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Degradation of nucleic acids and nucleotides in several conditions with perspectives of retrieval: A review

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ABSTRACT

Deoxyribonucleic acid (DNA) or oligonucleotides, can be modified in several ways as chemical degradation by electrophilic reaction, attack of radicals, hydrolytic deamination or oxidative damage caused by ionizing radiation. This work discussed these degradation mechanisms, determining the effects on these biomolecules. The actual knowledge about DNA damages only permits partial enzymatic repair treatments.

KEYWORDS

DNA; Chemical; Degradation

1. INTRODUCTION

Biological markers (biomarkers) are complex molecular fossils from biomolecules in living organisms. They are generally resistant to weather, the biodegradation, evaporation and other biological processes. As commonly preserved in rocks, they can be used by geologists, geochemists, archaeologists, evolutionist biologist, etc. for information on organic matter in source rocks, the presence of oil, environmental conditions during sedimentation (diagenetic process), the thermal maturity experienced by the oil and/or rock (catagenetic process), the degree of biodegradation, some aspects of mineralogy of the source rock (lithology), the age of fossils and characterization of biomarkers.

Biological markers can be DNA (DeoxyRibonucleic Acid) or oligonucleotides, which are stretches of DNA molecules of simple fixed-length string.

The continuous advances in DNA sequencing techniques allow faster and complete studies of sequenced DNA for fields as the evolutionist biology provide indirect evidence on the comparison of DNA sequences from living organisms, of the historical processes that have formed them over long periods of time. The study of DNA from fossils organisms offers a partial way out to this problem, because many technical pitfalls need to be innovated to allow the reconstruction and/or study of the molecules. By example, DNA from fossils can form cross-links among themselves or with other molecules to the passage of time, hindering the use of techniques such as PCR for study [1,2].

Therefore, this work discussed some degradation mechanisms of nucleic acids, oligonucleotides and nucleotides, determining the effects on these biomolecules by agents of degradation and finally exposed the major techniques available for the retrieval of ancient and damaged DNA.

2. CHEMICAL DEGRADATION OF DNA

There are some functional groups or chemical structures that can modify the DNA. These molecules possess sufficient *reactivity* to make changes and break covalent bonds within DNA. Almost all the DNA reactions fall into just two general categories: 1) the reaction of a DNA nucleophile with an electrophile or 2) the reaction of a DNA pi bond or c-h bond with a radical [3-6].

2.1. Electrophilic Degradation Reactions

Potentially, all of the heterocyclic bases in DNA, could to act as nucleophiles in reaction with electrophiles. as is expected, access to some sites is limited in double-stranded DNA relative to single-stranded DNA [7,8], but, reactions are not completely precluded even at locations

on Watson-Crick hydrogen bonding surfaces of the bases that reside near the helical axis of the duplex. The factors that determine the atom site selectivity for a given DNA-alkylating agent are complex [7-11]. A recent detailed study of alkylation by diazonium ions led to the conclusion that atom site selectivities seen in duplex dna do *not* reflect intrinsic nucleophilicities of the heteroatoms in the nucleobases. Rather, placement of the nucleobases into the environment of the double helix substantially alters the nucleophilicity of base heteroatoms. factors that alter the nucleophilicities of various heteroatoms in the dna bases, when placed within the context of double helix, include proximity of the polyanionic sugar-phosphate backbone, lower dielectric constants in the dna grooves relative to bulk water, and interaction of the inherent dipoles of the nucleobases with the electrostatic environment of the double helix (e.g., charges of the backbone and neighboring bases) [11].

2.2. Reactions of Radicals with the Heterocyclic Bases

Radicals react with bases frequently by addition to the pi bonds in the heterocyclic nucleobases or by hydrogen atom substraction. These reactivity has been extensively studied in the context of hydroxyl radical (HO•), which is generated by radiolysis of water. When DNA is exposed to the hydroxyl radical, approximately 80% of the reactions occur at the bases [12-14]. Many base damage products arising from the reaction hydroxyl radical with DNA have been characterized [13,15-19]. Radical attack yields nucleobase radical adducts that must undergo either oxidation or reduction to yield a stable final product. The cellular oxidant in these reactions may be molecular oxygen or high-valent transition metal ions (e.g., Fe^{3+}), while the reductant may be either thiols, superoxide radical, or low-valent transition metal ions (e.g., Fe^{2+}). In many cases, the base remains largely intact and the sequence of chemical events can be readily inferred. In some other cases, more extensive base decomposition occurs.

2.3. Reactivity in Archaeological Deposits

Ancient DNA contains only a small fraction of specimens endogenous [20], the reason for this is damage to the DNA that accrues over. Mainly two kinds of modification are likely to affect dna in an archaeological environment. First, hydrolytic reactivity will result in deamination of bases and in depurination and depyrimidination [21]. In second place, oxidative damage, caused by the direct interaction of ionizing radiation with the DNA, as well as mediated by free radicals created from water molecules by ionizing radiation, will result in modified bases [21,22]. Other mechanisms, for example alkylation or uv irradiation, are less likely to affect buried remains. Ancient DNA is degraded to a small average size containing abasic sites and oxidation products of pyrimidines [23]. Gas chromatography/mass spectrometry (GC/MS) is particularly suited to identify and quantify modifications in DNA [24].

3. RETRIEVAL OF ANCIENT AND DAMAGED DNA

The formulation of theories and deductions about the evolution of species are inferred from studies of genetic diversity in contemporary populations. The retrieval of ancient DNA from archaeological remains holds the promise to add a new tool to such studies, with the invention of PCR [25,26], as mentioned ancient DNA contains only a small part of sequences that can be amplified by the polymerase chain reaction (PCR) [20]. The PCR is the main technique to retrieve ancient DNA sequences.

It became possible to study ancient DNA sequences [23]. Contributing mainly to areas as phylogenetic relationships of extinct animals [20,27,28], whereas results in other areas have remained controversial [21,29] or difficult to authenticate. This is the situation, for example, for the retrieval of DNA sequences from ancient human remains [30].

Biochemical methods can identify *ancient* DNA alterations and inadequate sequencing [31].

There are evidence that inter-strand crosslinks, prevent amplification, may accrue more quickly *post-mortem* than the single-stranded nicks that are largely responsible for fragmentation. For this reason, DNA sequences may be present in fossil remains long after negative amplification results are obtained [32,33].

Some methods have been used to revert damages of ancient dna and improve the amplifiable dna templates and sequence reliability. As example, *PFU* and *TAQ hifi*, high fidelity polymerase enzymes leading a sequencing with minimal errors [34,35].

Similarly, uracil-*n*-glycosylase (UNG) takes out deamination products of cytosine and is an important means to determine the origins of sequence variation [31-36]. *n*-phenacylthiazolium bromide (PTB) appears to break intermolecular cross-links caused by advanced glycosylation end products, although the exact mode of operation remains unclear [37].

The actual knowledge about DNA damages only permit partial enzymatic repair treatments for DNA [38].

4. CONCLUSIONS

Nucleic acids, oligonucleotides and nucleotides are mainly damaged by mechanisms as chemical degradation by electrophilic reaction, attack of radicals, hydrolytic deamination or oxidative damage caused by ionizing radia-

tion.

With the actual knowledge about DNA, damages are the only possible partial enzymatic repair treatments.

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