LARGE SCALE PRODUCTION FERMENTER DESIGN :-

Fermenter it is a system consisting of different types of equipment's to provide microbial growth by controlling environmental condition. A topical large scale fermenter consist of three parts such as the culture vessel, associate supply and environmental systems and measurement and control system.

IDEAL FERMENTOR PROPERTIES:-

1. Provide operation free from contamination
2. Adequate mixing and aeration
3. Maintain specific temperature and PH
4. Access points for inoculations and sampling.
5. Non-toxic to microorganisms and safety.
6. Minimize liquid loss from the fermenter.
7. Monitoring and control of dissolvent oxygen
8. Allow feeding of nutrients solution and reagent
9. Suitability for wide range of microbial cultures.

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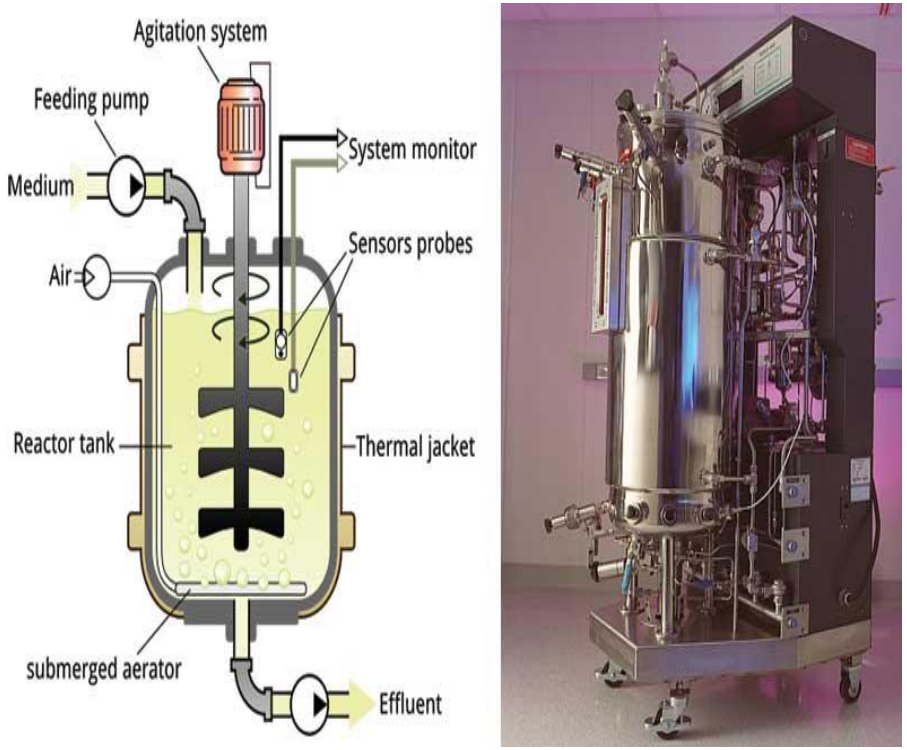


Fig.1 Production of fermenter design

The fermenter is made up of stainless steel or borosilicate glass. They are non-corrosive, non-toxic and easily cleanable. The head plates provide parts of nutrients medium probes, gas input and waste product removal. Head plates and other accessories are fitted

to the vessel by making use of gaskets, lip-seal and silicon rubber o rings.

Agitation in fermenter is most important for oxygen transfer, develop larger interface for oxygen dissolution, mixing of media contains and maintain uniform environment inside the production tank. Fermenters have impellers present to bring about agitation in the medium. Position and number of impellers are depended on size, volume and height of fermenter. Stirrer shaft can enter the vessel form the top or from side or from the bottom. Stirrer is rotated by the motor through adjustable pulley and belt or through direct drive.

The aeration capacity of the medium can be enhance by stirring. The aeration capacity of the stirred fermenter is proportional to the stirring speed, rate of air flow and the internal pressure.

Agitation result into vertex formation and escape the bubbles into hallow cone impeller action causes spinning of liquid as a mass. Vertical plates or baffles are present on inside wall of fermenter to correct situation. Speed of impeller depends on size of fermenter vessel and nature of microorganisms.

TYPES OF IMPELLERS

Fig. 2 Impellers

FERMENTATION MONITORING AND CONTROLS

Measurement and control of environmental conditions and biological variable is called fermentation monitoring. New developments in digital electronics have permitted a high level of monitoring and control of fermentation process. The computer can be a vital instrument for process optimization and control.

Process parameters are the optimum condition which is to be maintained for the production organisms. These conditions may be depended on types of organisms such as bacteria, actinomycetes, yeast, mould etc. it also depends on fermentation process.

CONTROLLED PARAMETERS AND MONITORING DEVICE IN FERMENTATION

1. Temperature control :-
   The temperature control in the fermenter or pipe is an important parameter for a good fermentation process.
2. PH monitoring and control :-Many microbial cells growth optimally between PH 5.5 – 8.5 microbial cells grow rapidly in fermentation medium and release the metabolites which are responsible for change in PH.
3. Dissolved oxygen :-
   In most aerobic fermentations it is essential to ensure that the dissolved oxygen concentration does not fall below the specified minimal level.
4. Pressure measurement :-
   Positive pressure is maintained in fermentation vessel and it may differ from proses to proses

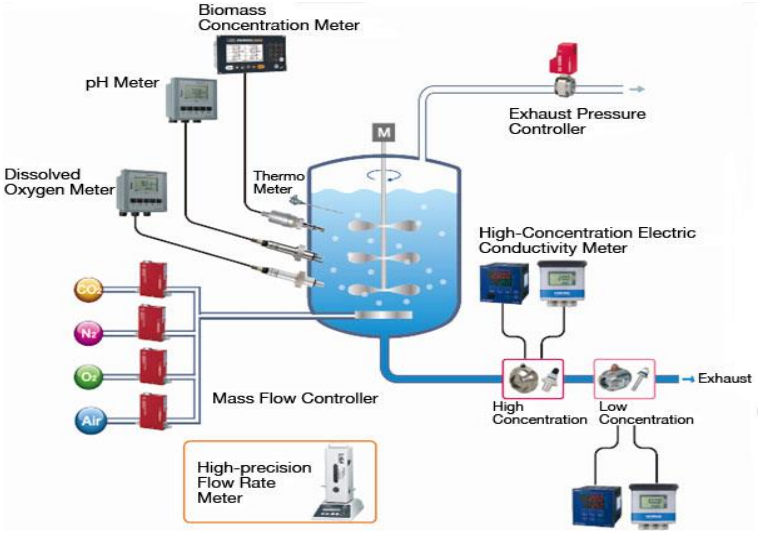


Fig.3 Monitoring device in fermentation

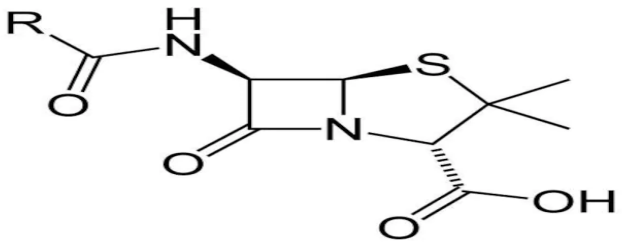
STUDY OF PRODUCTION OF PENICILLIN

PENICILLIN:-

Productions of penicillin begin in the United States 1941 by surface culture fermentation of penicillium notatum. During world war 2nd, penicillin producing fungi where studied extensively increase yields of penicillin. Penicillin is effective against gram - positive bacteria and also some large viruses and rickettsia. Natural penicillin is effective against several gram- positive bacteria. They inhibit the bacterial cell wall synthesis and destroy the cell.

The basic structure of penicillin is 6 amino penicillanic acids which consist of a thiazolidine ring with a condensed β- lactam ring. The β- lactam ring – thiazolidine ring of penicillin contains to amino acids such as L-cysteine and D- valine.

Structure of penicillin:-



PRODUCTION OF PENICILLIN:-

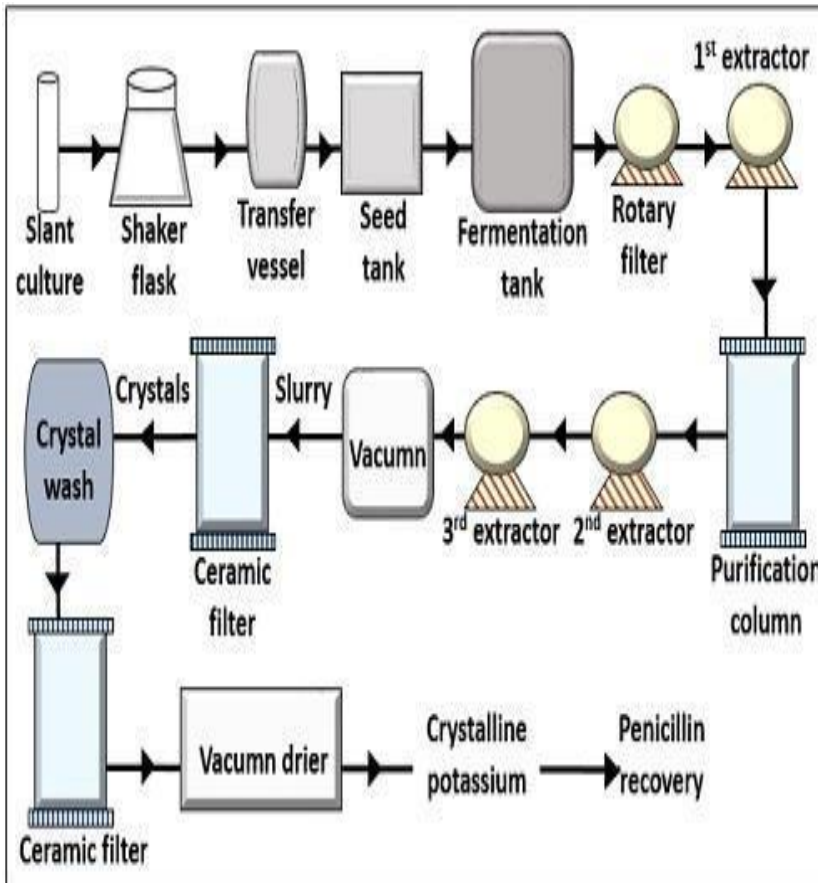


Fig.4 Production of penicillin

STUDY OF PRODUCTIN OF VITAMINE B-12

Vitamin B- 12:-

Vitamin B- 12 is a water soluble vitamin, commonly known as cobalamin. It is an important dietary component for normal growth in human beings and animals. Ricke E. L. and Smith L. (1948) isolated small amount of active material from liver and crystalized it as vitamin B-12 which was active in the treatment of penicillin of pernicious anemia

Vit. B12 is one of the largest and the most complex molecules. Vitamin B-12 is one of the largest and the most complex molecules. The main part in the structure of vit. B-12 is porphyrin ring containing cobalt as the central element.

Vit.B-12 is produce by bacteria and actinomycetes. Streptomyces olivaceus , pseudomonas denitrifiacans, propionibacterium shermaniiand propionibacterium freudenreichii are mainly used to commercial production of vit B12.

VIT. B12 PRODUCING MICROBIAL SPECIES

Microbial group :- actinomycetes

Species: - stetomyces olivaceus, nocardia species, steptomyces albidoflavus, S. antibioticus, s. aureofacieus, s. griseus, s. roseochromogenus.

Microbial group: - Bacteria

Species: - Pseudomonas denitrificants, Aerobacter aerogenes, Bacillus subtilis, Bacillus megaterium, Propinibacterium shermanii, Clostridium butyrium.

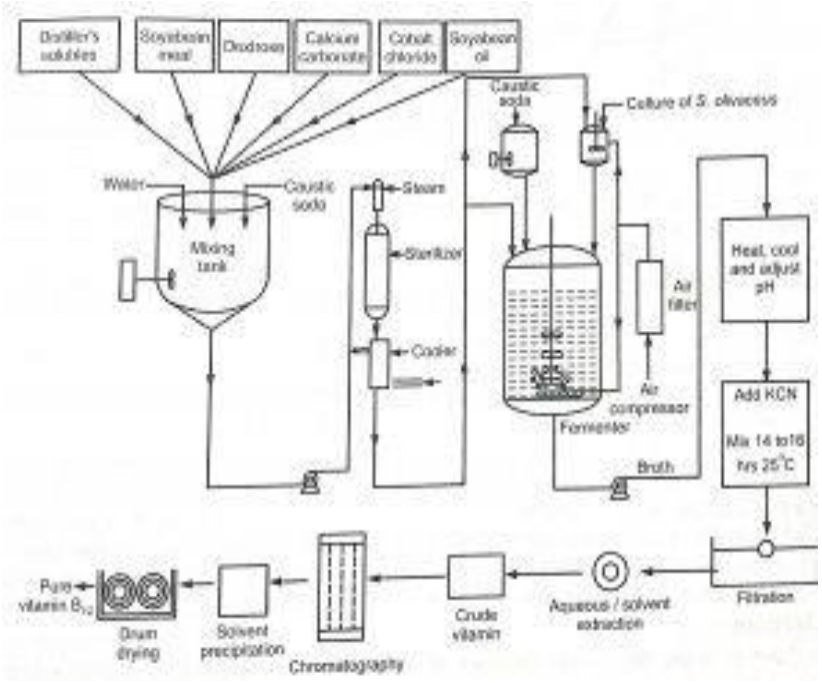


Fig. 5 Production of Vit. B-12

STUDY OF PRODUCTIN OF GLUTAMICACID

Glutamic acid:-

L- glutamic acid was the first amino acid to be produced by microorganisms, Corynebacterium glutamic. Glutamic acid is widely used in the production of monosodium glutamate which is commonly know is commonly known as the 'seasonal salt'. Monosodium glutamate is condiment and flavor enhancing agent and it commonly used in convenient food-stuffs.

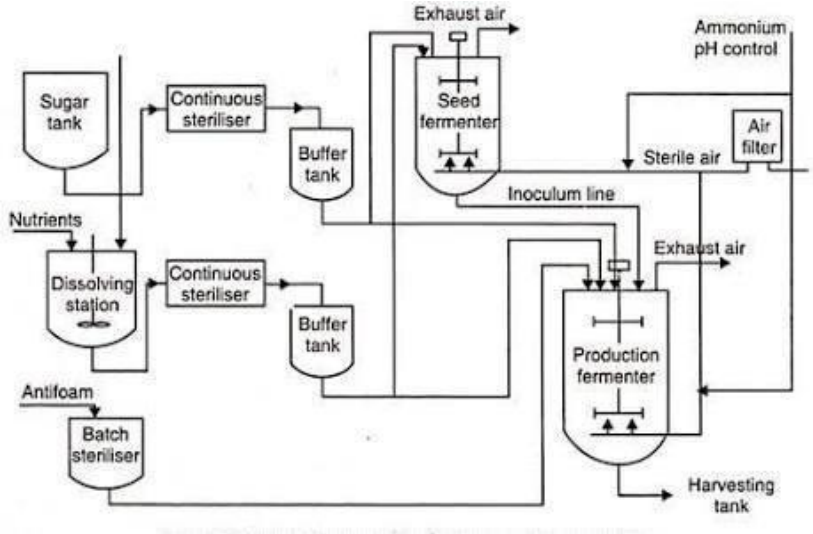


Fig.6 Production of glutamic acid

SYNTHESIS OF GLUTAMIC ACID :-

Acrylonitrile

$$N{\equiv}C{-}CH{=}CH_2 + C{\equiv}O + H{-}H$$

↓ oxo reaction

β- cyanopropionaldehyde

$$N{\equiv}C{-}CH_2{-}CH_2{-}\underset{\underset{O}{\|}}{C}{-}H + NH_4^+ CN^-$$

↓

Strecker intermediate

$$N{\equiv}C{-}CH_2{-}CH_2{-}\underset{\underset{NH_2}{|}}{\overset{\overset{H}{|}}{C}}{-}C{\equiv}N$$

↓ NaOH neutralize, $+ 2H_2O$

Glutamic acid

$$HO{-}\overset{\overset{O}{\|}}{C}{-}CH_2{-}CH_2{-}\underset{\underset{NH_2}{|}}{\overset{\overset{H}{|}}{C}}{-}\overset{\overset{O}{\|}}{C}{-}OH + 2NH_3$$

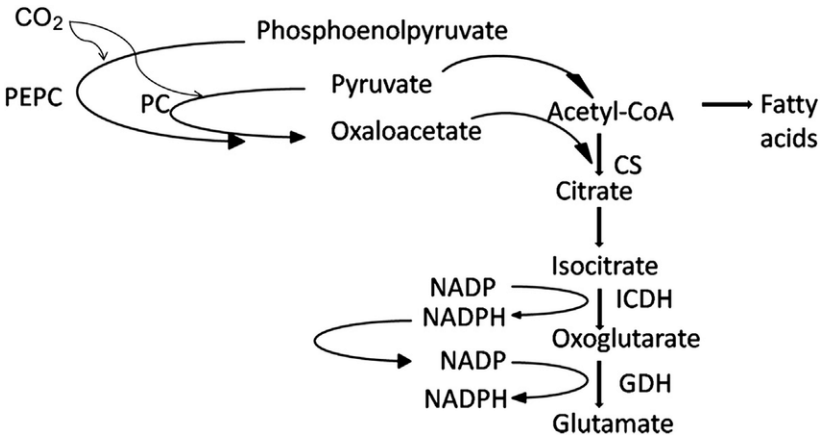
This amino acid can be synthesized by number of techniques such as :-

1) Hydrolysis of wheat glutin, soyabean cake or by other protein rich food components.
2) Cleavage of pyrrolidone carboxylic acid found in stiffens molasses.
3) One step fermentation process uing single microbes.
4) Two steps process involving α-ketoglutaric acid by fermentation and its conversion to glutamic acid by enzymatic process or used of another microbes.

MICROBIAL STAINS AND BIOSYNTHESIS :-

L- glutamic acid can be synthesized from a wide species of bacteria. Actinomycetes and fungi. In addition of acid such as Escherichia coil bacillus subtilis, Cephalosporium salmosynnematum, Bacterium α-ketoglutorium, Bacillus megatherium, Aerobacter cloacae, Pseudomonas fluoresences, Serratia marcescens, Microbacterium species etc. C. glutamicum is a gram-positive, non-motile bacterial strain and its mutants are developed to produce high yield of acid.

METABOLIC PATHWAY OF GLUTAMIC ACID

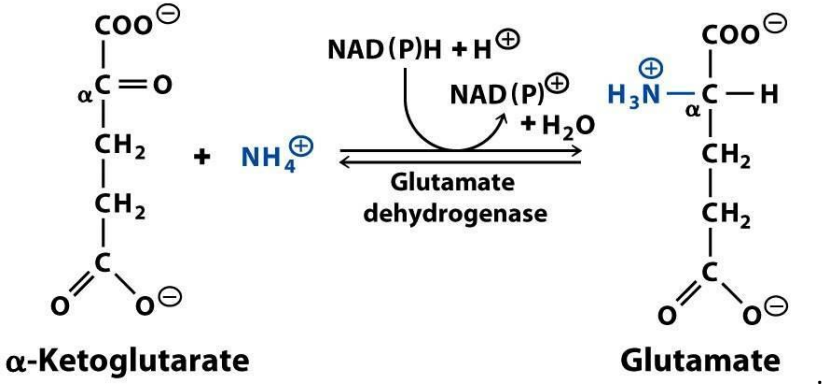


The pathway for the synthesis of glutamic acid from glucose as the carbon source is an given diagram. The glucose is broken down into fragments by microbes through the Embden Meyerhof-Parnas (EMP) pathway and the pentose-phsophate pathwaway. The key precursor of glutamic acid is α-ketoglutarate is converted to L- glutamic acid through reductive amination (NH4).

INOCULU PRODUCTION :-

A suitable stain of Corynebacterium glutamic from stock culture is used for inoculum development. The strain is inoculated in sterilized medium and incubated at 35˚C for 16 hours. Sufficient inoculum (6%) can be developed and then added in final production fermenter.

Conversion of α-ketoglutaric acid to L-glutamic acid :-



REFERENCE :- Prof. Chandrakant Kokare book of Pharmaceutical Biotechnology Page no. 196-210

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