Anticancer efficacy of phenolics based structurally related compounds and their radical scavenging action

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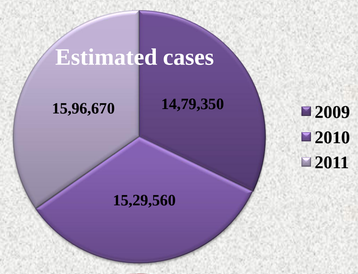
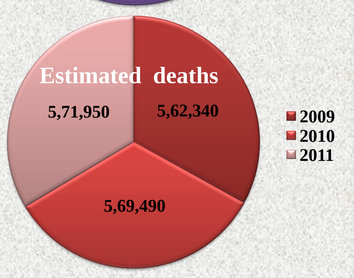
INTRODUCTION

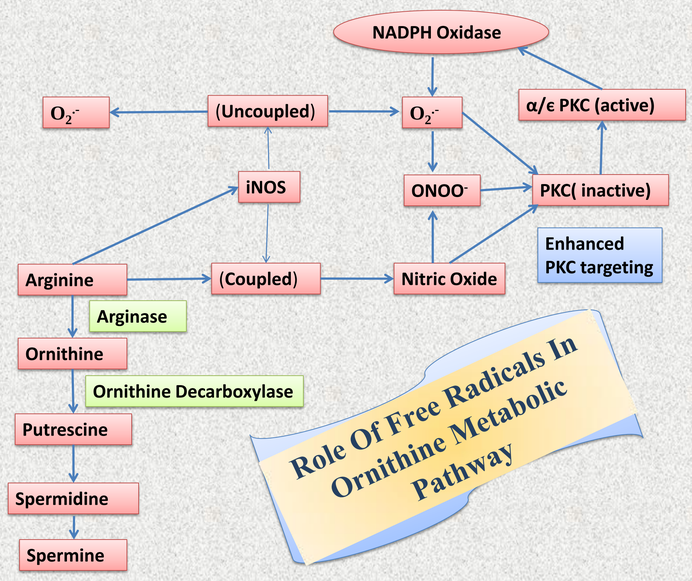
- Cancer, one of the leading cause of death worldwide, is an abnormal cell proliferation that fails to respond to the normal signals.
- In an effort to eradicate the growing menace of cancer, a clear understanding of fundamental biology and molecular mechanism of carcinogenesis is essential for targeted therapies.
- Among the devised strategies being in use for cancer treatment, the one that is of immense interest is the development of plant based novel anticancer agents.
- Due to their tremendous availability, biological activity and efficacy, the phytochemicals deemed a gibbous future in chemoprevention.
- In the present study, several phenolics based structurally related compounds of steroidal and non-steroidal skeleton were synthesized and tested for their modulatory effect on ornithine decarboxylase activity, an enzyme highly upregulated in cancer.
- Additionally, these compounds were also examined for radical scavenging action to establish a correlation with the anticancer property.

CANCER STATISTICS

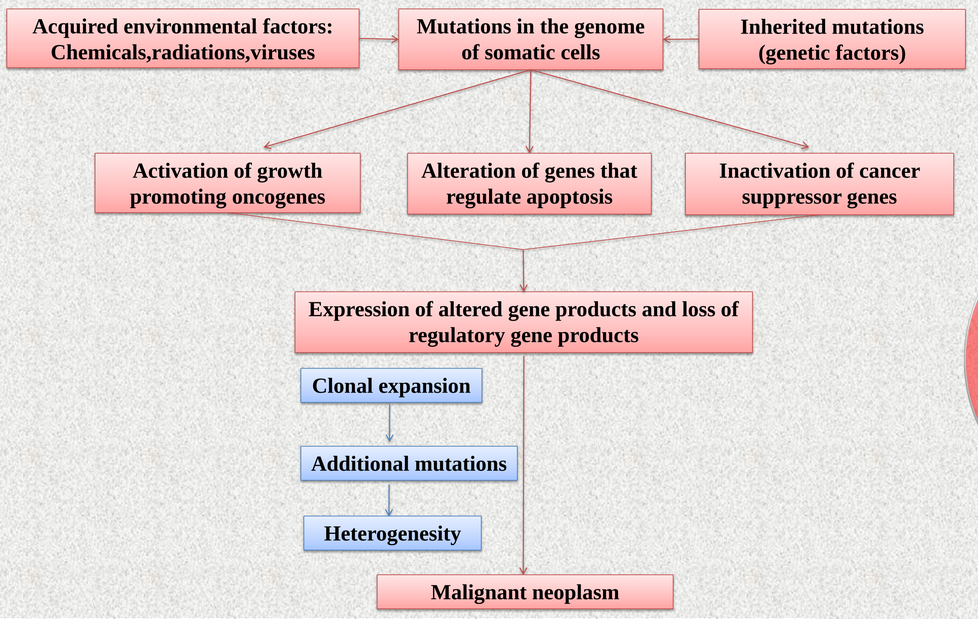




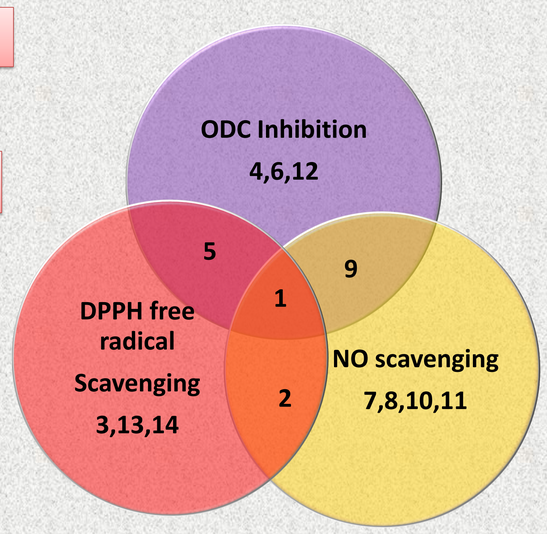
Role Of Free Radicals In Ornithine Metabolic Pathway



MOLECULAR MECHANISM OF CANCER



RESULTS



1-(3,-methoxy, 4-hydroxyphenyl)-3-[3-methoxyestra 1, 3, 5 (10)-trien-17-acetate, 2-yl] -2-propen-1-one (NBA-1)

3- (3', 4', 5'-trimethoxyphenyl)- 4, 5, 6 -trimethoxyindan-1-one oxime (NBA-6)

1-(3,4, 5-trimethoxyphenyl)-3-(2,4,5-trimethoxyphenyl)-2-propen-1-one(NBA-10)

1-(3,4,5-trimethoxyphenyl)-3-(2,3,4-trimethoxyphenyl)-2-propen-1-one (NBA-2)

3-(3',4', 5'-trimethoxyphenyl)- 4,5,6-trimethoxyindan-1-ol (NBA-7)

3-(3',4', 5'-trimethoxyphenyl)- 4,5,6-trimethoxyindan-1-one(NBA-11)

1-(4-methoxyphenyl)-3-[3-methoxy,17-hydroxyestra 1,3,5(10)-trien, 2-yl] -2-propen-1-one (NBA-3)

Phenolic based steroidal and non steroidal structurally related compounds

2-Hydroxy, 3- (3', 4', 5'-trimethoxyphenyl)- 4, 5, 6-trimethoxyind-2-en-1-one (NBA-12)

1-(3,4-methylenedioxyphenyl)-3-(3,4,5-trimethoxyphenyl)-2-propen-1-one(NBA-4)

1-(3,4,5-trimethoxyphenyl)-3-phenyl-2-propen-1-one (NBA-8)

1-phenyl-3-[3-methoxy, 17-hydroxyestra 1,3,5(10)-trien, 2-yl]-2-propen-1-one (NBA-13)

1-(2,4-dibromophenyl)-3-[3-methoxyestra 1,3,5(10)-trien-17-acetate, 2-yl]-2-propen-1-one (NBA-5)

1-(3,4, 5-trimethoxyphenyl)-3-(3,4,5-trimethoxyphenyl)-2-propen-1-one (NBA-9)

1-(3-methylphenyl) -3- [3-methoxy, 17-hydroxyestra 1,3,5 (10)-trien, 2-yl]-2-propen-1-one (NBA-14)

MOLECULAR TARGETS IN CANCER CHEMOPREVENTION

Class	Primary target
Cyclooxygenase -2 inhibitor	Cyclooxygenase -2
Selective Estrogen Receptor Modulators	Estrogen receptor
5-alpha reductase inhibitor	5-alpha reductase (type -1)
Ras inhibitor	Farnysyl transferase
Tyrosine kinase inhibitor	Tyrosine kinase
Matrixmetalloproteinase inhibitor	Matrixmetalloproteinase
Polyamines biosynthesis inhibitors	Ornithine decarboxylase, Aromatase, S-Adenosine decarboxylase
PPAR-γ agonist	PPAR-γ
RXR selective ligand	RARs, RAXs
Cellular retinol binding protein ligand	Cellular retinol binding protein
AP-1 inhibitors	AP-1
Jun kinase inhibitor	Jun kinase
Cyclin dependent kinase inhibitors	Cyclin dependent kinase
Monoclonal Abs	Her-2,EGFR,VEGF
Gene therapy	p53

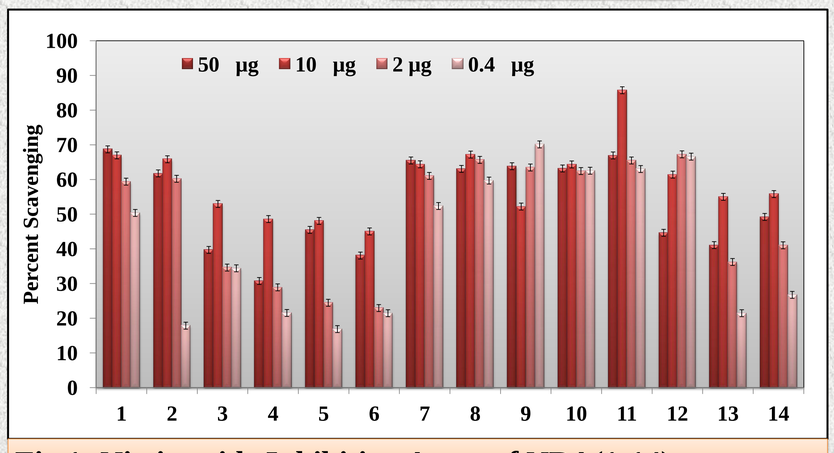


Fig 1: Nitric oxide Inhibition Assay of NBA(1-14)

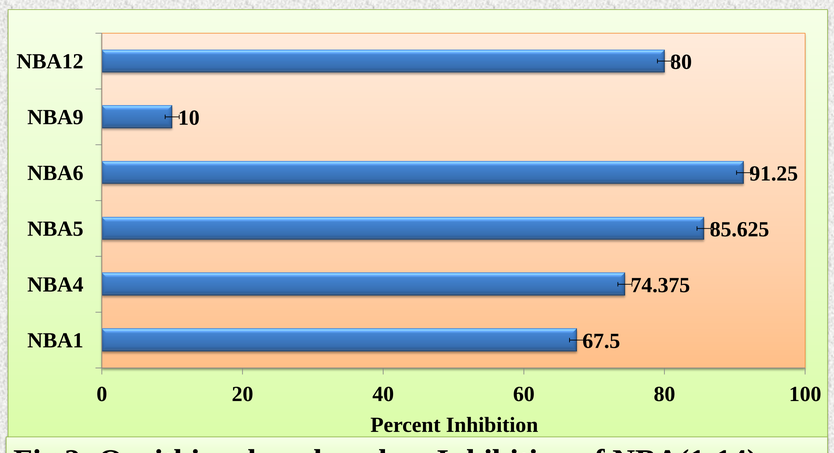


Fig 2: Ornithine decarboxylase Inhibition of NBA(1-14)

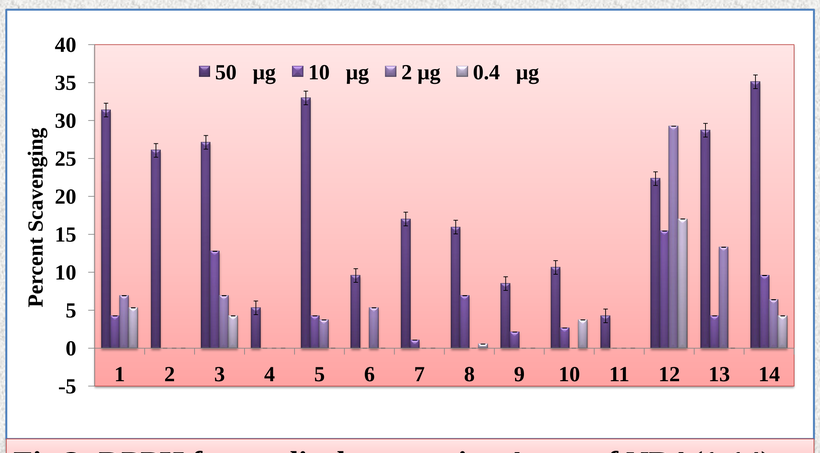


Fig 3: DPPH free radical scavenging Assay of NBA(1-14)

CONCLUSION

Phenolics based chalcones and indanone derivatives synthesized on steroidal and non steroidal skeletons were tested for their chemopreventive and radical scavenging action.
Most of these compounds possessed a 3,4,5- trimethoxyphenyl unit which might be inducing enzyme inhibition and scavenging radical formation.
Further investigations are on the way to establish the structure-activity relationship, so that these compounds can be developed as anticancer agents.

EXPERIMENTAL REFERENCES

Ornithine Decarboxylase Inhibition Assay
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Journal of Agricultural Food Chemistry (2002) 50: 2454-2458

ACKNOWLEDGEMENT

Council of Science &Technology(CST), Uttar Pradesh
Council of Scientific & Industrial Research (CSIR),New Delhi