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Involvement of Mutagens in the Production of Bioethanol by *Saccharomyces cerevisiae*: A Review

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Abstract

A mutagen is a physical or chemical agent that changes the genetic material, usually DNA, of an organism and thus increases the frequency of mutations above the natural background level. nowadays many chemical mutagens like 1, 2-dimethyl hydrazine, Quercetin, Bromo acetaldehyde, Ketoconazole etc. in the production of bioalcohol. It was observed that in presence of mutagens the production of bio alcohol by *Saccharomyces cerevisiae* Rb-39 increased by 2.5% to 17.5%.

Keywords: Mutagens; Fermentation; 1, 2-dimethyl hydrazine; Quercetin; Bromo acetaldehyde; Ketoconazole

Review

The term mutation refers both to the change in the genetic material and to the process by which the change occurs. Mutation is the ultimate source of all genetic variation; it provides the raw material for evolution.

A number of chemicals were found to be mutagenic in both plants and animals [1-3]. Friedrich and Zimmermann [4], for example, found that nitrous acid was effective in causing mutations in Aspergillus. In Drosophila that mutation could be induced by nitrogen and Sulphur mustards [5].

Lawley [6] and others discovered mutagenic activity in formaldehyde, diethylsulphate, diazomethane, and other compounds. Most of these chemicals also caused severe skin irritations in mammals and many were cancer-producing as well. In fact, many chemicals were first tested for mutagenic activity simple on the basis of prior skin or cancer tests. Since then hundreds of chemical agents have been found to produce mutagenic activity in a variety of organisms and important new methods have been devised for discovering such activity.

In general, however, prediction of mutagenic activity cannot be made on the basis of chemical structure alone. Some compounds, for example, affect certain organisms but not others, while some are restricted in action to specific developmental stages or to a specific (e.g., formaldehyde).

The search for genes that respond differently to mutagenic agents had some success, but no mutagen was found that confined its effects to only one particular gene on a chromosome and affected no others at all [7]. Thus, the wide array of compound that because mutations made it difficult for a long period to assign any specific reaction in the cell to a particular mutagen.

A crioline dyes such as proflavine and acridine orange are other mutagens that seem to produce direct effects on the DNA molecule. According to Loeber [8], acridine dyes act by inserting themselves between two neighboring purine bases in single DNA strand. The consequence of such incorporation, according to Stumpf and Copeland [9], is to cause either the insertion or deletion of a single nucleotide. Thus, acridine mutations would not be expected to cause transitions as do base analogues, nitrous acid, hydroxylamine, and alkylating agents [10].

Miller [11] performed a classic experiment or r II mutations in phase T_4. His procedure was to induce and collect R-99 mutations caused by all these agents and then test whether reverse mutation to normal (r^+) could be induced by the 2-aminopurine and 5-bromouracil that they themselves produced. Similarly, they could revert high percentages of r-99 mutation that had been caused by hydroxylamine, nitrous acid, and alkylating agents. The most revealing findings about mutation have come from the studies of some mutagenic chemicals as well radiation energy [11,12]. General reviews reveal that there is a rather widespread agreement as to the best strategy for a program of strain development of screening designed to improve best and potent mutant of micro-organism [13-16]. Singh [17] in his investigation on microbial biosynthesis of lactic acid by *Lactobacillus acidophilus* acid found that only hydrazine sulphate enhances the microbial biosynthesis of lactic acid while p-nitrophenylhydrazine-2,4-dinitrophenythydrazine and lithium fluoride has been found almost detrimental valueless for the microbial synthesis of lactic acid.

Billoval [18] also worked on a few chemical mutagens and found that only methoxy caffeine enhances the fungal synthesis of ergot-alkaloids while sodium azide, hydrazine hydrochloride, and lithium fluoride has been found almost detrimental and valueless for the fungal synthesis of ergot-alkaloids by Arnold [19].

A large variety of compounds like peroxides, caffeine, gaseous butadiene, Ethelene and thiourea chemicals were also reported by a group of workers as very specific mutagens [20-24]. Nishi et al. [25] have worked on microorganisms and fermentation process such as N-methyl-N-nitroso urea, EMS, or X-rays to induce the microbial process and achieved the improved yields. Dubey and Tiwari [26,27] have also reported the mutagenic properties of ethyl methyl sulphonate (EMS). Tiwari et al. [27,28] found that lactic acid fermentation process was inhibited with increasing concentration of camphor.

Several phenolics flavonids and aldehydes were also found mutagenic in variety of strain of different fungi and bacteria [29-32]. Some urethanes also behave as a typical mutagen. Its mutagenic properties have been established by Stankowski et al. [33].

Indophenols also has inhibitory effect on anaerobic fermentation using yeast suspension. Rizwan [34] found appreciable mutagenic action of hydrazine at 1.0 M optimum concentration. The alkylated hydrazine has also been found to be specific mutagen but was not as effective as hydrazine. Hydroxylamine [35] has been found to be most specific mutagenic chemical for a number of microbes.

Singh and Harigae [36] in their investigations reported chloralhydrate as a growth inhibitor chemical mutagen. Ang et al. [37] also reported chloralhydrate as a strong mutagenic chemical for styphimurian but it has been found weak mutagenic. in many other cases. Sorensen et al. [38] reported Chloralhydrate as a retards production of lactic acid by delbrueckii [38]. Colchi-mutation has also been reported by Xu et al. [39,40].

Proflavin and acridine orange are two important mutagenic dyes [41]. The mechanism of dyes action is not fully understood, and it may take place during recombination. The influence on various dyes on activity of different microbes have been reported by a group of workers [42-46].

Yim et al. [47] demonstrated the influence of the ionizing radiations to induce mitosis gene conversion by using diploid strain of *S. cerevisiae*. Gamma rays and ultrasonic waves were found as effective mutagens for lactic culture and the fungus *A. niger* [47-51].

Guo and Li [51] has also studied some chemical mutagens or fermentation processes and has reported only benzyl carbamate has significant influence while 2, 4- dinitrophenyl hydrazine, acetone phenyl hydrazone and Acetaldehyde phenylhydrazone insignificant for fermentative process, especially for citric acid fermentation.

Chin et al. [52] studied efficacy of P-toluene sulphonyl azide and p-toluene sulphonyl hydrazine on microbial synthesis of bio alcohol and found that p-toluene sulphonyl azide retards that yield of bio alcohol while p-toluene sulphonyl hydrazine enhances the yield significantly.

Dan et al. [53] reported salicyloyl hydrazine and benzoyl hydrazine as a specific mutagen for fermentative production of tactic acid by Lactobacillus bulgaricus-2056. Li et al. [54] again reported 2-aminofluorene and dimethyl nitrosamines as a Chemicals mutagen for lactic acid fermentation. Chan and Liu [55] observed ethylene oxide and butyl carbamate as an effective chemical mutagen for alcoholic fermentation.

Novy et al. [56] has reported Et Br very useful chemical mutagen for homolactic acid fermentation. They further found Nitrofurazone as a strong chemical mutagen for homolactic acid fermentation [57].

Thus, it is obvious that most of the chemical mutagens are very useful for different fermentation process.

It is obvious from the above review of literature that various chemical mutagens and some other mutagenic agents are used to produce mutants. If microbial population exposed to the effect of mutagens differs in cultural properties, then these mutations may be differentiated according to size, shape, structure, and color of the colonies. Mutations of biochemical properties are revealed by means of minimal media containing only salts and carbohydrates (Table 1).

Comparative study of the influence of 1, 2-demethyl hydrazine, Quercetin, bromo acetaldehyde and ketoconazole on alcoholic fermentation by *Saccharomyces cerevisiae* Rb-39 in 50 hrs Ghulam [58].

S. No	Chemical mutagens used	Optimum concentration of mutagens used	Maximum yield of Bioalcohol in control ml/100 ml	Maximum yield of bioalcohol in presence of Different mutagens ml/100 ml	% Difference in the yield of bioalcohol inorase (+) in 50 hours of incubation period	Reference
1	1,2-dimethyl hydrazine	6.0×10^{-5} M	6.98	7.15	(+)2.43553	[57]
2	Quercetin	6.0×10^{-5} M	6.93	7.5	(+)8.22510	[57]
3	Bromo acetaldehyde	3.0×10^{-5} M	6.95	7.28	(+)4.74820	[57]
4	Ketoconazole	6.0×10^{-5} M	7.03	8.28	(+)17.78093	[57]

Table 1: Each value represents mean of three trials, where (+) values indicate % increase in the yield of bio alcohol.

Conclusion

Thus, it is concluded that a large number of mutagens have been employed to generate the mutants of different microbes but still there are chemical inorganic mutagens whose influence on alcoholic fermentation by species of yeast have not been well studied and established. Moreover, a survey of the literature reveals that there has been not enough mention to study the alcoholic fermentation exposed to mutagens especially chemical mutagens.

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