LIST OF TABLES

Tables	Page No.
Table 1: Estimated incidence, mortality and 5-year prevalence of top five ranked cancer	10
Table 2: Estimated incidence, mortality and 5-year prevalence of top five ranked cancer	11
Table 3: Estimated incidence, mortality and 5-year prevalence of top five ranked cancer: women	12
Table 4: Selected chemopreventive agents with their molecular targets	18
Table 5: List of chemopreventive and anticancer drugs that are in advance stages of clinical trial	f 21
Table 6: Chemotherapeutic drugs approved by FDA, USA in 2015	22
Table 7: Chemically induced carcinogenesis models that are currently being used in chemoprevention study	n 25
Table 8: UV-VIS peak values of FENA and LEPT	60
Table 9: FTIR peak values and functional groups of FENA and LEPT	61
Table 10: Effects of FENA on general body weight gain profile and relative organ weight in untreated <i>Swiss albino</i> mice	85
Table 11: Effects of FENA on general body weight gain profile and relative organ weight in DMBA and croton oil treated <i>Swiss albino</i> mice	86
Table 12: Effects of FENA on general body weight gain profile and relative organ weight in Benzo(a)pyrene treated <i>Swiss albino</i> mice	87
Table 13: Modulatory influences of FENA on the activity/level of xenobiotic metabolizing enzymes, antioxidants and toxicity related parameters in hepatic tissues of <i>Swiss albino</i> mice	88
Table 14: Modulatory influences of FENA in hepatic tissue against DMBA induce and croton oil promoted skin papillomagenesis	ed 89
Table 15: Modulatory influences of FENA in hepatic tissue against B(a)P induced forestomach papillomagenesis	91
Table 16: Modulatory influences of FENA in papilloma bearing tissue against DMBA induced and croton oil promoted skin papillomagenesis	92
Table 17: Modulatory influences of FENA in papilloma bearing forestomach tissue against B(a)P induced forestomach papillomagenesis	94

Table 18: Modulatory influences of FENA on the activity/level of xenobiotic metabolizing enzymes, antioxidants and toxicity related parameters in lung and kidneys of Swiss albino mice	95
Table 19: Modulatory influences of FENA on the activity/level of xenobiotic metabolizing enzymes, antioxidants and toxicity related parameters in forestomach and spleen of <i>Swiss albino</i> mice	96
Table 20: Modulatory influences of FENA in lung tissue against DMBA induced and croton oil promoted skin papillomagenesis	97
Table 21: Modulatory influences of FENA in kidneys tissue against DMBA induced and croton oil promoted skin papillomagenesis	98
Table 22: Modulatory influences of FENA in forestomach tissue against DMBA induced and Croton oil promoted skin papillomagenesis	99
Table 23: Modulatory influences of FENA in lung tissue against B(a)P induced forestomach papillomagenesis	100
Table 24: Modulatory influences of FENA in kidney and spleen tissue against B(a)P induced forestomach papillomagenesis	101
Table 25: ADME/Tox profile of phytochemicals present in FENA	102
Table 26: Effects of LEPT on general body weight gain profile and relative organ weight in untreated <i>Swiss albino</i> mice	111
Table 27: Effects of LEPT on general body weight gain profile and relative organ weight in DMBA and croton oil treated <i>Swiss albino</i> mice	112
Table 28: Effects of LEPT on general body weight gain profile and relative organ weight in Benzo(a)pyrene treated <i>Swiss albino</i> mice	113
Table 29: Modulatory influences of LEPT on the activity/level of xenobiotic metabolizing enzymes, antioxidants and toxicity related parameters in hepatic tissues of <i>Swiss albino</i> mice	114
Table 30: Modulatory influences of LEPT in hepatic tissue against DMBA induced and croton oil promoted skin papillomagenesis	115
Table 31: Modulatory influences of LEPT in hepatic tissue against B(a)P induced forestomach papillomagenesis	117
Table 32: Modulatory influences of LEPT in papilloma bearing tissue against DMBA induced and croton oil promoted skin papillomagenesis	119
Table 33: Modulatory influences of LEPT in papilloma bearing forestomach tissue against B(a)P induced forestomach papillomagenesis	121
Table 34: Modulatory influences of LEPT on the activity/level of xenobiotic metabolizing enzymes, antioxidants and toxicity related parameters in lung and kidneys of Swiss albino mice	123

Table 35: Modulatory influences of LEPT on the activity/level of xenobiotic metabolizing enzymes, antioxidants and toxicity related parameters in forestomach and spleen of <i>Swiss albino</i> mice	124
Table 36: Modulatory influences of LEPT in lung tissue against DMBA induced and croton oil promoted skin papillomagenesis	125
Table 37: Modulatory influences of LEPT in kidneys tissue against DMBA induced and croton oil promoted skin papillomagenesis	126
Table 38: Modulatory influences of LEPT in forestomach tissue against DMBA induced and croton oil promoted skin papillomagenesis	127
Table 39: Modulatory influences of LEPT in spleen tissue against DMBA induced and croton oil promoted skin papillomagenesis	128
Table 40: Modulatory influences of FENA in lung tissue against B(a)P induced forestomach papillomagenesis	129
Table 41: Modulatory influences of FENA in kidneys tissue against B(a)P induced forestomach papillomagenesis	130
Table 42: Modulatory influences of FENA in spleen tissue against B(a)P induced forestomach papillomagenesis	132
Table 43: ADME/Tox profile of phytochemicals present in LEPT	132
Table 44: Effects of fractionated extract on viability of lung, prostate and colon cancer cell lines	145

LIST OF FIGURES

Figures	Page No.
Figure 1: World map showing the distribution of age standardized rate of cancer	
incidence	8
Figure 2 : World map showing the distribution of age standardized rate of cancer mortality	9
Figure 3: World map showing the distribution of prevalence of cancer	9
Figure 4: Basic Progression Model of cancer and its windows for chemoprevention	n 13
Figure 5: Mode of action of chemopreventive agents	14
Figure 6: Chemical structure of few chemopreventive and anticancer phenolic compounds	27
Figure 7: Chemical structure of few chemopreventive and anticancer flavonoids	29
Figure 8: Chemical structure of few chemopreventive and anticancer alkaloids	31
Figure 9: Map of India showing biodiversity hotspots	33
Figure 10: Map of Assam showing the investigated area in blue dots	36
Figure 11: Photographs of Nyctanthes arbor-tristis Linn.	37
Figure 12: Photographs of <i>Phlogacanthus tubiflorus</i> Nees.	38
Figure 13: Photographs of <i>Phlogacanthus thyrsiflorus</i> Nees.	39
Figure 14: Protective effect of the REPT against oxidative stress induced by H_2O_2	48
Figure 15: Protective effect of the FENA against oxidative stress induced by H ₂ O ₂	49
Figure 16: Antioxidative and free radical scavenging activity of FENA	58
and LEPT	20
Figure 17: Fe ³⁺ reducing ability of FENA and LEPT	59
Figure 18: Ultraviolet-visible and FTIR spectra of FENA and LEPT	60
Figure 19: Timeline of treatment schedule of modulatory influence of FENA/LEP	T 66
Figure 20: Timeline of treatment schedule of chemopreventive potentials of FENA/LEPT against DMBA induced and croton oil promoted skin papillomagenesis	68
Figure 21: Timeline of treatment schedule of chemopreventive potentials of FENA/LEPT against Benzo(a)pyrene induced forestomach papillomagenesis	69
Figure 22: FENA inhibit the papilloma incidence and multiplicity, papilloma yield and burden against DMBA induced and croton oil promoted skin papillomagenesis	1 77

Figure 23: FENA inhibit the papilloma multiplicity, papilloma yield and burden against B(a)P induced forestomach papillomagenesis	78
Figure 24: Hematoxylin and eosin stained sections of skin tissues of normal and papilloma bearing mice:	79
Figure 25: Hematoxylin and eosin stained sections of forestomach tissues of normal and papilloma bearing mice:	78
Figure 26: Heat map showing the modulatory influence of FENA	82
Figure 27: Total ion Chromatogram (TIC) of FENA	84
Figure 28: LEPT inhibit the papilloma incidence and papilloma yield and burden against DMBA induced and croton oil promoted skin papillomagenesis	103
Figure 29: LEPT inhibit the papilloma incidence and papilloma yield and burden against DMBA induced and croton oil promoted skin papillomagenesis	104
Figure 30: Hematoxylin and eosin stained sections of skin tissues of normal and papilloma bearing mice	105
Figure 31: Hematoxylin and eosin stained sections of forestomach tissues of normal and papilloma bearing mice	106
Figure 32: Heat map showing the modulatory influence of LEPT	108
Figure 33: Total ion Chromatogram (TIC) of LEPT	110
Figure 34: Proposed mode of chemopreventive potentials of FENA and LEPT	134
Figure 35: F ³ NAF inhibit the growth of PC3 cells	148
Figure 36: F ³ NAF inhibit the growth and caused death of LNCaP cells	149
Figure 37: F ³ NAF inhibit the proliferation of PC3 and LNCaP cells	150
Figure 38: Effects of F ³ NAF on apoptosis in PC3 cells	152
Figure 39: F ³ NAF cause arrest in progression of cell cycle of PC3 cells and modulates regulators of cell cycle	153
Figure 40: F ³ NAF inhibit the clonogenicity of PC3 cells	154
Figure 41: F ³ NAF modulate the regulators of growth, proliferation and survival in PC3 cells	155
Figure 42: F ³ NAF inhibit the migration and invasion of PC3 cells	157
Figure 43: Chemical characterization of F ³ NAF:	158

LIST OF ABBREVIATIONS

Abbreviation	Full form
μg	micro gram
μl	micro litre
μΜ	micro mole
$^{0}\mathrm{C}$	⁰ Celsius.
0 N & 0 E	⁰ North & ⁰ East
ABTS	2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid)
Ad libitum	Without restraint.
AD	Anno Domini
AhR	Aryl hydrocarbon receptor
Akt	Protein kinase B (PKB)
ANOVA	Analysis of variance
AOEs	Antioxidant enzyme systems
AP1	Activator protein 1
ARE	Antioxidant response elements
ARNT	Aryl Hydrocarbon Receptor Nuclear Translocator
ATCC	American Type Culture Collection
B(a)P	Benzo(a)pyrene
BC	Before Christ
BHA	Butylated hydroxyanisole
BHT	Butylated hydroxytoluene
BrdU	5-bromo-2'-deoxyuridine
BSA	Bovine serum albumin
BSI	Botanical Survey of India
CAM	Chorioallantoic Membrane
CAPE	Caffeic acid phenethyl ester
CAT	Catalase
Cdc	Cell-division cycle protein
CDK	Cyclin-dependent kinase
COX	Cyclooxygenase
CPCSEA	Committee for the Purpose of Control and Supervision of Experiments on Animals
DCFDA	2',7'-Dichlorofluorescin diacetate
de novo	From the beginning

DMBA 7,12-Dimethylbenz[a]anthracene

DMSO Dimethyl sulphoxide

DPPH 2,2-diphenyl-1-picrylhydrazyl

DTD DT-diaphorase

ECE Epicatechin equivalent

ECL Enhanced chemiluminescence

ECM Extracellular matrix
EGCG Epigallocatechin gallate

EGFR Epidermal growth factor receptor
ERK Extracellular signal regulated kinases

et ali (and others)

F³NAF Free flavonoid fraction of flowers of *Nyctanthes arbor-tristis*

FACS Fluorescence-activated cell analyzer

FBS Fetal bovine serum

FDA Food and Drug Administration

FENA Flower extract of Nyctanthes arbor-tristis

FITC Fluorescein isothiocyanate

FOXO Forkhead box

FTIR Fourier transform infrared spectroscopy

GAE Gallic acid equivalent

GCMS Gas chromatography—mass spectrometry

gm gram

GPx Glutathione peroxidase
GR Glutathione reductase
GSH Reduced glutathione
GSSG Glutathione oxidized
GST Glutathione-S-transferase

HPLC High performance liquid chromatography

HPV Human Papilloma virus

HR LCMS High resolution liquid chromatography mass spectrometry

Hr hour

HRP Horseradish peroxidase

i.e. id est (that is)

IC₅₀ Inhibitory concentration (50%)

In silico Performed on computer

In situ On site

In vitro Outside a living SYSTEM

In vivo Within the living system

Inj. Injection

IP Intraperitoneal

JNK Jun N-terminal kinase LD_{50} Lethal dose (50%) LDH Lactate dehydrogenase

LEPT Leaf extract of *Phlogacanthus thyrsiflorus* Nees.

LP Lipid peroxidation

MAPK Mitogen-activated protein kinases

MDA Malondialdehyde

MEK Mitogen/extracellular signal-regulated kinase

mg mili gram
ml milli litre
mM mili mole
mm milli meter

MMP Matrix metallopeptidase

mTOR Mammalian target of rapamycin

MTT 3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide)

NADH Reduced nicotinamide adenine dinucleotide

NF-κB Nuclear factor κB

nm nano meter
nM nano mole
NO Nitric oxide

 $\begin{array}{ccc} Nrf & Nuclear \ receptor \ factor \\ O_2^- & Superoxide \ radical \\ OD & Optical \ density \\ OH^* & Hydroxyl \ radical \\ ONOO^* & Peroxynitrite \\ \end{array}$

PAHs Polyaromatic hydrocarbons
PARP Poly ADP ribose polymerase

PBS Phosphate buffer saline

PCa Prostate cancer
PI Propidium iodide

PI3K Phosphoinositide 3 kinase

PKC Protein kinase C

RAF Rapidly accelerated fibrosarcoma

Ref. Reference

REPT Roots of *Phlogacanthus tubiflorus*

RFU Relative fluorescence units
ROS Reactive oxygen species
rpm Revolution per minute
SD Standard deviation

SDS-PAGE Sodium dodecyl sulfate polyacrylamide gel electrophoresis

Sec second

sem Standard error of the mean SOD Superoxide dismutase SPTs Secondary primary tumors

STAT Signal transducer and activator of transcription

TBARS Thiobarbituric acid reactive substances

TGF Transforming growth factor
TIC Total ion chromatogram

TPA 12-O-Tetradecanoylphorbol-13-acetate

UHPLC Ultra high performance liquid chromatography
UPLC Ultra performance liquid chromatography

UV-VIS Ultraviolet—visible spectroscopy
VEGF Vascular endothelial growth factor

Viz. Namely

w/v Wight/volume

WHO World Health Organization
XRE Xenobiotic responsive element