enhanced since 2019 after COVID-19 pandemic, and the development of an economic technology with simultaneous pretreatment, hydrolysis, and fermentation alternates for the production of low-cost disinfectants. On one hand, the utilization of lignocellulosic wastes for the production of value-added products such as bioethanol, disinfectants, and hand sanitizers helps to reduce environmental pollution caused by their improper disposal; on the other hand, their

utilization also contributed to the nation's economy by marketing and export of these value-added products.

Red River Biorefinery (RRB), North Dakota, U.S.A, which utilizes 500,000 tons of agricultural by-products per year for the production of ethanol, has recently started producing pharmaceutical grade (USP) ethanol for production of disinfectants and hand sanitizers (<http://www.prnewswire.com/news-releases/red-river-biorefinery-now-producing-pharmaceutical-grade-usp-ethanol-for-hand-sanitizers-and-disinfectants-301146352.html>). Apart from specially cultivated food grains, wasted grains during transportation, processing, and storage are also utilized for ethanol refinery. Food grains have been exploited by Indian companies for ethanol production, and based on the sources utilized, Indian ethanol market has been categorized into grain-based ethanol, and mixed grain-based ethanol in addition to the molasses and sugar-based ethanol (<https://www.techsciresearch.com/report/india-ethanol-market/3860.html>). The Government of India has approved the utilization of rice available with Food Corporation of India (FCI) for ethanol production at a meeting of the National Biofuel Coordination Committee (NBCC) held under the Chairmanship of the Minister of Petroleum and Natural Gas. The bioethanol, produced from rice, has aimed to be utilized for blending with petrol, and manufacturing of alcohol-based hand sanitizers (<https://www.livemint.com/news/india/fci-s-surplus-rice-stocks-to-be-converted-into-ethanol-to-make-hand-sanitisers-11587408039897.html>). The central government has taken a decision to convert surplus rice lying in the warehouses of the FCI to ethanol for production of hand sanitizers to help India's fight during the COVID-19 public health emergency (<https://qrius.com/india-is-using-rice-for-hand-sanitisers-as-millions-go-hungry/>)

6.2 Use of hydrated ethanol in sanitizers

Some of the by-products present in the fermentation media during ethanol production from lignocellulosic feedstock are ketones (diacetyl), aldehydes (acetaldehyde), aromatic compounds (phenol, styrene, benzoic acid), alcohols (propanol, butanol, methylpropanol, conifer alcohol, sinapyl alcohol, p-coumaryl alcohol), fatty acids (acetic acid, propionic acid, butyric acid, butanoic acid, pentanoic acid, hexanoic acid, octanoic acid, decanoic acid, dodecanoic acid), and esters (ethyl acetate, ethyl formate, propyl acetate, hexyl acetate, ethyl octanoate, ethyl dodecanoate), and these by-products need to be removed by purification to get fuel grade ethanol. The technologies used in ethanol purification are distillation, adsorption, pervaporation, and ozonation. Distillation is the most commonly used step in purification for the separation and concentration of ethanol from the azeotropic mixtures, containing two or more compounds, based on volatilities [102–104]. Sanitizers, used in healthcare sector, contain 70% (v/v) ethanol that is less in concentration required in

biorefinery area (95.63%, v/v). The low-concentration ethanol can be obtained from primary distillation and thereby bypass the subsequent steps of purification. The energy-demanding purification steps, required to obtain purified ethanol from binary azeotrope water-ethanol, can be omitted for the production of disinfectants, which further reduces its production cost and makes the process cost and energy efficient. Therefore, 2G ethanol plants can be integrated with sanitizer production plants to fulfill its global demand.

7 Health issues of ethanol-based sanitizers

The excessive use of hand hygiene products namely soaps and sanitizers may damage the skin by reducing the stratum corneum water-binding capacity, altering intracellular lipids, denaturing stratum corneum proteins, and decreasing the number of corneocytes [105]. These lipid-dissolving alcohols and emulsifying detergents penetrate deeper into the skin layers which result in depletion of lipid barrier and alteration of normal skin flora [106]. The use of ABHS commonly results in skin reactions including allergic contact dermatitis with manifestations of anaphylactic symptoms and respiratory distress, and irritant contact dermatitis with symptoms of erythema, dryness, bleeding, and pruritus, and these symptoms may range from mild to severe [107]. ABHS may also dry the hands, which may further lead to cracks or peeling of skin [108]. The regular application of ethanol on the skin through disinfectants results in the accumulation of small amount of ethanol and its metabolites (acetaldehyde) in blood at acute levels [109]. Ethanol-based hand sanitizers are proved to show less skin-irritant property as compared to sanitizers containing isopropanol and n-propanol [110]. Some of the common measures to prevent the skin irritation and other adverse effects of ABHS are avoiding habits that may cause skin irritation, selection of hand hygiene products with less irritating agent, and moisturizing of skin after using hand sanitizers [111, 112]. There can be inhalation and/or dermal absorption (passive alcoholism) in healthcare workers and people in hospitals due to regular use of ethanol-based hand sanitizers [113]. Similarly, the occupational use of alcohol-based antiseptics could generate detectable amount of ethanol in the blood (contributed from both inhalation and absorption of volatilized product) as proved by physiologically based pharmacokinetic and epidemiological studies [114]. Some common clinical effects such as nausea, abdominal pain, headache, loss of coordination, decreased level of consciousness, and blurred vision are observed to be similar with methanol and ethanol poisoning. Severely adverse health effects have been reported in Arizona and New Mexico with alcohol-containing hand sanitizers. There is higher risk for esophageal cancer after alcohol consumption in populations which lack in the activity of aldehyde dehydrogenase (ALD), involved in ethanol

catabolism, compared to the populations with fully functional ALD [115]. There are several previous reports which have proved the presence of ethanol in blood and urinary ethyl glucuronide after exposure to ethanol-based hand sanitizers [116–118]. Recently, Yangzes and his coworkers have reported the ocular injury in children after using alcohol-based hand rubs [119].

8 Conclusion

Alcohol-based (specifically ethanol) hand sanitizers and disinfectants exhibit high potential of killing or inactivating broad range of pathogens, and led to the rise in demand of ethanol-based formulations by 1400% all across the world from December 2019 to February 2020 as reported by the WHO. They have been emerged as the first line of defense against latest SARS-CoV-2 virus and have therefore triggered the demand of ethanol manifolds. Ethanol is globally (including India) produced by using sugar- or starch-rich food crops or their processed by-products as 1G ethanol, and utilized as biofuel, ingredient of pharmaceuticals, household products (paints, detergents, inks, and coatings), food and beverages, and cosmetics and beauty products. Large production of 1G ethanol from food crops and by-products led to the major issues of food scarcity worldwide, which necessitates the exploration of non-food LCB to be utilized for 2G ethanol production causing a major research focused on the particular area. In India, a foreseeable amount of lignocellulosic waste is generated annually in the form of agro-residues, forestry residues, weeds etc., which is mostly burnt or left in the fields unutilized, which could be utilized for sustainable 2G ethanol production. Therefore, the recent paradigm of ethanol production has shifted from edible grains/molasses towards non-edible lignocellulosic feedstocks eliminating the challenges of food crisis. Moreover, the availability of LCB in abundance throughout the year offers a sustainable biotechnological solution to the escalating ethanol demand in India and across the globe. In the present time of COVID-19 outbreak, the 1G and 2G ethanol could be extremely useful to cater the burgeoning demand of hand sanitizers. This seems a viable and judicious fit in the on-going campaign of *Atmanirbhar Bharat* (Self-reliant India) by Government of India, which will leverage the multiple benefits to the rural and micro, small and medium enterprises driven economy.

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