



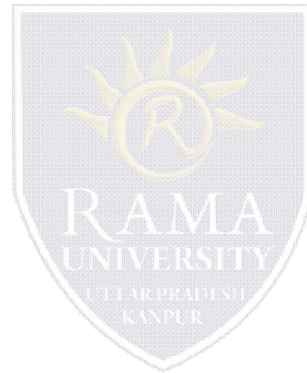
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Chemical Mutagen:

A chemical mutagen is a substance that can alter a base that has already been incorporated into DNA and thereby change its hydrogen bonding specificity.



i. Base Analogues:

A base analogue is a chemical compound similar to one of the four bases of DNA.

It can be incorporated into a growing polynucleotide chain when normal process of replication occurs.' These compounds have base pairing properties different from the bases.

They replace the bases and cause stable mutation.

A very common and widely used base analogue is 5-bromouracil (5-BU) which is an analogue of thymine.

The 5-BU functions like thymine and pairs with adenine.

The 5-BU undergoes tautomeric shift from keto form to enol form caused by bromine atom. The enol form can exist for a long time for 5-BU than for thymine. The tautomer form of the base hydrogen-bond to an incorrect base, and so the base laid down will be wrong. If 5-BU replaces a thymine, it generates a guanine during replication which in turn specifies cytosine causing G: C pair.

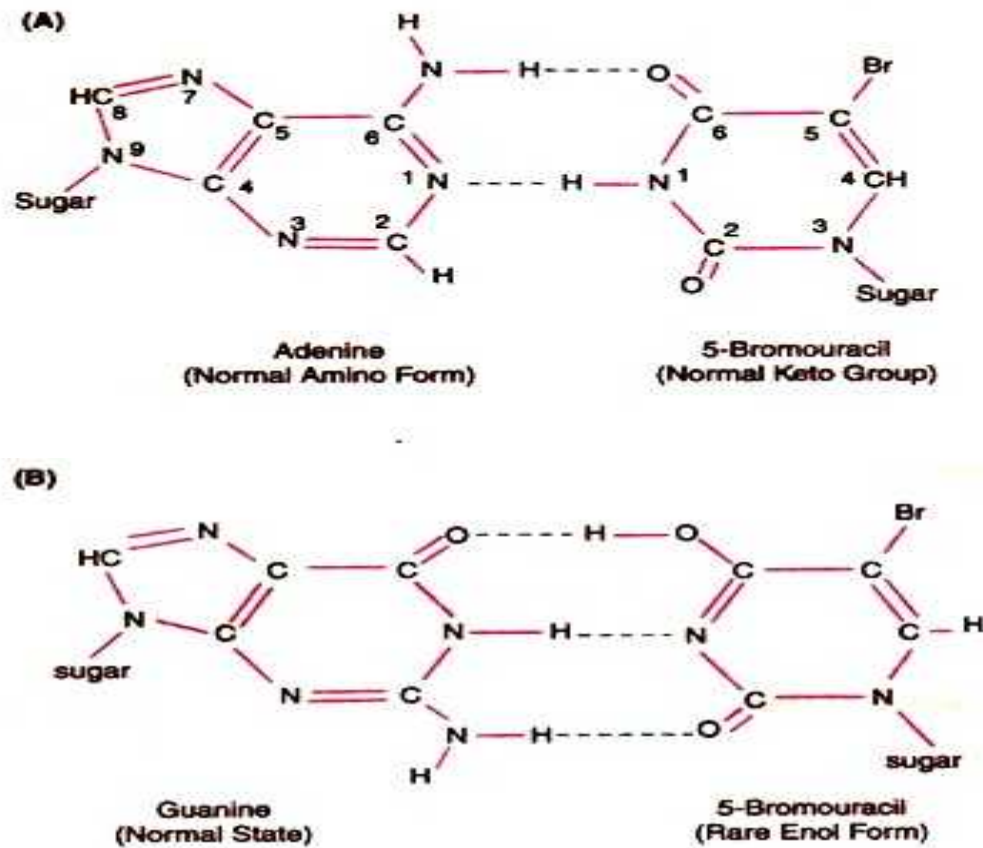


Fig. 9.6 : Mutagenesis by base analogue 5-bromouracil. A, the keto form of 5-BU pairs with adenine; B, 5-BU is tautomerised to enol form and pairs with guanine rather than adenine.

- ❖ During the replication, keto form of 5-BU substitutes for T and the replication of an initial AT pair becomes an A: BU pair.
 - ❖ The rare enol form of 5-BU that pairs with G is the first mutagenic step of replication.
 - ❖ In the next round of replication G pairs with C.
 - ❖ Thus, the transition is completed from AT→GC pair
 - ❖ The 5-BU can also induce the conversion of GC to AT.
 - ❖ The enol form infrequently acts as an analogue of cytosine rather than thymine. Due to error, GC pair is converted into a G: BU pair which in turn becomes an AT pair.
 - ❖ Due to such pairing properties 5-BU is used in chemotherapy of viruses and cancer.
 - ❖ Because of pairing with guanine it disturbs the normal replication process in microorganisms.
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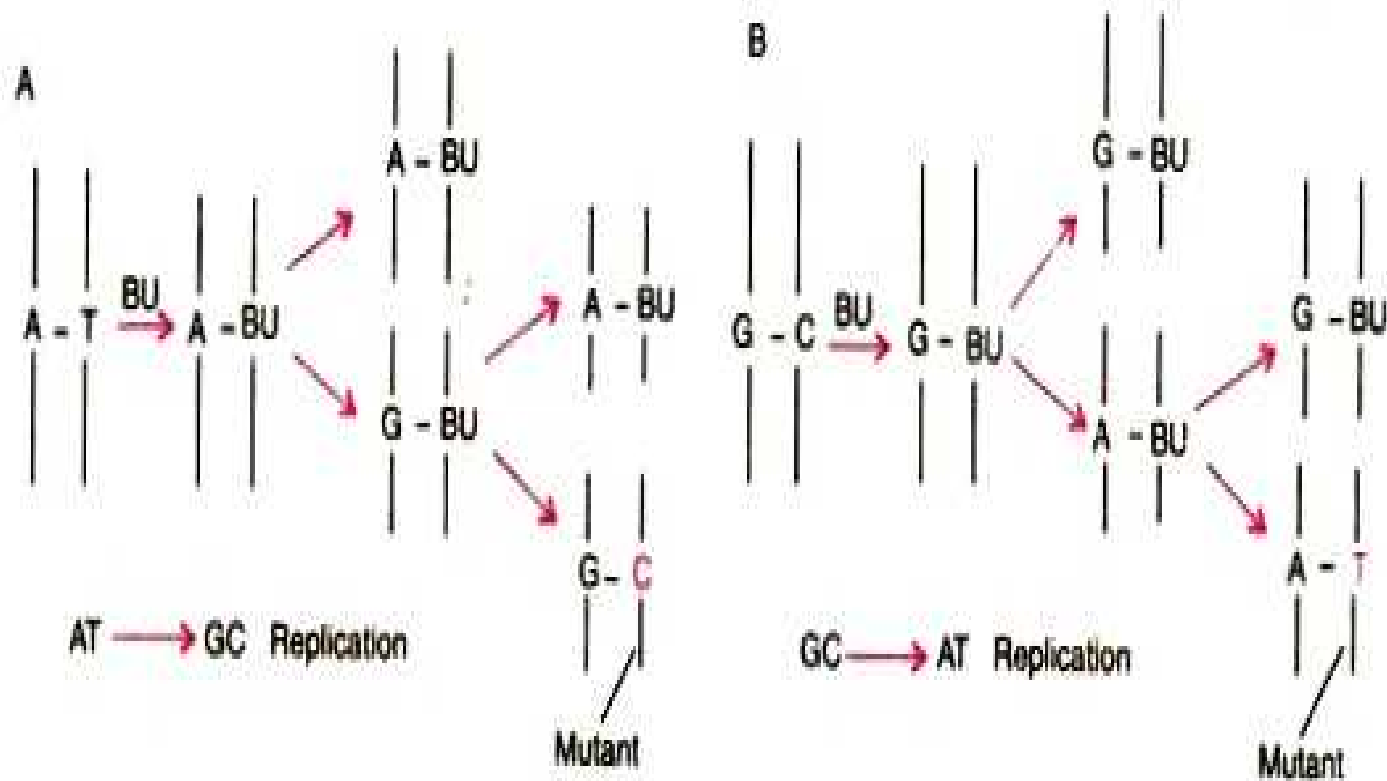


Fig. 9.7 : Mechanism of 5-bromouracil (BU)-induced mutagenesis. A, AT→GC replication; B, GC→AT replication.

