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Review Article

SMOKING CARCINOGENS AND LUNG CANCER – A REVIEW

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ABSTRACT

Smoking ambiguity contributes to a certain revelation regarding the process by which cancer is induced. In the laboratory, carcinogens induce clear lung tumor to lung cancer induction. For instance, carcinogenic chemicals, namely, 4(methyl nitrosomine)-1-(3-pyridyl)-1-butanol, and nitrosonornicotine (NNN) cause tumor malignancy. It is evident from the mechanistic studies that the carcinogens have a stronger tendency to mutate the genes like suppresser gene, a gene that encodes the receptor of the cell surface to the nucleus, thus, giving way to the proliferation of mutation leading to neoplastic cells. In this analysis article, we have discussed molecular mechanics that can cause cancer by nitrosamines such as nicotine-derived nitrosamine ketone and NNN regarding a variety of significant cigarette combustion carcinogens and the effort to introduce a different dimensional approach to the prevention of cancer, by understanding the perspective of various treatments.

Key words: 4(methylnitrosomine)-1-(3-pyridyl)-1-butano nitrosonornicotine, Carcinogen, Carcinogen, Cigarette, Mutant, Nitrosamine ketone, P53, Tumor.

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INTRODUCTION

The major cause of mortality from cancer among males and females is due to lung cancer in 2018, with over 234,030 cases (12,680 in males and 112,350 in females). Around 90% in males and 75.90% in female death are estimated common death rate from cancer were shown in Fig. 1 [1]. In general, nicotine is deemed as a carcinogen because of its tumor-inducing property, including such specific cases such as hyperoxia nicotine-derived nitrosamine ketone (NNK) [2]. More strict carcinogenic materials induce oxygen atomic addiction to carcinogenic compounds, which improves the water solubility and allows it more readily extricable [3]. Other cell pollutants have been supported by the phase 2 enzyme to transform oxygenated carcinogenic substances into liquids. Some of the cytochrome P450-formed intermediates (HEM as a cofactor) with carcinogenic substances were reactivated since their intermediate reactions are electro deficient center and deoxy ribonucleic acid (DNA) lead to the formation of a covalent product known as a DNA adduct [4].

The carcinogenic agents associated with the tobacco primarily responsible to cause lung cancer. The process of association with DNA and genetic alteration in the gene has a clear understanding of how to respond to oncogene and tumor-suppressor gene exposures to tobacco smoke. Each cigarette contains a minor dose of "polycyclic chromatic hydrocarbons" (PAH) and NNK in the cigarette smoke [6]. To exercise the cancer effects, NNK and PAHs involve activation of metabolism and there is a contest among hepatic metabolism and detoxifying the risk of cancer differs between individuals [7]. Further, carcinogenic metabolism promotes DNA adduct production [8]. As DNA adducts are an escape and survive from the mobile repair system, miscoding may lead to permanent mutation. DNA impaired cells may be killed by programmed cell death [9]. In the critical area of oncogenes or tumor suppressors, a permanent mutation leads to activation or decapitation of the tumor suppressor gene. Such multiple occurrences will lead, ultimately to lung cancer, into the aberrant cell that is controlled by growth loss. Scheme related to nicotine addiction of cigarette smoke carcinogens and lung cancer and several mutations in essential genes [10]. Many reports are available on the mutation of the human beings KRAS and P53 genes in smoker tumors and targeted at the association of mutations with specific carcinogenic substances in tobacco smoke [11]. If any step-in horizontal steps are blocked or stopped, even people who continue to smoke may reduce lung cancer (Fig. 2).

Carcinogens linked to lung cancer

The carcinogen is a molecule that induces or increases the occurrence of cancer, whether chemically, physically, or virally [13]. More than 55 of the 4000 chemicals found in cigarette smoke have been carcinogenic, according to international cancer research agency assessments [14]. This chemical carcinogenic substance induces cigarette smoke cancer. The flow out of the cigarette's mouthpiece is an aero solution that holds 1010 particle/ml water. The most frequently contained carcinogenic substances are estimated to be 95% of smoke made up of O_2, CO_2, and nitrogen polycyclic aromatic hydrocarbons, N-nitrosamines, and aromatic amines. For small quantities, they are usually 5–200 mg/cigarette. Aldehyde and other organic fluid molecules including benzene and butadiene are more frequently contained. The polycyclic aromatic hydrocarbons (PAH) and Tobacco-specific N-nitrosamines (TSNA) play an important role in development of human lung cancer with relate to smoking [15].

Nicotine use and lung cancer are related to carcinogens. Nicotine allows people to Smoke keep on despite the notorious health problems consequences, and it can lead to tumors in particular circumstances, such as hyperoxia [16]. Nicotine is not typically a carcinogen. Nicotine may also be found in the body as a carcinogenic agent such as NNK. Cigarettes are a catastrophic nicotine delivery instrument because in every puff nicotine includes more than 55 carcinogens, such as PAH and NNK was shown in Fig. 3 [17]. The accumulated smoking over a lifetime is significant, although the dosage per cigarette for any carcinogen is very low. The organism has a similar reaction to carcinogen exposure to any external compound or medication. Cytochrome enzymes P450 facilitates an oxygen atom introduced to cancer, enhances its solubility in water, and increases its excitability. Furthermore, Phase 2 enzymes contribute to

this metabolic detox cycle, transforming the oxygenated carcinogen into a shape that is highly water-soluble. This oxidation is further facilitated by phase 2 enzymes, which convert oxygenated carcinogens into a highly soluble shape in the water [18]. The individual is safeguarded insofar as this mechanism is successful. Some of the cytochrome P450 enzytes intermediate products react to carcinogens but typically have an electrophilic core [19].

Such metabolites or intermediates that react with DNA, such that products called DNA adducts are formed covalently. Cells have DNA repair mechanisms that can eliminate adduct and restore DNA to its usual form [20]. Variations in DNA repair can influence the likelihood of cancer between people. Not functional repair solutions are usable. Any adducts fail and appear to be in DNA. Such persistent DNA supplements can contribute to miss codification. For example, the resulting DNA adduct (methylguanine) misreads deoxyadenosine DNA polymerases after metabolic activation of DNK and inserts thymidine during replication [21]. As a result, the G – C side chains permanently converted to the A – T base pair. These types of mutations are frequently

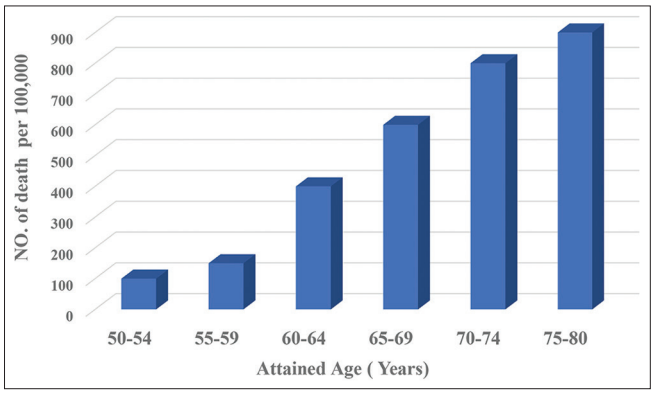

Fig. 1: Graphical representation of smoking deaths from 2009 to 2018 [5]

observed in the KRAS oncogene in lung cancer and in the TP_{53} gene in a variety of cancers induced by cigarette smoke [22]. Changes in RAS and p53 are also shown directly to result from the reaction of those genes with metabolic carcinogens. This relentless attack on genes is entirely compatible with the genetic disruptions which have led to six proposed characteristics of cancer growth signals autonomous, insensitivity to anti-growth signals, apoptosis evasion, tissue invasion, and metastasis, persistent angiology, and infinite replicative capacity.

ADDUCT FORMATION

Adducts in 4(methyl nitrosomine)-1-(3-pyridyl)-1-butanol (NNAL) and NNK

NNK and NNAL are condensed metabolic pathways. The sensitivity of humans is primarily to NNK, as it much exceeds the concentration of NNAL in tobacco material. Moreover, NNK in humans, animals, and primates has been commonly and efficiently transformed into metabolic NNAL. Among animals such as NNAL, NNAL is common lung cancer [24]. The key methods of metabolic NNK and NNAL enables the DNA adducts are by carbon a-hydroxylation next to group N-nitroso. This metabolic process is popular with certain nitrosamines. Methyl or methylene carbon NNK hydroxylating may be essential [3,25]. A-Hydroxylation creates methyl carbon-hydroxymethyl NNK which is relatively constant to be glucuronidase. This loses formaldehyde naturally, generates pyridyl-isobutyl diazohydroxide, that reacts with DNA yielding pyridyloxobutylation adducts [26].

The adducts are very soluble in DNA. They will release the drug by acid hydrolysis. HPB drug keto, hydroxy NNK generates methylene diazo-hydroxide, and keto aldehyde of methylene carbon-ethylene dioxide-NNK spontaneous development [3,27]. Methane diazo-dioxide is converted to methanediazonium ion which methylate's DNA. Thus, 7-mG, O6-mG, and O4-have been detected in tissues of animals treated with NNK. A large range of methylation agents, including a method bearing nitrosamines such as N-nitrosodimethylamine, N-nitroso-methyl benzylamine, and nitroamides or sulfur nitroxides such as N-methyl nitrosourea contain the same inducts [28]. A variety of P450s catalyze the NNK reactions

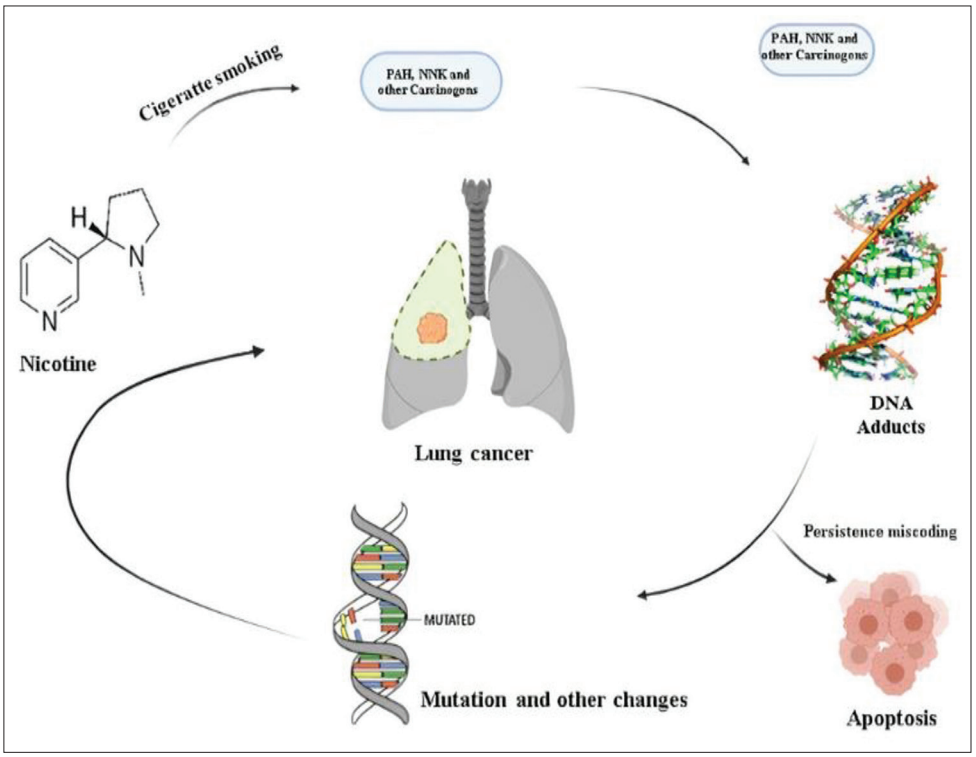

Fig. 2: Scheme manifesting the effect of nicotine produced during cigarette smoking on lung cancer and numerous defects in essential genes [12]

in hydroxylation. The association with NNK a-hydroxylation of common P450s is summarized NNAL similarly undergoes a -hydroxylation at the-methyl and-methylene carbons, producing DNA damage [29].

Formation of adducts in homosapien

Just 20% of smokers can get lung cancers, the sensitivity of smokers may rely on the patron equilibrium between mitochondrial activation of carcinogens and detoxification [30]. Cigarette smoke facilitates its carcinogenic effect which leads to mutations within tumor suppressor genes or oncogenes can cause lung carcinoma and tumorigenesis. The majority of studies of this type conclude that P53 plays an important role in the responsive balance between cell proliferation and death, and mutates into around half of all cancers [31]. Cancer in the lungs, in an exhibit of 550 p53 lung tumor mutations shows 33% transversions of G(guanine) to T(thymine) and 26% transitions of G(guanine) to A(adenain). Activated carcinogens react mainly to G and the resulting adduct repairs would be slower on the transcribed, stranded, and supported by the hypotheses [32]. Levels of 7-mdG in several studies have looked at the human lung. The mean 7-mdG level in the largest study is 2.11 per 107 nucleotides. It is a ratio of 7-mdG: HPB, equivalent to that of rat 7.52, relative to the 0.1 per 10 nuclear adducts of HPB release. The presence of 7-mG in the human pulmonary system is not the product of experiments that show greater numbers of smoking than non-smokers [33]. A link between the extensive metabolizing genotype of debrisoquine is observed. CYP2D6, 7 mdG higher intake rates as well as CYP2E1 and small all, particularly at low cotinine rates, between higher intake levels [34]. As P450 2D6 and 2E1 do not seem to act a significant role in the lung metabolism of the NNK, their significance is currently uncertain. The presence of methyl and pyridyloxobutyl (POB) pipes in smokers "lungs is compatible with humans" lung tissue's capacity to utilize all hydroxylation pathways; however, there is no specific quantitative dimension of the metabolism-to-DNA level connection [35]. 3-ethylene rates are also considerably higher in smokers relative to non-smokers, although the origins of the ethylated agent in cigarette smoke are unknown.

NIROSAMINE-INDUCED CANCER GENETIC PATHWAYS

Cancer activation NNK and nitrosonornicotine (NNN) encoded

Naturally, present NNK is a procarcinogen in cigarette smoke, to full fill its carcinogenic functions; an inactive form requires mitochondrial activation [35]. Various CYPs enable the active use of NNK in DNA metabolites which could cause methylation, pyridyl hydroxy butyl of nucleobases, DNA adduct forming, and pyridyl hydroxy butyl [36]. NNK-Methylene hydroxylation creates methane diazohydroxide and methyl diazonium ion, which reacts with DNA formed mainly by 7-Nmethylguanine (7-m Gua) and O6-methylguanine (O6-mGua) along with minimal amounts of O4-methylamine. 5-007-NNK hydroxylation can occur with either methyl or methylene oil. 5-007-Hydroxylation of methyl carbon produces 5-007 hydroxymethyl NNK; it is relatively constant to undergo glucuronidation. In spontaneity, formaldehyde is missing from the POB diazohydroxide and interacts with DNA adducts that form heavy POB [37]. Four were identified. 11-β-Hydroxysteroid dehydrogenase, the microsomal enzyme responsible for 11-hydroxyglucocorticoid interconversion, 2'-Hydroxy NNN initiates a random ring-opening to create the same structure as NNK methyl hydroxylation for pyridyloxobutyldiazohydroxyde. 5'-Hydroxylation frequently creates electrophilic diazohydroxide that is necessary for DNA to react, and CYPs primarily catalyze hydroxylation reactions to NNN [38]. The development of DNA adducts as the key stage in the NNK and NNN carcinogenesis processes is established, but the opportunity for specific DNA adducts to contribute to mutations, chromosome aberrations differ greatly from O6-methylguanine [39]. There is no direct proof of BER's role in the preparation of POB DNA damage, but POB DNA adducts could be resolved by nucleotide viewing reparation (NER) and BER pathways [40]. However, the lack of X-ray repair of the important BER fragrance protein cross complementary protein 1 (XRCC1) enhanced the mutagenic and toxicity of of 4-(acetoxymethylnitrosamine)-1-(3-pyridyl)-1-butanone (NNKOAc), which shows that XRCC1-Despite the absence of ERCC-2 it performed an essential part in protecting cells from the adverse impact of these additives [41]. 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and N^1-nitrosonornicotine (NNN) are the two major metabolic activation of tobacco carcinogens (Fig. 4) [42]. Adducts of DNA are incorrectly remedied, either remedied are required, A prerequisite for cancer induction if not necessary. There will be lung cancer in fewer than 20% of smokers.

Inflammation, infection, and immune reactions are often correlated with a range of procedures [43]. The susceptibility depends in part on the balance among the relation and growth of ROS and RNS. Smoking involves free radicals like nitrous oxide and hydroquinone mixtures, semiquinones, and quinones, which may contribute to redox cycling, oxidative smoking injury [44]. This is not well established among NNK-and NNN. Regulation and detoxification of carcinogenic activity in smoking. NNK's potential to cause oxidative stress, however, became apparent when increased levels of NNK induction to an A/J mouse were detected and 8-OHdG was a major ROS-generated lesion known to be the markers of Oxidative DNA impact 8 OHdG is deleted by the gene component Mmh/Ogg1, 8 HydG is a genetic component Mmh/Ogg 1 gene, and 8-OHdG is the product of the increased incidence of NNK 8-HdG [44].

Human tobacco carcinogen intake

We aim to understand the absorption of human tobacco-carcinogens more fully. We want to enhance our basic understanding of human carcinogenic doses and cancer mechanisms. We are also looking for a biochemical base to explore the connection between the smoking and cancer risk of the lungs. Regulatory smoking is the name used to describe the burning enclosed product [46]. Smoke (100–200 mg/cigarette), as reported in several international studies, it is available in both incomplete combustion cigarette smoke, 1–2 mg/g [47].

This should be seen in products linked to cigarettes. The NNK is the strongest lung-linked carcinogen that causes pulmonary tumors in which path rodents, mice, and hamsters through which rats are administered to be particularly susceptible to NNK cancer. The lower average dosage in rats with the potential to cause lung tumors (1.8 mg/Kg in dose trend) is comparable to that in a smoker with the maximum NNK (approx. 1.1 mg/kg) during their entire lives [48]. DNA activation trends in rats' lungs and people with NNK exposure are also similar [49]. Adenomalous tumors have been developed mainly in mice infected with NNK in the skin or rodents, for example, when carcinogen is purified in the oral cavity and inserted into the urinary bladder [50].

Human lung cancer is a popular form of lung cancer. NNK was attributed to adenocarcinoma which further causes the animals to have this type of cancerous tumor [50]. The main cause of lung tumors in humans is the production of adenocarcinoma. NNK seems to be the most prevalent type of cancer. Over the past 2 centuries, NNK rates in regular cigarettes have increased in combination with an increase in lung adenocarcinoma, whereas benzo[a]pyrene has decreased as a cause of squamous cell carcinoma in the lung [51].

This is more essential, as NNK is present in cigarettes only. The identification of NNAL in the urine and glucuronide may also be associated with nicotine consumption, since NNK is not found in the general setting, in the diet, or anywhere. The usage of NNK in non-smokers that are prone to smoke from the atmosphere [52]. NNAL and also its glucuronide levels in the urine substantially increased when exposed to such high levels of tobacco environmental smoke. For example, long-term hospital staff subjected to ambient cigarette smoke from smoking patients has large levels of NNAL glucuronide in their urine. NNK was ultimately investigated in people with the majority of ambient smoking cigarette observational tests and also in people with smoking couples [53]. The intake of NNK among women living with people who smoke was much greater than in non-smokers.

The link between the amounts of cotinine and NNAL plus glucuronide in urine has been repeatedly reported in non-smokers subjected to atmospheric cigarette smoke [54]. The usage of NNK by non-smokers

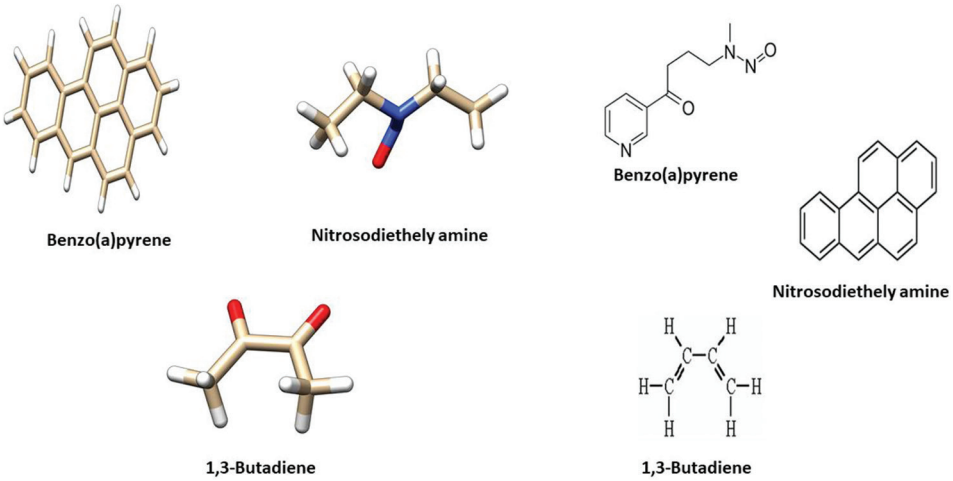

Fig. 3: 3D structure of lugs related carcinogens [23]

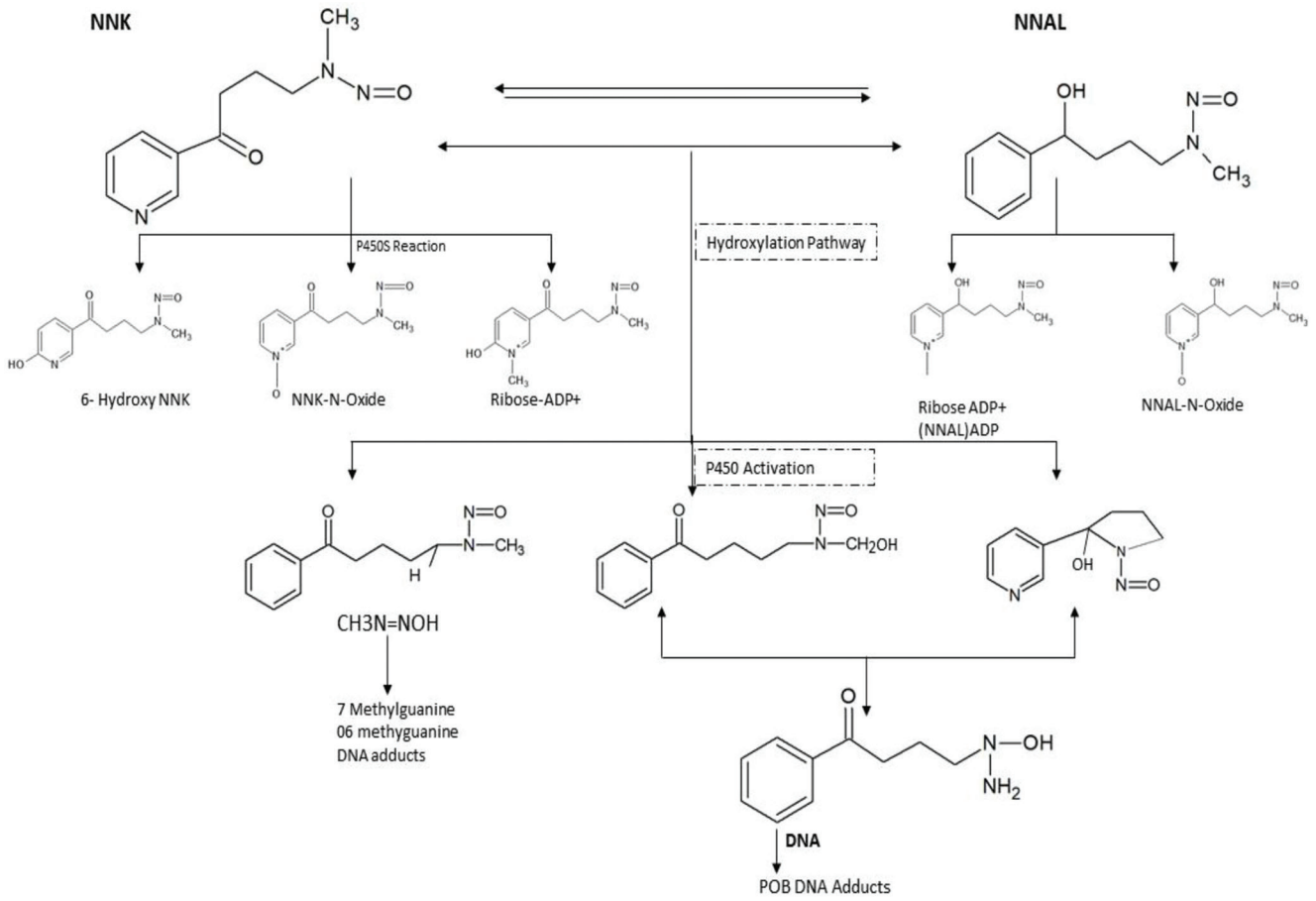

Fig. 4: Diagrammatic representation by laboratory animal and human study of NNK and NNN metabolism mechanisms and DNA formation of the adduct. NNK: N-1-(3pyridyl)-1-butanone, NNN: N-4-(methylnitrosamine) [45]

subjected to ambient tobacco smoke offers a biochemical correlation between such exposure and lung cancer, which firmly supports the notion that environmental tobacco smoke induces human lung cancer [55].

There has been a constant connection between the levels of cotinine and cotinine glucuronide in the urine of these chemicals with nicotine metabolites. A metabolite of nicotine, cotinine is widely used for human tobacco and other nicotine-containing drug uptake biomarkers. Nicotine and cotinine are nonetheless not cancerous [56].

DIAGNOSTICS

Cough, hard breathing, wheezing, blood in sputum, and diagnosis depend on the type of cancer, tumor position. Biomarkers – carcinoembryonic antigen in protein biomarkers for diagnosis [57]. It is better even combined with cytokeratin fragmentation –21 for more accurate results more than one biomarker is necessary. Tumor-infiltrating lymphocytes, complement split product, autoantibodies, circulating tumor cell, and miRNAs with CEA.

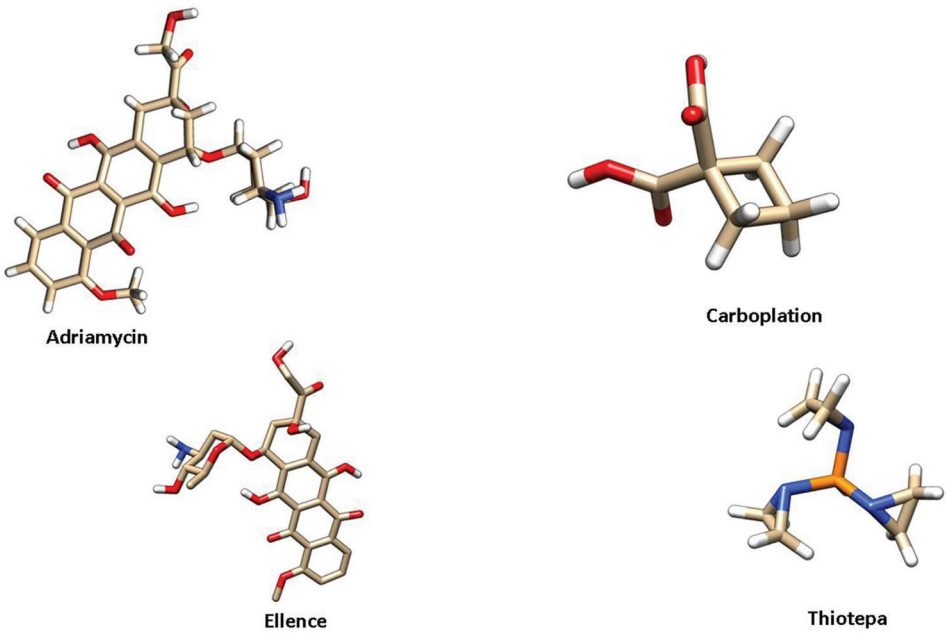

Fig. 5: Structure of some drugs used in chemotherapy [64]

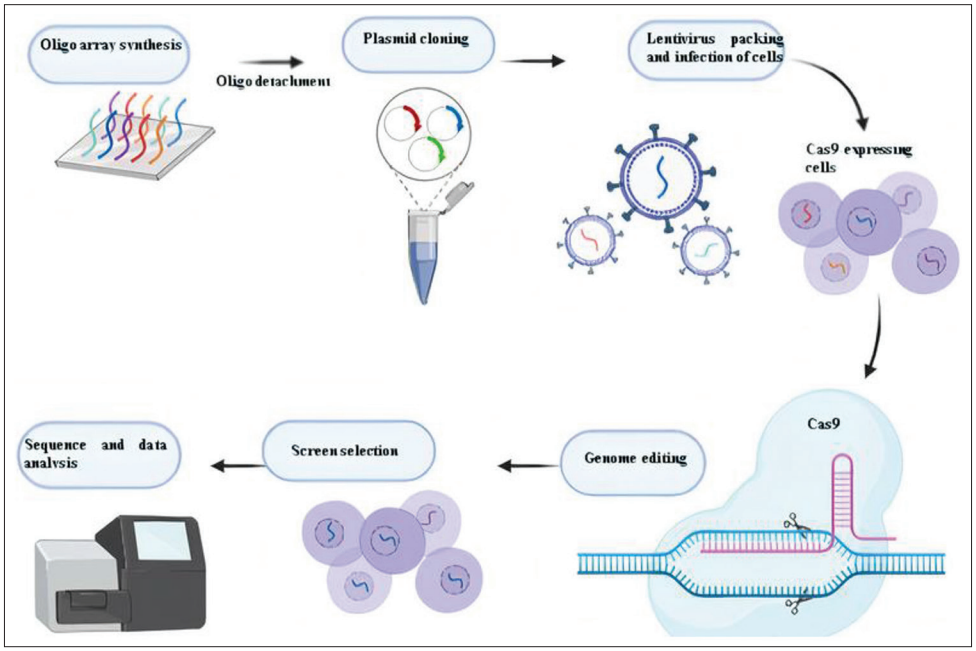

Fig. 6: CRISPR screening protocol [67]

Imaging technology-X-ray section emission tomography (positron emission tomography [PET]), magnetic resonance imaging, bone scan, bronchoscopy, biopsy, surgery will not refer to final stage patients. PET. CT is another important technique which is mainly used to locate and to identify the cancer tumor size [58].

CYTOGENETIC TECHNIQUE – FICTION

Fluorescence immunophenotyping and interphase cytogenetic are involved in detection of lung tumor which helps to identify the "genetic abnormalities", immunophenotypic markers. The cytogenetic analysis allows us to determine, genes, oncogenes, overexpressing cells, receptors, and ligands in the homoplastic area. Fluorescence *in site* hybridization comparative genetic hybridization, spectral karyotyping (SKY) chromosome analysis using SKY microarray [59]. One of the different arrays evaluations of the frequency of DNA methylation gene indicator of lung cancer is an early detection tool. Identification of volatile compounds in breath example of VOC3 emitted by neoplastic cells is methionine aldehydes, pentane, ammonia, detected by gas chromatography with the help of biomarkers, and cancer also be detected by blood and urine sample [60].

SCREENING

It is much more important to avoid lung cancer than screening this with. Randomized research tests found getting a chest X-ray do not increase. Survival in confirmed lung cancer cases [61]. However, research has shown that regular screening is for CT of the chest lung cancer reduces the death rate in suffers from a good profile dependence on the toxin. Effectiveness of intense control for identification by

regular chest CT scanning consequent cancers or metastatic of cancer did not exist Formal evidence, although a consequent yearly one The CT scans are frequently carried out but also suggested the Guidelines for a National Comprehensive Cancer Network [62]. However, these are the information not sufficient for it to be conclusive accept this custom popular to everyone. More rational treatment measurements such as fluorescence endoscopy of the lung they have been examined to show their effectiveness against synchronous tumor identification [63].

LUNG CANCER CARE OR REHABILITATION

Based on how far pulmonary cancer progresses, lung cancer is managed in several forms. NSCL cancer patients diagnosed with surgery, chemotherapy, and radiation therapy.

CHEMOTHERAPY

Chemotherapy is an active type of chemical drug treatment designed to kill cells that are fast-growing in the body (Fig. 5). The main form of chemotherapy is to decrease the body's gross cancer cell count, reduce cancer, propagation probability, shrink the scale of the tumor, and reduce signs now.

CRISPR cas9 variants

The another most important modern technique-CRISPR/Cas9 is used in several methods [65]. Many variations have been added in many modifications to the CRISPR system's basic structure such as the Cas9 RNA scaffold (DCas9) and dead RCas9 RNA scaffold, siRNA have RNA scaffolds connected to sgRNA Scaffolds are built to recruit specifically engineered RNA proteins interacting with cellular effectors for different active molecule-module modulation. AMPK α1 and α2 exclusion [66]. The editing in murine lung adenocarcinoma cells controlled by CRISPR Cas9 showed a substantial decrease in the level of the lung tumour were shown in Fig. 6 [67].

The editing in murine lung adenocarcinoma cells controlled by CRISPR Cas9 showed a substantial decrease in the level of the lung tumor (KRASG12D p53f/F controlled non-small cell lung cancer).

VACCIENS

Instead of a fixed causal link, there is a potential association between HPV and cancer. However, HPV is involved as a causative factor in several cancer types and a preventive was created. After 2006, the centers for Disease Care and Prevention (CDC) has advised that all pre-teen teens between the ages of 11 and 12 should be regularly vaccinated and that young people between the ages of 13 and 26 should also be vaccinated with HPV to avoid genital cancer [66]. The CDC also recommends daily vaccination for males aged from 11 to 12, plus young adults aged 13 to 21. Where the vaccination is not already completed, high-risk males up to 26 years old vaccinated by the increasing data on the widespread prevalence of HPV and HPV diseases [67]. Further work indicates that HPV and the lung are more associated and beneficial.

DISCUSSION

Even though smoking is a major causative agent of lunger cancer in humans, yet there is no proper evidence proves the relationship between smoking and lung cancer [68]. The purpose of this review study was to investigate relationship between tobacco and its mechanism by which carcinogens that reacts against DNA. The studies suggest that, the tobacco is involved in high risk of lung cancer, pancreas, gallbladder, brain, liver, hematologic malignancies etc [69-70]. Though study conclude that cancer is an inherited disease, Smoking has been the subject of most genetic epidemiological studies, attempting to create gene carcinogenic associations and to clarify phenomena, carcinomic cycle elements [71]. It is equally amenable to know the clarity of the factor that adzed which chain smoker inclined to the advancement of lung cancer and to find native medication [72]. While these findings have been of considerable significance to the date, these experiments have not yet attained their maximum potential [73,74]. Many of them also concentrated on human genotypes that may be predicted to trigger different reactions including activation of metabolism. Some works were motivated by fairly easy techniques of genotyping. As this area progresses, it is increasingly clear that this method can only produce minimal knowledge [75]. More thorough incorporation of biomarkers of genotypes and phenotypes into epidemiological observation is needed. DNA microarray will support these studies which enable the quick result of genotyping. In the end, control of the metabolic pathways outlined in Fig. 1 should also be feasible. 1 Hybrid genotyping – phenotyping strategy of smoking and other individuals exposed to tobacco carcinogens [76]. Blocking either of the horizontal pathways in Fig. 1 will result in reduced prevalence and mortality of lung cancer. Avoiding the tolerance to nicotine and developing smoking prevention approaches are goals but only marginally effective ones are found. Human DNA metaphylaxis is almost certainly caused by NNK or NNN exposure [77]. The function of tobacco-specific nitrosamines is uncertain to ensure that they are protected against the oxidative harm caused by the human lungs. DNA-methylating nitroid compounds are more probable origins. The precise source of DNA methylation damage from human pulmonary tobacco-specific nitrosamines needs more research to be identified. [78]. Carcinogenic symptoms are less typical of SSB and 8-oxo-dG. Chemoprevention is an effective method for addicted smokers and former smokers. There are now several agents identified that can inhibit carcinogenic activation or promote detoxification [79]. Many chemopreventive substances impede downstream activities from the development of adduct DNA [80]. Further production of successful chemopreventive agents which are less toxic would be a big goal in reducing the occurrence of lung cancer [81]. There are many techniques used to cure lung cancer, such as scanning, radiation, guided treatment, screening, targeted therapy, and the CRISPR system allows deteriorating malignancy [82]. This type of controlled cell approaches the gene and what form of the disease will develop and produce.

CONCLUSION

Smoking causes multidimensional effect on lung cancer. This lung cancer is often closely associated to inflammation and tobacco smoking. Thus, it remains the most reliable causal agent for developing disease and holds a definitive predictive and prognostic value. Chemoprevention is an efficient means of treating addiction and ex-smokers. If some of the horizontal pathways are blocked in Fig. 1, the incidence is reduced and the lung cancer mortality is reduced. Avoiding nicotine tolerance and improving approaches to smoking prevention are priorities but only moderately successful ones are established. A major aim is to reduce lung cancer further and produces effective chemoprevention agents that are less harmful. There are several methods used in the treatment of lung cancer, for example, scan, radiation, direct treatment, screening, and targeted therapy. This regulated cell type discusses the gene and how the disease evolves and produces.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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