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CANCER, MUTAGENS AND CARCINOGENS

Dr. Ranjana Shukla
Professor & Head Department Of Chemistry, Babu Banarasi Das National Institute of Technology And Management Lucknow-227105, (U.P.) India

ABSTRACT

Cancer has been defined as an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of the normal tissue and persists in the same excessive manner, after the cessation of the stimuli which evoked the change.

Keywords: *Cancer, Mutagens, Carcinogens, Tumor.*

I. INTRODUCTION

Cancer may be of two kinds: malignant and non-malignant (benign). A malignant tumor leads to a dangerous disease[1,2,3] of multicellular organism in which certain cells start replicating in an uncontrolled fashion and in most cases forming malignant tumors which in turn give rise to daughter tumors (metastasis).[4,5]

It is a well-known fact that cancer may be caused by certain external physical and chemical factors, such as, cell damage through strong pressure, radiations and a large number of chemical compounds called carcinogens.[6,7] The chemical carcinogens can be divided into six main groups:

i) Automatic polycyclic hydrocarbons, their derivatives, and related compounds.
ii) Amino derivatives of aromatic hydrocarbons.
iii) Derivatives of 4-aminostilbene.
iv) Derivatives of azobenzene.
v) Certain aliphatic and heterocyclic compounds (e.g. urethane, nitrogen mustards).
vi) Miscellaneous inorganic salts of arsenic, zinc, nickel, etc.

The structural and other properties of the carcinogens have been reviewed by several authors.[8-11]Some of the significant chemical carcinogens are summarized in table:

Chemicals Recognized as Carcinogens in Human and Experimental Animals

Sl. No.	Carcinogens	Human and Experimental Animals	References
1	Benzidine 3,3 Dichlorobenzidene 4-Aminobi-phenyl	Urinary bladder Urinary bladder Urinary bladder	12-14
2.	4-aminobiphenyl-4-nitro-biphenyl	Urinary bladder	
3.	1-and 2-Naphthyliamine	Lungs	15
4.	Estrogens (DES) Diethylstilbestrol	Mammary organs	16,17
5.	4-Ethylsulphonyl naphthalene-1-sulfonamide (ENS or 4-ENS)	Epithelial hyperplasia of bladder	18-22
6.	2-Acetylaminoflourene	Specific organs	23,24
7.	Soots, tar, oils	Skin, lungs	
8.	Betel quid (Betel nut)	Buccalmuscosa (oral organs)	25
9.	Bis (2-chlorethyl) –sulfide	Lungs	
10.	Nickel powder	Fibrosarcoma	26,27
11.	Cobalt Powder	Fibrosarcoma	28, 29
12.	Cadmium powder	Fibrosarcoma	30

13.	p-Dimethylaminoazo benzene	Liver	31
14.	1,2,5,6-Dibenzanthracene	Skin	32
15.	2-Phenyl phetnanthrene -3, 2^{1}–dicarboxylic acid	Skin	32
16.	N- Nitrosodimethyl amine (DEN)	Kidney, Lung	33
17.	N- Nitrosoethyl amine (DEN)	Kidney, Lung	33
18.	N-Nitroso-N-methyl urea (DMH)	Kidney, Lung	33
19.	4-Nitroquinoline-1-oxide (4-NQO)	Liver Oral keratinocytes Peritoneal cavity Bacterial and bacterial Genomes Mouse liver cytosol Mammalian cells	34 35 36 37 38 39
20.	Cigarettes Smoke	Lungs, other sites	
21.	Urethane	Liver	40
22.	Asbestos	Lungs, Pleura, other sites	

These chemicals are primary and secondary carcinogens. The primary carcinogens produce tumors in the immediate region of application, and they are capable of producing such tumors in many different tissues and organs, and in several species of animals. By contrast the secondary carcinogens are generally less potent and more specific in their activity, which is often confined to particular organs or particular animal species. In many cases they produce tumors chiefly in organs remote from the point of application, suggesting that their metabolites, rather than the original compounds are responsible for the carcinogenic action.[41,42]

The mechanism of chemical carcinogenesis (scheme) may be divided into three broad phases:

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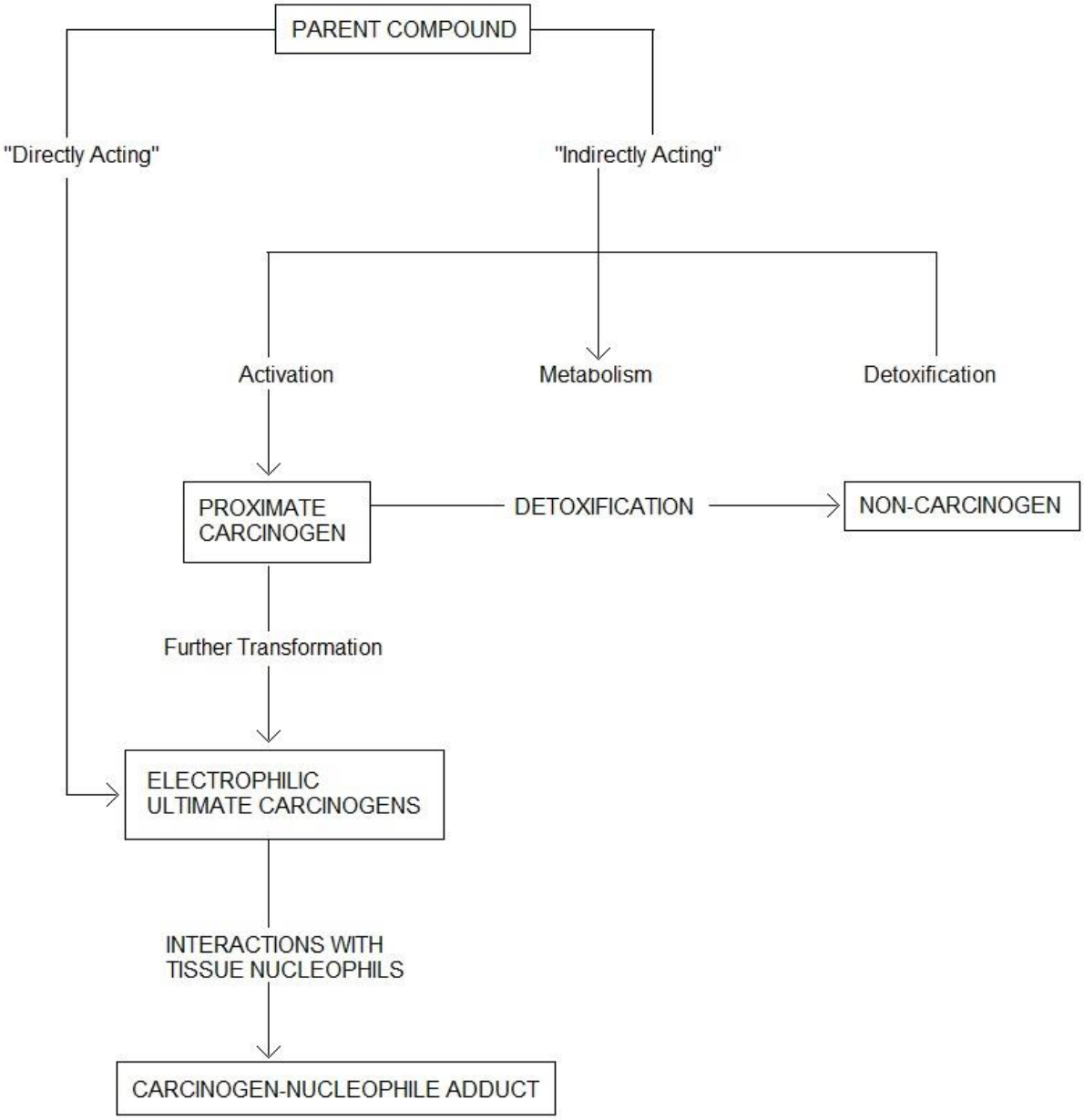
Schematic pathway for chemical carcinogens



Examples of Electrophilic Activation Of Major Class of Chemical Carcinogens

a) Enzymatic activation of the administrated procarcinogen into an active electrophilic form.
b) The interaction of the electrophile with critical receptors in the affected cells.
c) Development of such cells into clinically apparent tumors (scheme). Alkylating agents such as the nitrosamides, spontaneously decompose to electrophiles and do not, therefore require metabolic activation in contrast to other major groups of carcinogens such as the aromatic amines, polycyclic aromatic hydrocarbons, nitrosamines etc.

II. CONCLUSION

A few carcinogens, such as asbestos which induces pleural and peritoneal mesotheliomas in man, have not yet been shown to interact directly with critical cell target. Otherwise this scheme seems to be of general application. Thus chemical carcinogenesis is a two step process: the metabolic activation of procarcinogens and their interaction with cellular macromolecules (DNA, RNA and proteins).

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