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Escherichia coli as Model Organism and its Application in Biotechnology: A Review

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Abstract: *Escherichia coli* (*E. coli)* is a short Gram-negative, facultative anaerobic and rod shaped bacterium of the genus *Escherichia* that is commonly found in the lower intestine (Colon) of warm-blooded organisms. Itis most widely studied prokaryotic model organism in the fields of biotechnology and microbiology. The bacterium has the ability to take up nutrients from its environment but also to synthesize many nutrients when they are not available, enabling growth on a minimal medium. *E. coli* K-12 is first *E. coli* strain to have its genome sequenced used for several decades as a model bacterium as well as an industrial workhorse due to its relatively short doubling time and easiness in genetic modification. Nonpathogenic strains of *E. coli* serve as probiotic agents in the field of medicine especially to treat various diseases of gastrointestinal tract. The bacterium cells can be genetically modified so that they have the gene for producing human insulin. The presence of *E .coli* in environmental samples, food, or water usually indicates recent fecal contamination or poor sanitation practices in food-processing facilities.In conclusion, *E. coli* are a natural mammalian gut bacteria used as a model organism for scientific research. It is the most preferred microorganism to express heterologous proteins for therapeutic use. It's advisable to encounter *E. coli*, in to Antibiotic production since polyketides favoring the process of antibiotic production with high rates in *E. coli*.

Key words: Biotechnology · *E. coli* · Model Organisms · Non Pathogenic Strain

INTRODUCTION

A microorganism is a living thing that is so small to be viewed with a microscope. Many of these are useful to human and nature while some are harmful and cause diseases. *E. coli* is the microorganism belongs to a group of bacteria known as coliforms that are found in the gastrointestinal tract of warm-blooded animals. a model organism is a species that has been widely studied, usually because it is easy to maintain and breed in a laboratory setting and has particular experimental advantages [1].

In eukaryotes, several yeasts, particularly *Saccharomyces cerevisiae* (baker's or budding yeast), have been widely used in Genetics and Cell Biology largely because they are quick and easy to grow. The cell cycle in simple yeast is very similar to the cell cycle in humans and is regulated by homologous proteins. The fruit fly, e.g., *Drosophila melanogaster* (one of the most famous subjects for experiments) is studied again, because it is easy to grow for an animal and has various visible congenital traits and has a polytene (giant) chromosome in its salivary glands that can be examined under a light microscope. A roundworm (nematode), *Caenorhabditiselegns*is studied because it has very defined development patterns involving fixed numbers of cells and it can be rapidly assayed for abnormalities [2].

Escherichia coli are the frequently used model organism in microbiology study.As compared to other living organisms more is known about *E. coli* because of its simple nutritional requirements, rapid growth rate and most important it's well established genetics. Rate of cell division of *E. coli* is average of once in every 20 min, thus enabling quick environmental adaptation. This fast division rate has helped in evolutionary experiments which are conducted in the laboratories [3]. Plasmids are

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extra chromosomal molecules that are self-replicative and sometimes provide interesting features to its host.

Nonpathogenic organisms are organisms that do not cause disease, harm or death to another organism and is usually used to describe bacteria. Pathogenic organisms are an organism which is capable of causing diseases in a host (person). Non-pathogenic *E. coli* strains provides the host benefits by producing vitamin K, B_{12} and preventing disease by colonizing the intestinal part however, certain *E. coli* strains can cause disease [4]. Nonpathogenic strains of *E. coli* serve as probiotic agents in the field of medicine especially to treat various diseases of gastrointestinal tract [5].

Most nonpathogenic *E. coli* live in our intestines assist waste processing and food absorption [6] and various protein expression systems have been developed which allow the production of recombinant proteins in *E. coli*. One of the applications of recombinant DNA technology was the manipulation of *E. coli* to produce human insulin [7]. Modified *E. coli* cells also used in production of biofuels [8]. Therefore the objectives of these papers are to review *E. coli* as model organism and its application in bio technology because most of the students in our colleges written on pathogenic strains of *E. coli*.

In 1885, the German-Austrian pediatrician Theodor Escherich discovered this organism in the feces of healthy individuals. He called it Bacterium *coli commune* because it is found in the colon [9]. *E. coli* is a Gram-negative, facultative anaerobic that makes ATP by aerobic respiration if oxygen is present, but is capable of switching to fermentation or anaerobic respiration if oxygen is absent and non-sporulation bacterium [10]. The Bacterium is typically rod-shaped and is about 2.0 µm long and 0.25 -1.0 µm in diameter with a cell volume of 0.6-0.7 µm [11].

Genes in *E. coli* are usually named by 4-letter acronyms that derive from their function. For instance, recA is named after its role in homologous recombination plus the letter A. Functionally related genes are named recB, recC, recD etc. The proteins are named by uppercase acronyms, e.g. RecA, RecB, etc. When the genome of *E. coli* was sequenced, all genes were numbered (more or less) in their order on the genome and abbreviated by b numbers, such as b2819 (=recD) etc. The "b" names were created after Fred Blattner who led the genome sequence effort [12]. Optimum growth of *E. coli* occurs at 37°C (98.6°F), but some laboratory strains can multiply at temperatures up to 49°C (120°F) [13]. *E. coli* grows in a variety of defined laboratory media, such as lysogeny broth, or any medium that contains glucose, ammonium water [14]. Therefore, the aim of this seminar is to review *E. coli* as model organism and its application in bio technology.

***Escherichia coli* as Model Organisms:** *Escherichia coli (E. coli)* is a short Gram-negative, facultative anaerobic, rod shaped bacterium of the genus *Escherichia* that is commonly found in the lower intestine (Colon) of warm-blooded organisms [15]. Model organisms are non-human species that are used in the laboratory to help scientists understand biological processes. They are usually organisms that are easy to maintain and breed in a laboratory (lab) settingand have particular experimental advantages [2]. In a laboratory setting, the *E. coli* can be grown inexpensively and easily. It iswidely studied for about 60 years. So, the bacterium is the most extensively investigated model organism and considered to be very important species in biotechnology and microbiology [1].

E. coli has the ability to take up nutrients from its environment but also to synthesize many nutrients when they are not available, enabling growth on a minimal medium (a simple medium with only the essential nutrients for *E. coli* growth). This versatility allows the identification of mutants that cannot grow on minimal media but can grow when specific nutrients are added. The attributes that make Escherichia coli an excellent model organism are: Single-celled organism, its ability to reproduce rapidly, it's growing very Easily, its survival in variable growth conditions, Presence of naturally occurring harmless *E. coli* and its ability to manipulate very easily [16].

***E .coli* As Single-Celled Organism:** There are no ethical concerns about growing, manipulating and killing bacterial cells, unlike multicellular model organisms like mice or chimps. They are also tiny cells, so in a small laboratory we can have flasks containing billions of cells that take up very little room, allowing many experiments [17].

Abilities of *E. coli* to Reproduce and Grow Very Rapidly: *E. coli* doubling its population about every 20 minutes. This is helpful in a laboratory (Lab.) situation where waiting for subsequent generations to produce experimentaldata that can be the rate-limiting step. With *E. coli* it is as easy and fast as letting them grow overnight. The nutrient mixtures in which *E. coli* divide most rapidly include glucose, salts and various organic compounds, such as amino acids, vitamins and nucleic acid precursors [18].

However, the bacterium can also grow in much simpler media consisting only of salts, a source of nitrogen (such as ammonia) and a source of carbon and energy (such as glucose). In such a medium the bacteria grow a little more slowly (with a division time of about 40 minutes) because they must synthesize all their own amino acids, nucleotides and other organic compounds. The ability of *E. coli* to carry out these biosynthetic reactions in simple defined media has made them extremely useful in elucidating the biochemical pathways involved. Thus, the rapid growth and simple nutritional requirements of *E. coli* have greatly facilitated fundamental experiments in both molecular biology and microbiology [19].

Genetic Manipulation of *E. coli:* *Escherichia coli* have been especially useful to molecular biologists because of both its relative simplicity and the ease with which it can be propagated and studied in the laboratory. The genome of *E. coli*, for example, consists of approximately 4.6 million base pairs and encodes about 4000 different protein. The human genome is nearly a thousand times more complex (approximately 3 billion base pairs) and encodes about 100,000 different proteins. The small size of the *E. coli* genome provides obvious advantages for genetic analysis and the sequence of the entire *E. coli* genome has been determined [20].

Plasmid and the *E. coli* Revolution: The term Plasmid was first coined by Joshua Lederberg in 1952 referring to genetic elements in bacteria that remained as an independent molecule from the chromosome at any stage of their replication cycle. Plasmids are extra chromosomal molecules that are self-replicative and sometimes provide interesting features to its host. These molecules are present not only in eubacteria but also are found in Archea and some lower eukaryotic organisms. Many bacteria contain self-replicating DNA molecules that can be harnessed for molecular biology applications. *E. coli* plasmids were the first ones to be extensively modified for such purposes [21].

Plasmids must contain several important features to be used in research: proper size for ease to transform or transfect, selection markers, a replication origin, regulatory elements to control expression and transcription termination. All features are important when designing a plasmid vector for the desired application, the reader can imagine the goal and there will always be a way to create the molecular tool for achieving such a goal and that is possible due to the basic structure of most plasmids used in molecular biology and their modularity [22].

Nonpathogenic *Escherichia coli*: Nonpathogenic strains of *Escherichia coli* serve as probiotic agents in the field of medicine especially to treat various diseases of gastrointestinal tract [5]. Cultivated strains (e.g. *E. coli* K12) are well-adapted to the laboratory environment and unlike wild-type strains have lost their ability to thrive in the intestine. The harmless strains are part of the normal flora of the gut and can benefit their hosts by producing vitamin K and preventing colonization of the intestine with pathogenic bacteria. Most *E. coli* live in our intestines, where they help our body breakdown the food we eat as well as assist with waste processing and food absorption [6].

Escherichia coli K-12 is first *E. coli* strain that its genome was sequenced used for several decades as a model bacterium as well as an industrial workhorse due to its relatively short doubling time and easiness in genetic modification. SacC enzyme in *Mannheimiasucciniciproducens* hydrolysis the sucrose in extra cellular space to confer the sucrose utilizing capability to other organisms which do not have the ability to utilize. Many researchers to Attempt to develop an *E. coli* K-12 derivative possessing sucrose-metabolizing capability by transfer SacC enzyme from *Mannheimiasucciniciproducens* (*M. succiniciproducens*) for producing Sucrose [23]. It has great advantages as a raw material for biotechnological applications. It is less expensive than other common carbohydrates and can be used as a protectant of proteins from many types of stresses [24].

Therapeutic Use of Nonpathogenic *Escherichia coli*: Bacterial flora plays an important role in the treatment inflammatory bowel disease (IBD) [25]. *E. coli* Nissle 1917 was isolated by AlfredNissle in 1917 from the feces of a soldier for prevention ortreatment of GIT diseases [26]. It contains active component of the microbial drug Mutaflor used in several European countries as a probiotic drug for the treatment of IBD. Nissle 1917 had equivalent efficacy to mesalazine for the treatment ulcerative colitis [27].

The anti-inflammatory effect of *E. coli* Nissle 1917 on pro-inflammatory cytokine production from intestinal epithelial cells is by suppressing IL-8 production from Intestinal epithelial cells (IEC) [28]. These suppressive functions of the non-pathogenic bacteria contribute to maintaining the intestinal homeostasis or to show the therapeutic effects as a probiotics. Generally Nissle 1917 treatment prevent either acute and chronic colitis via suppression of the pro-inflammatory cytokines production by mesenteric lymph node (MLN) or lamina propria mononuclear cells (LPMCs) [29].

Table 1: List of biopharmaceuticals produced in *E. coli*

Biopharmaceutical products	Therapeutic indication	Year of approval	Company
Humulin (rh insulin)	Diabetes	1982 US	Eli Lilly
IntronA (interferon α2b)	Cancer, hepatitis, genital warts	1986 US	Schering-Plough
Roferon (interferon α2a)	Leukemia	1986 US	Hoffmann-La-Roche
Humatrope (somatropin rh growth hormone)	hGH deficiency in children	1987 US	Eli Lilly
Neupogen (filgrastim)	Neutropenia	1991 US	Amgen Inc.
Betaferon (interferon β-1b)	Multiple sclerosis	1993 US	Schering Ag
Lispro (fast-acting insulin	Diabetes	1996 US	Eli Lilly
Rapilysin (reteplase)	Acute myocardial Infraction	1996 US	Roche
Infergen (interferon alfacon-1)	Chronic hepatitis C	1997 US	Amgen
Glucagon	Hypoglycemia	1998 US	Eli Lilly
Beromun (tasonermin	Soft sarcoma	1999 EU	Boehringer
Ontak (denileukindiftitox)	Cutaneous T-cell Lymphoma	1999 US	Seragen Inc.
Lantus (long-acting insulin glargine	Diabetes	2000 US	Aventis
Kineret (anakinra)	Rheumatoid arthritis	2001 US	Amgen
Natrecor (nesiritide)	Congestive heart failure	2001 US	Scios Inc.
Protect (human parathyroid hormone	Osteoporosis	2006 EU	Denmark

Source: [36].

Applications of *Escherichia coli* in Biotechnology: *Escherichia coli* hold an important position in industrial microbiology and modern biological engineering because of its easy manipulation and also long history of its laboratory cultures [30]. Used for the production of heterologous proteins [31] and various protein expression systems have been developed which allow the production of recombinant proteins in *E. coli*. One of the first useful applications of recombinant DNA technology was the manipulation of *E. coli* to produce human insulin [32].

However, several disadvantages limit its use for production of recombinant biopharmaceuticals. Various post-translational modifications (PTMs) such as glycosylation, phosphorylation, proteolytic processing and formations of disulfide bonds which are very crucial for biological activity do not occur in *E. coli* [7].

Many folded forms of proteins have been successful in expressing them in *E. coli* which was previously thought to be difficult and even impossible [33]. Proteins that need post-translational modification glycosylation for function or stability use the system of N-linked glycosylation which is found in *Campylobacter jejuni*engineered into *E. coli* for their expression [34]. As a result, Engineering of *Campylobacter* N-linked glycosylation pathway into *E. coli* provides an opportunity to express heterologous proteins in glycosylated form in *E. coli.* The bacteriumcells in modified form are also used in the development of vaccine and biofuels production [8].

Production of Biopharmaceuticals in *E. coli*: *Escherichia coli* is one of the most desirable hosts for the expression of several recombinant proteins due to its rapid growth rate, easier genetic manipulations and high level of recombinant protein synthesis rates. It is the host used for manufacturing a biopharmaceutical [35]. (Table 1 show List of biopharmaceuticals produced in *E. coli*).

Post-Translational Modifications: *Escherichia coli*is a favorite microorganism of biotechnologists for the large-scale production of therapeutic proteins [37]. However, the absence of post-translational modification processes in *E. coli* limits its use for the production of recombinant biopharmaceuticals. Various post-translational modifications, including glycosylation and phosphorylation, which are critical for functional activity, do not take place in *E. coli* due to its lack of such cellular machinery [38]. N-Linked glycosylation of proteins is one of the most important post-translational modifications in eukaryotes [39]. Identified as a novel N-linked glycosylation pathway in the bacterium *Campylobacter jejuni* show the successful transfer of a functionally active Nglycosylation pathway into *E. coli*. *Campylobacter jejuni* harbors pgl gene clusters, which are involved in the synthesis of various glycoproteins. By successfully transferring the pgl pathway into *E. coli*, various glycosylated proteins were produced in *E. coli*. The molecular engineering of the glycosylation pathway of *C. jejuni* into *E. coli* has paved the way for expressing glycosylated proteins in *E. coli* [40].

Bacterial oligosaccharyltransferase PglB from *C. jejuni* were expressed in *E. coli* for synthesizing glycan which were then successfully transferred to asparagine residues in the target eukaryotic protein [41]. To develop glycol-conjugate vaccines against several

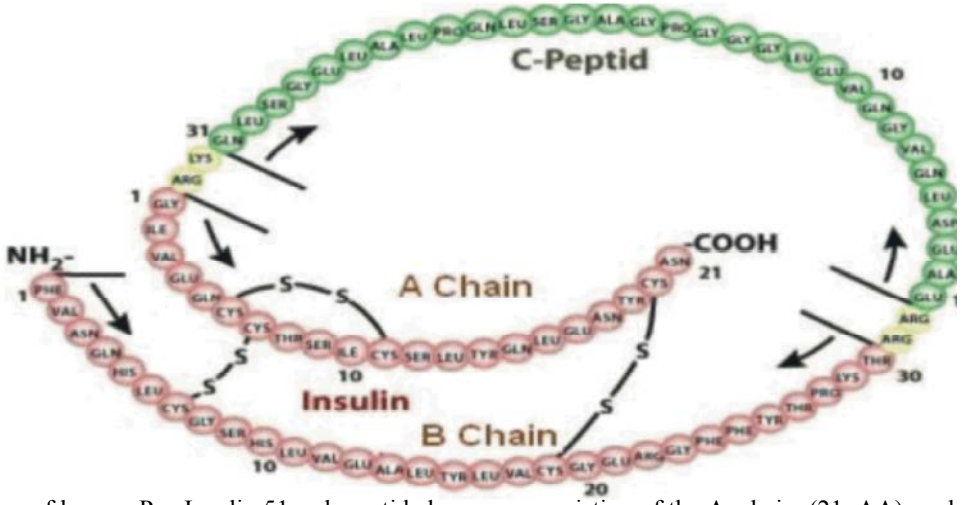

Fig. 1: Structure of human Pro-Insulin 51-polypeptide hormone consisting of the A chain (21 AA) and the B chain (30 AA).
Source: Preparative Biochemistry and Biotechnology [45].

bacterial pathogens, which could be a more cost-effective and convenient alternative method to presently employed chemical-based methods of vaccine production. aglycoconjugate vaccine against *Shigelladysenteriae O1* developed using this technology. Initial efficacy and safety studies demonstrated that the glycoconjugate vaccine was safe and also elicited a strong immune response. This novel approach for glycoconjugate vaccine production using the engineered N-linked glycosylation system of *Campylobacter jejuni* can be exploited to produce vaccines against both gram-positive and gram-negative pathogens [37].

Synthesis of Human Insulin Production in *E. coli*: Genetic Engineering is the transfer of DNA from one organism to another using biotechnology. *E. coli* cells can be genetically modified so that they have the gene for producing human insulin. The insulin is introduced into an *E. coli* cell. In *E. coli* B-galactosidase is the enzyme that controls the transcription of the genes to make the bacteria produce insulin, the insulin gene needs to be tied to this enzyme. When these modified bacteria grow they produce human insulin then the protein can be purified and supplied to diabetics [42].

Human Insulin is a 51-polypeptide hormone consisting of the A chain with 21 Amino Acids and B chain with 30 Amino Acids and has a molecular weight of 5.8 kDa linked by two disulfide bridges. Insulin is biosynthetically derived from the single-chain, 86-residue precursor, named Pro-Insulin (Figure 1). Human Insulin hormone Secreted from beta cells in the islets of Langerhans in the pancreas, the hormone is the first responsible for the process of adjusting the level of blood glucose. Diabetes mellitus describes a metabolic disorder characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. Resulting in many Diabetic complication such; neuropathy, vision disorders, heart disease and metabolic difficulties [43].

Designing of the suitable gene sequence for the Human pro-Insulin, genetic codons optimized using computer program to be compatible with abundant codons used by *E. coli* in which the protein produced. human pro-Insulin gene were assembled and amplified using PCR based techniques, then synthesized gene were inserted into cloning vector plasmid and transformed into *E. coli*, which were chosen carefully for the cloning step, to maximizing the number of cloned gene. Cloned gene isolated and purified then inserted into an expression vector then suffering transformation again in another bacterial *E. coli* strain [44].

Codon Optimization and Primer Design: Gene Optimization of human pro-Insulin gene codons to be used by *E. coli* was performed using optimizer a web server for online optimizing the codon usage of DNA sequences by replacing the rare codon with the most abundant codon used by *E. coli* to obtain the most suitable human Pro-Insulin gene sequence of 261 Nucleotide for 87amino acid residues. Long primers were designed using DNA works software a computer program that automates the design of oligonucleotides for gene synthesis [46].

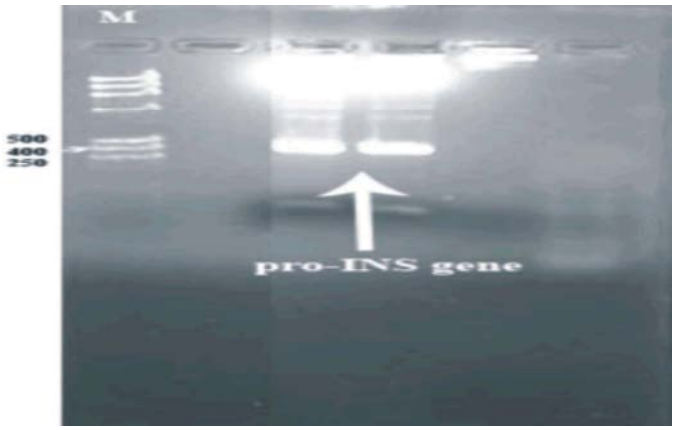

Fig. 2: DNA Gel Electrophoresis showing the Digested plasmid pCR2.1 TOPO vector and pro- Insulin gene fragment after enzymatic digestion by *Eco R1*.
Source: [48].

Gene Assembly and Amplification: GC-Rich system and 10 Long oligonucleotides and Two short outermost primers used in this step, the assembly step called Polymerase Cycling Assembly (PCA), where the second step were ordinary PCR reaction for the gene Amplification, then the product has been checked by 2 % agarose gel electrophoresis [44].

Human pro-Insulin Gene Cloning: Synthetic gene with 261 bp undergoes cloning into PCR2.1-TOPO cloning vector then transformation into TOP10F` *E. coli* cloning host. The cloned gene suffering Isolation and cloned again in pET101/D/TOPO expression vector plasmid then transformed into BL21star (DE3) *E. coli* as an expression host strain induction using IPTG were performed to the BL21star (DE3) *E. coli* that carry target gene inserted into the vector for the expression of the human pro-Insulin protein [47].

Human Pro-insulin Protein Expression: SDS-PAGE was performed for both "induced" and "noninduced" bacterial cultures then stained by commasie blue dye and imaged using gel documentation system [48].

Use of *Escherichia coli* as Indicator Organism: *Escherichia coli* are the predominant member of the facultative anaerobic portion of the human colonic normal flora [49]. The bacterium's only natural habitat is the large intestine of warm-blooded animals and since *E. coli,* with some exceptions, generally does not survive well outside of the intestinal tract, its presence in environmental samples, food, or water usually indicates recent fecal contamination or poor sanitation practices in food-processing facilities [50].

The population of *E. coli* in these samples is influenced by the extent of fecal pollution, lack of hygienic practices and storage conditions. The mere presence of *E. coli* in food or water does not indicate directly that pathogenic microorganisms are in the sample, but it does indicate that there is a heightened risk of the presence of other fecal-borne bacteriaand viruses, many of which, such as *Salmonella spp.* or hepatitis A virus, are pathogenic [51]. For this reason, *E. coli* is widely used as an indicator organism to identify food and water samples that may contain acceptable levels of fecal contamination [52].

But Methods used to isolate *E. coli* as an indicator organism from food have not proved to be efficient for isolating pathogenic strains of *E. coli* [53]. This is largely because pathogenic strains often differ considerably from nonpathogenic *E. coli* in growth patterns. Pathogenic strains frequently show delayed growth at 44 and 45.5°C, particularly when initially present in low populations [13].

Role of *Escherichia coli* in Biofuel Production: *Escherichia coli* strains can naturally utilize a variety of carbon sources (including sugars and sugar alcohols) under both aerobic and anaerobic conditions and is best suited for a variety of industrial products in addition to biofuels. *E. coli.* improve natural pathways to construct new biosynthetic pathways denovo for the optimal production of the desired biofuel products. The development of new sequencing technologies enabled the identification of the genetic variations, understanding the diversity and characterization of the genetic makeup of organisms could play a role in generating new classes of biofuels [54]. All the biofuels derived from *E. coli* are derived from the modification

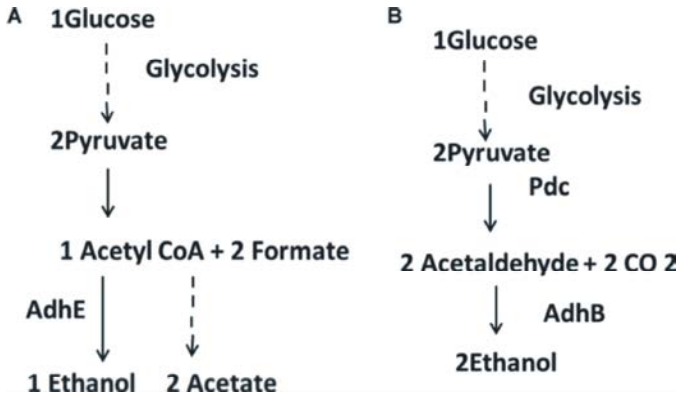

Fig. 3: Strategies for the production of bioethanol from *E. coli*.
Source: [60].

of central carbon catabolism and the process includes the conversion of hexose/pentose sugar molecule into C_2 molecules and the further modification of C_2 molecules [55].

Engineering *E. coli* to Produce Bioethanol: The major source of ethanol production is lignocellulosic feed stock material (composed of lignin, hemicellulose and cellulose) and is considered a cheaply available renewable energy source for ethanol production. The hemicellulose component of lignocellulosic biomass hydrolyzes into hexose sugars (mannose, glucose and galactose) and pentose sugars (xylose and arabinose), which are ultimately converted into ethanol through the fermentation process [56].

Organisms such as *Saccharomyces cerevisiae (S. cerevisiae) and* Zymomonasmobilis *(Z. mobilis)* are currently used as front runners to produce ethanol through fermentation. However, these organisms cannot use pentose sugars and thus limit our ability to harness maximum productivity. However, organisms such as *E. coli* and *Clostridia* species are considered because of their ability to use both pentose and hexose sugar to produce ethanol. The native *E. coli* is producing ethanol through an endogenous process in which under anaerobic conditions one mole of glucose is metabolized into two moles of formate, two moles of acetate and one mole of ethanol. The last step in the endogenous ethanol production process (Fig. 3A) involves the reduction of acetyl-coA into ethanol by AdhE [57].

The reduction reaction consumes two NADH molecules, while the initial glycolysis in order to convert glucose to pyruvate produces only 1NADH (1NADH for each glyceraldehyde 3 phosphate to 1,3-Bisphosphoglycerate) leading to redox imbalance. To overcome the redox imbalance, the native *E. coli* balances the production of ethanol by oxidation of acetyl-coA into acetate, which requires no NADH. This native fermentation process leads to the sub-optimal level of production of ethanol, which is estimated to be 0.26 g ethanol/g of glucose, whereas the maximum possible theoretical yield is 0.51 g ethanol/g of glucose [58].

To mitigate the problems existing in the endogenous ethanol production process the successful attempts of genetic engineering in *E. coli* to produce high quantities of ethanol is by inserting genes such as *pdc* and *adhB* from *Z. mobilis*. The *pdc* and *adhB* genes were expressed in operon from a plasmid under a constitutively expressed artificial *pet* (production of ethanol) promoter to produce pyruvate decarboxylase and alcohol dehydrogenase II, respectively. This heterologous fermentation pathway shown in Figure 3B produces 95% of the final products as ethanol without creating any redox imbalance (consumes only one NADH) [59].

CONCLUSION

Escherichia coli are a natural mammalian gut bacteria used as a model organism for scientific research. *E. coli* is a single-celled organism that can be manipulated and killed with no ethical concerns. It has a rapid growth rate and is very easy to culture in laboratory. Most strains of *E. coli* are harmless, posing no threat to the scientists that use them and most importantly its genetics are well-studied and can be manipulated easily. *E. coli* appears to be the best indicator of bacteriological quality of water. However, the fact remains that the life span of *E. coli* in water is short, thus it best determines, recent contaminations. The bacterium is most preferred microorganism to express heterologous proteins for

therapeutic use. The metabolic engineering and synthetic biology also improve the production of biofuels from *E. coli*.

Based on the above conclusion the following recommendations are forwarded.

- *E. coli* should use for production of desired protein since it is less cost and easy to handle.
- It's advisable to encounter *E. coli*, in to Antibiotic production since polyketides favoring the process of antibiotic production with high rates in *E. coli*.
- In order to utilize *E. coli*, in different biotechnology application further in-depth investigation has to be conducted.

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