



CSIR-CIMAP

Ornithine Decarboxylase activity, a clinical biomarker for evaluating cancer chemopreventive efficacy of phytomolecules

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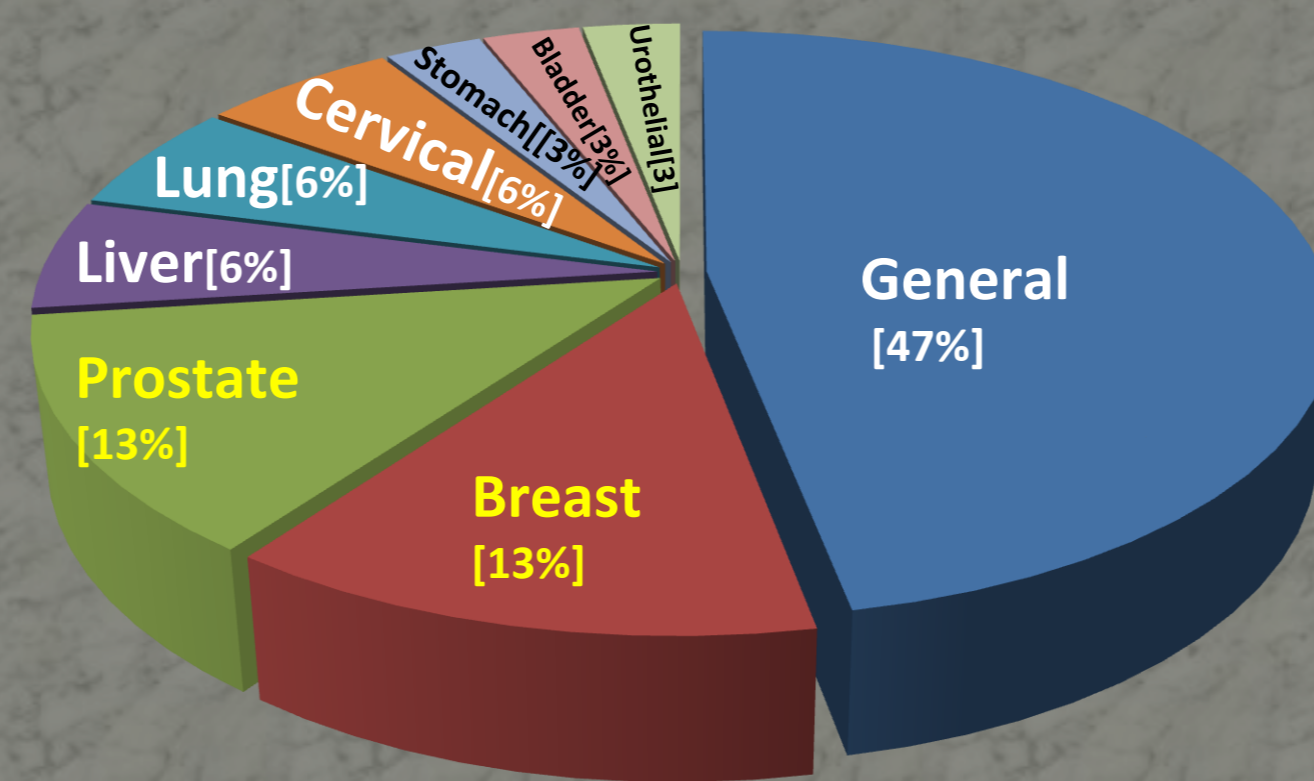
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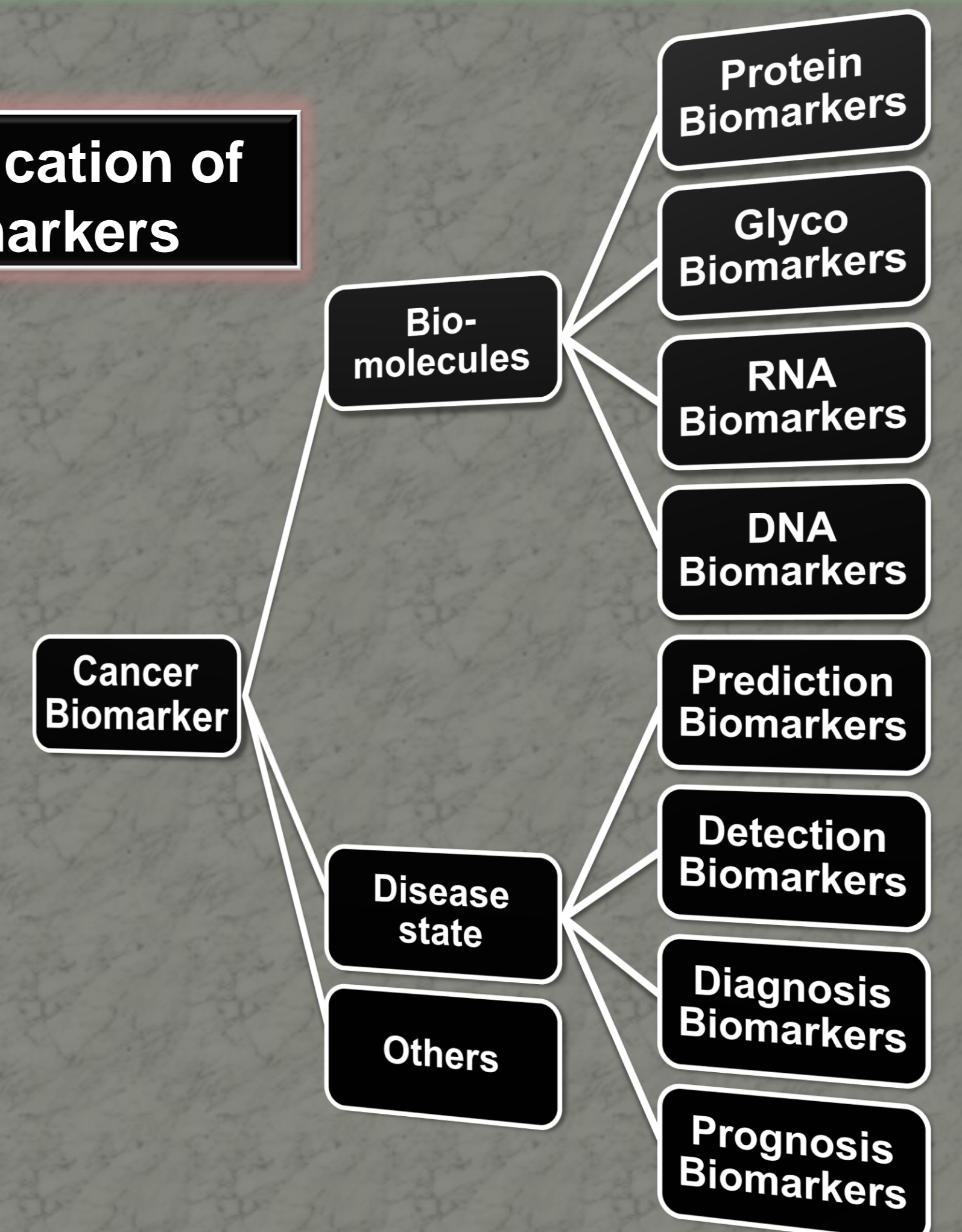
INTRODUCTION

- Biomarkers of cancer has made a strong traipse in predicting the disease pattern and contributed significantly to the understanding of tumour state, progression, characteristics and response to therapies.
- Ornithine decarboxylase (EC 4.1.1.17) catalyzes the pyridoxal 5-phosphate (PLP)-dependent decarboxylation of ornithine to putrescine, the first critical step in biosynthetic pathway of polyamines.
- Expression of this enzyme is transiently increased upon stimulation by growth factors, but becomes constitutively activated during cell transformation induced by carcinogens, viruses or oncogenes.
- Lots of research says that the phytomolecules having antioxidant property may have antimutagenic or anticarcinogenic activity. Therefore a need is there to find their interactive mode on known signature markers of cancer like ornithine decarboxylase enzyme.

Biomarker patent filings according to type of cancer



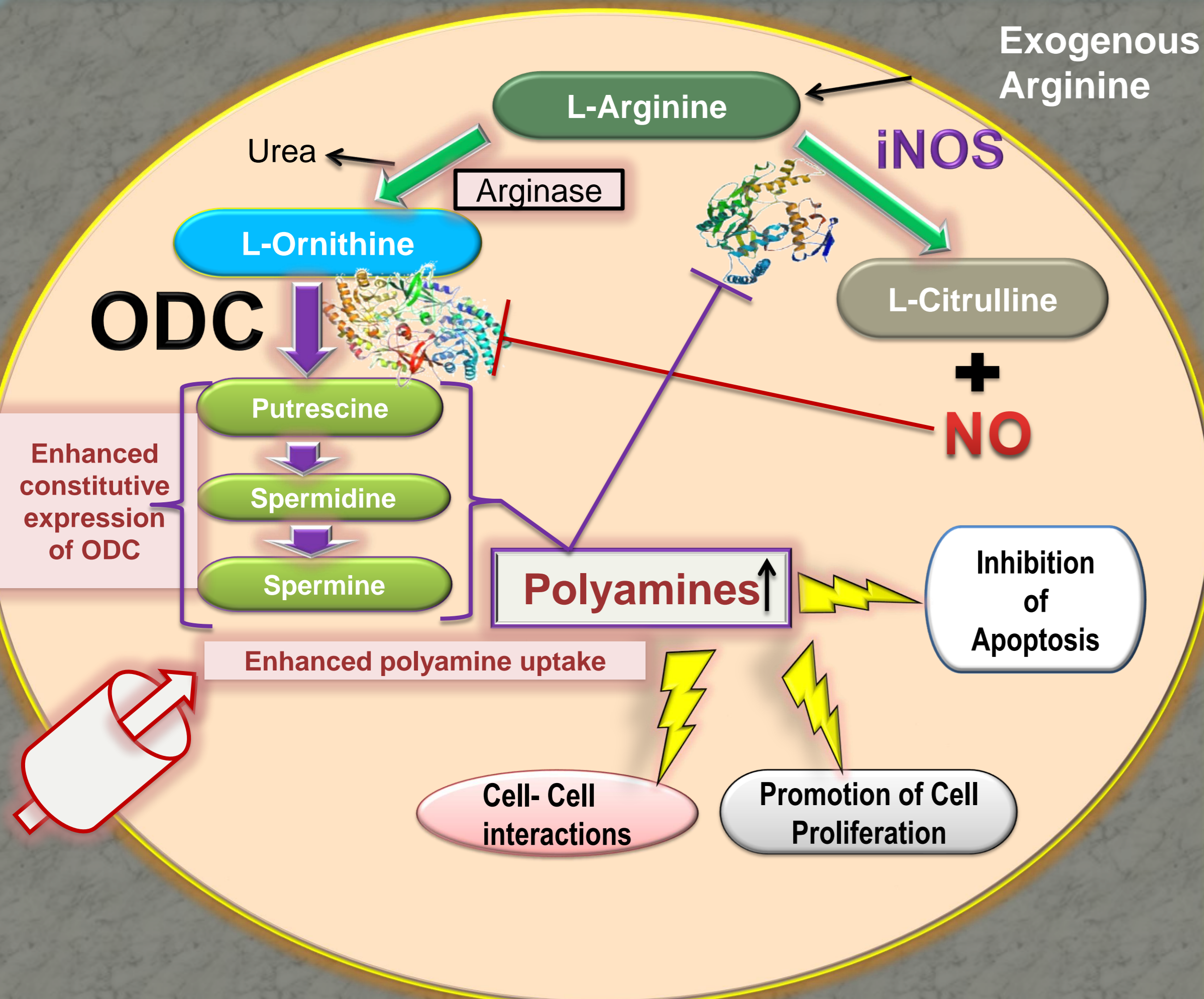
Classification of Biomarkers



REFERENCE

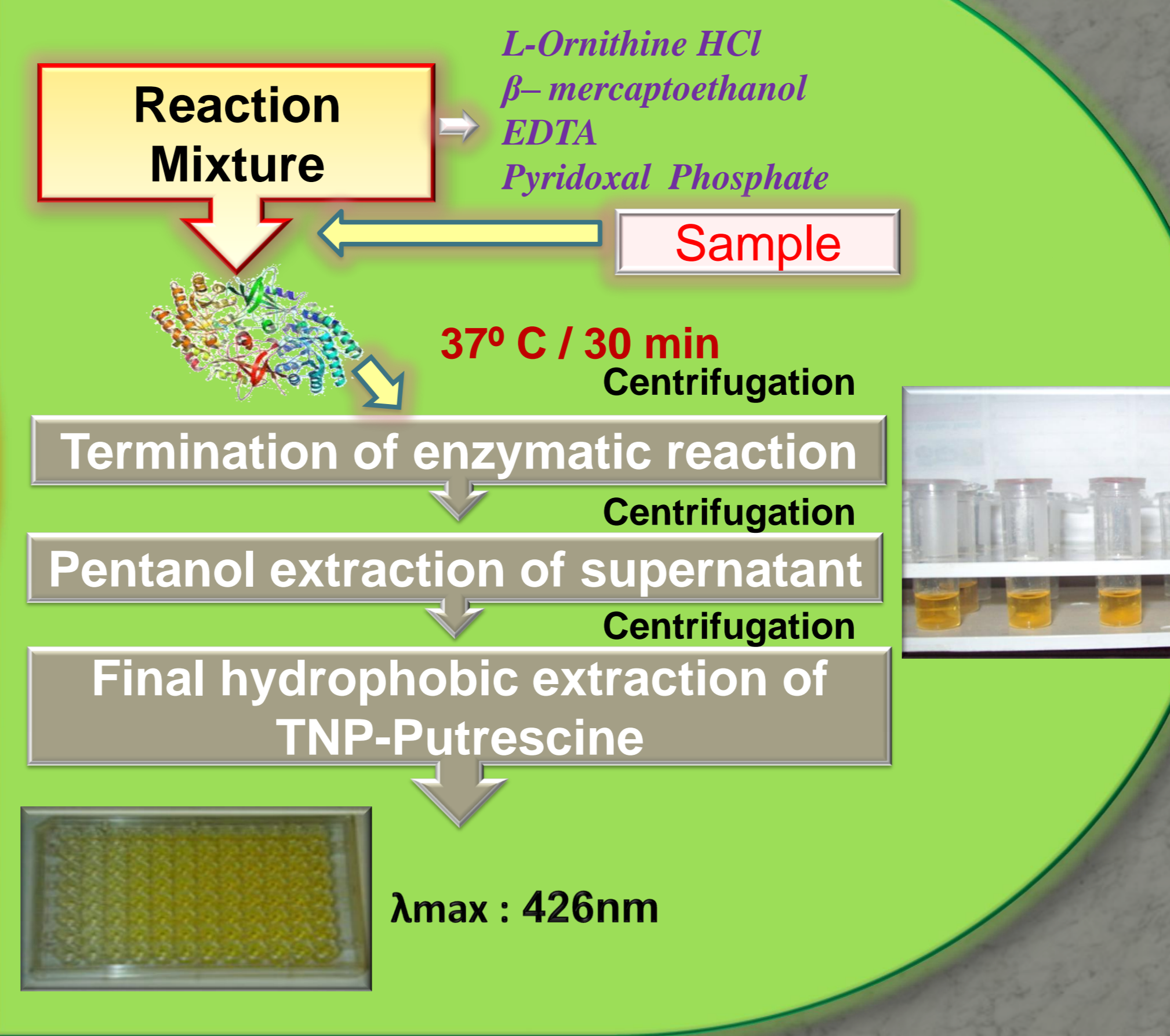
- Analytical Biochemistry (1987)160:290-293
- Biochem.Biophys.Res.Comm.(1994)201:748-755
- J.Agric.Food Chem.(2002)50:2454-2458

Reactions inside the cell

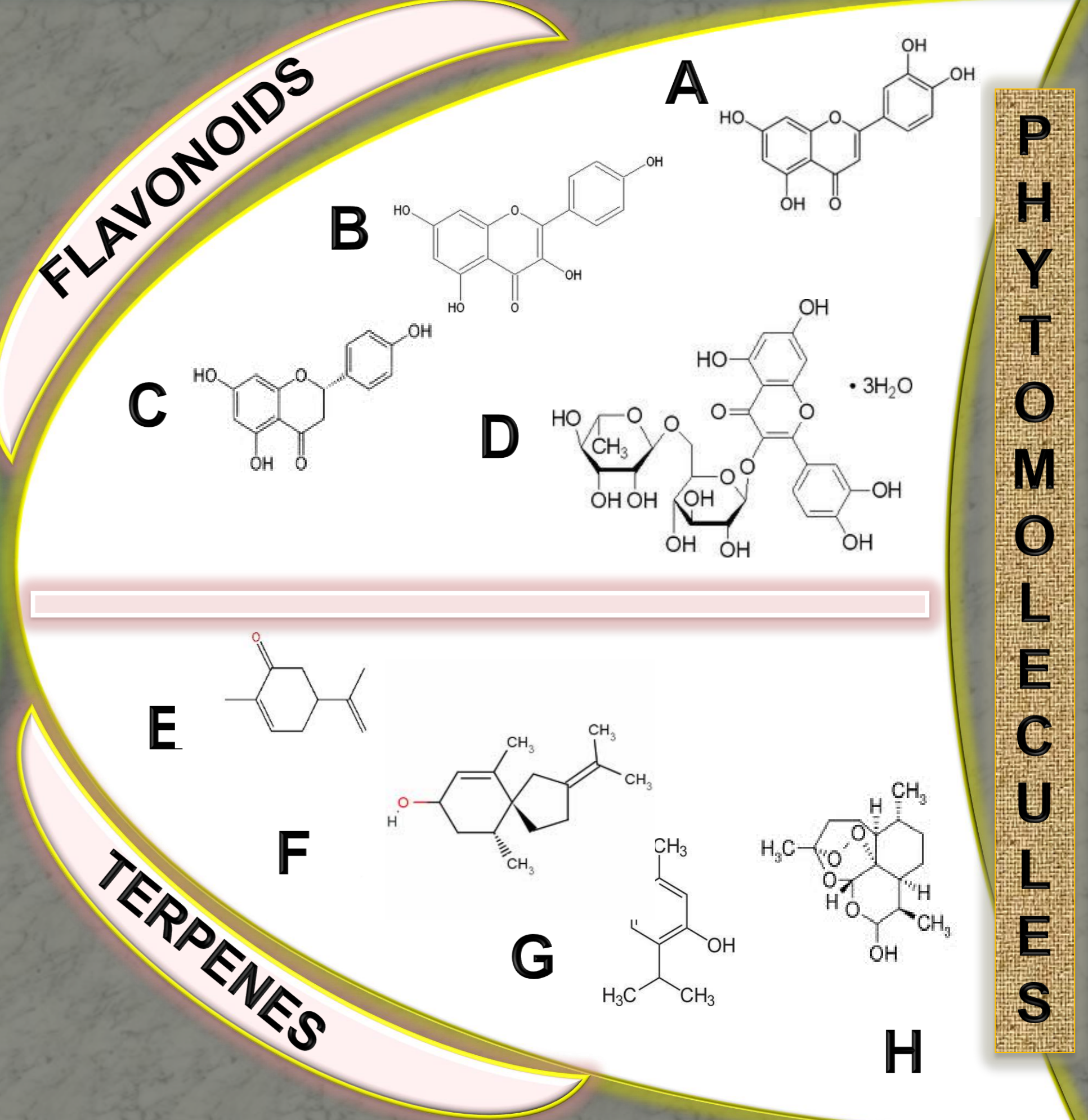


METHODOLOGY

EXPERIMENTAL SCHEME

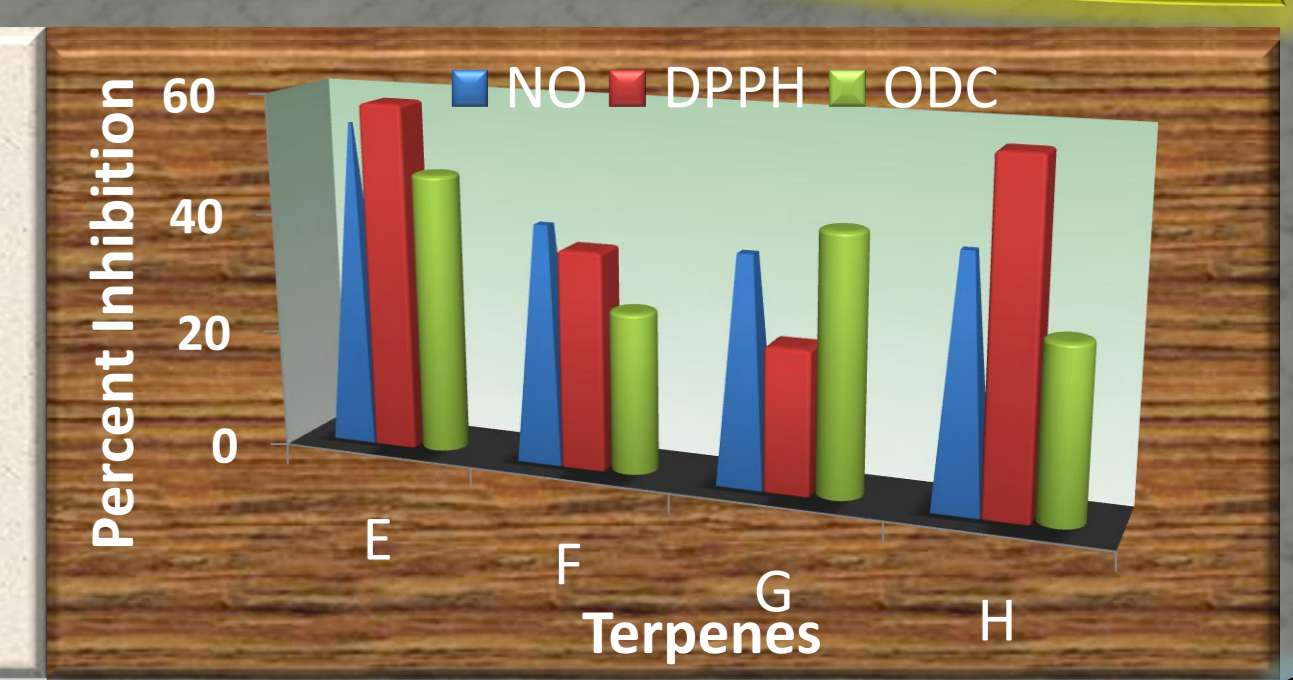
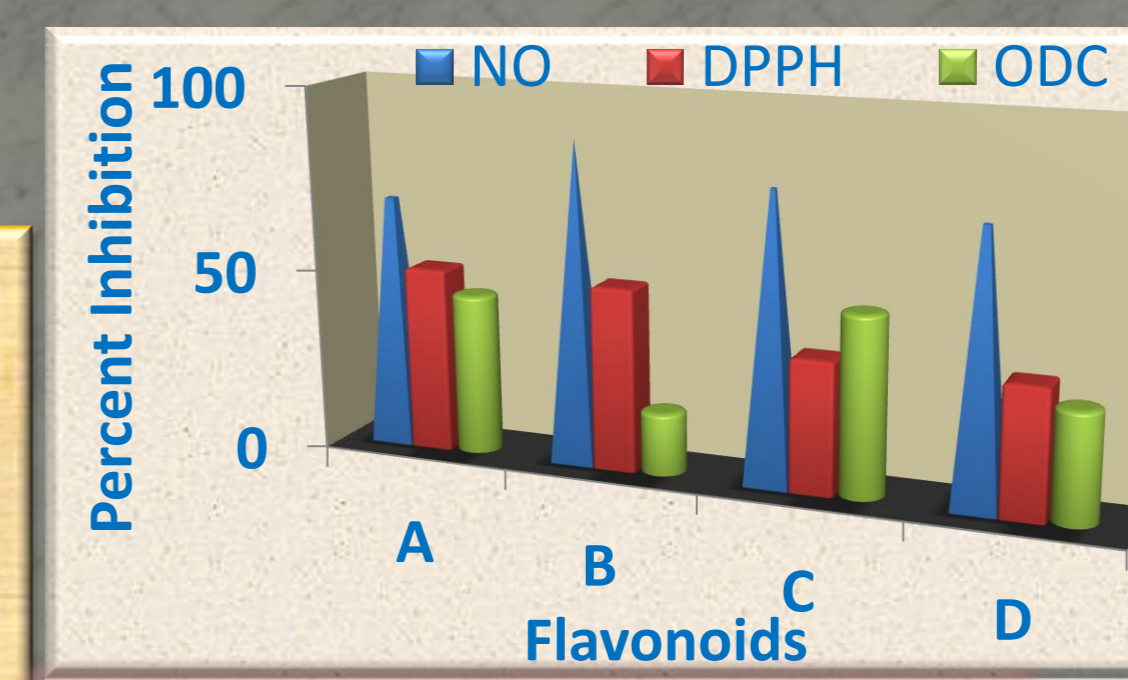


Structures of positive leads

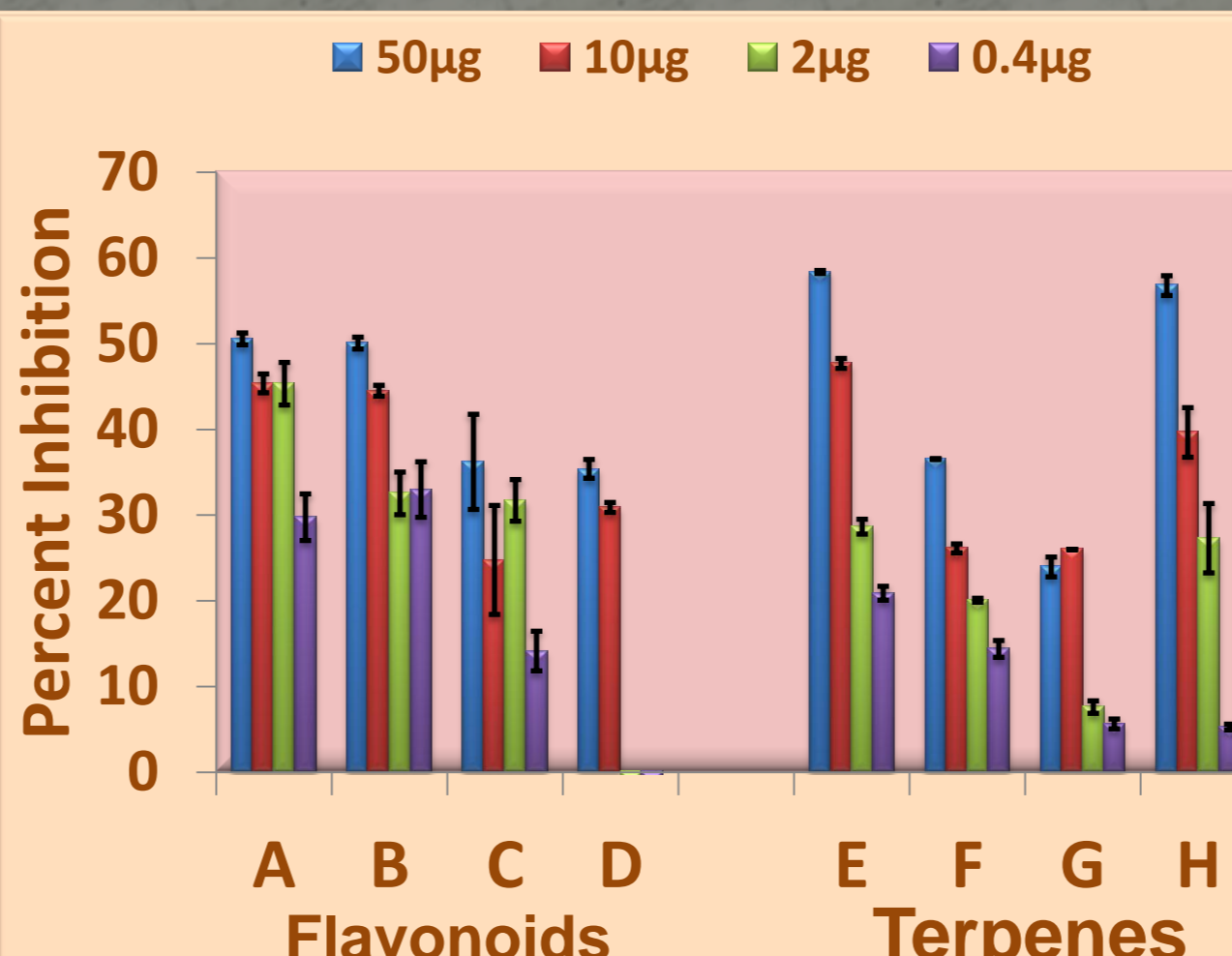
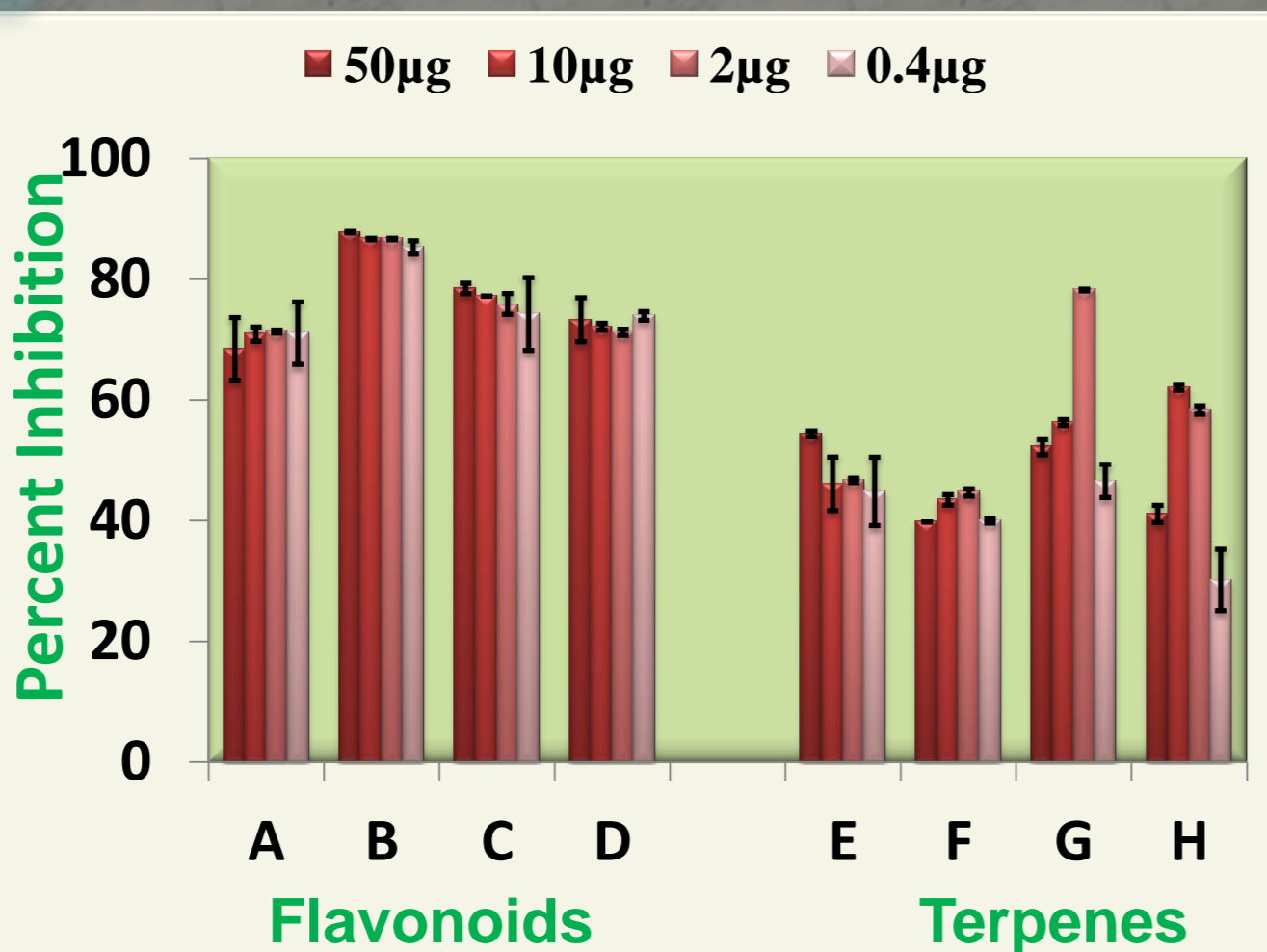
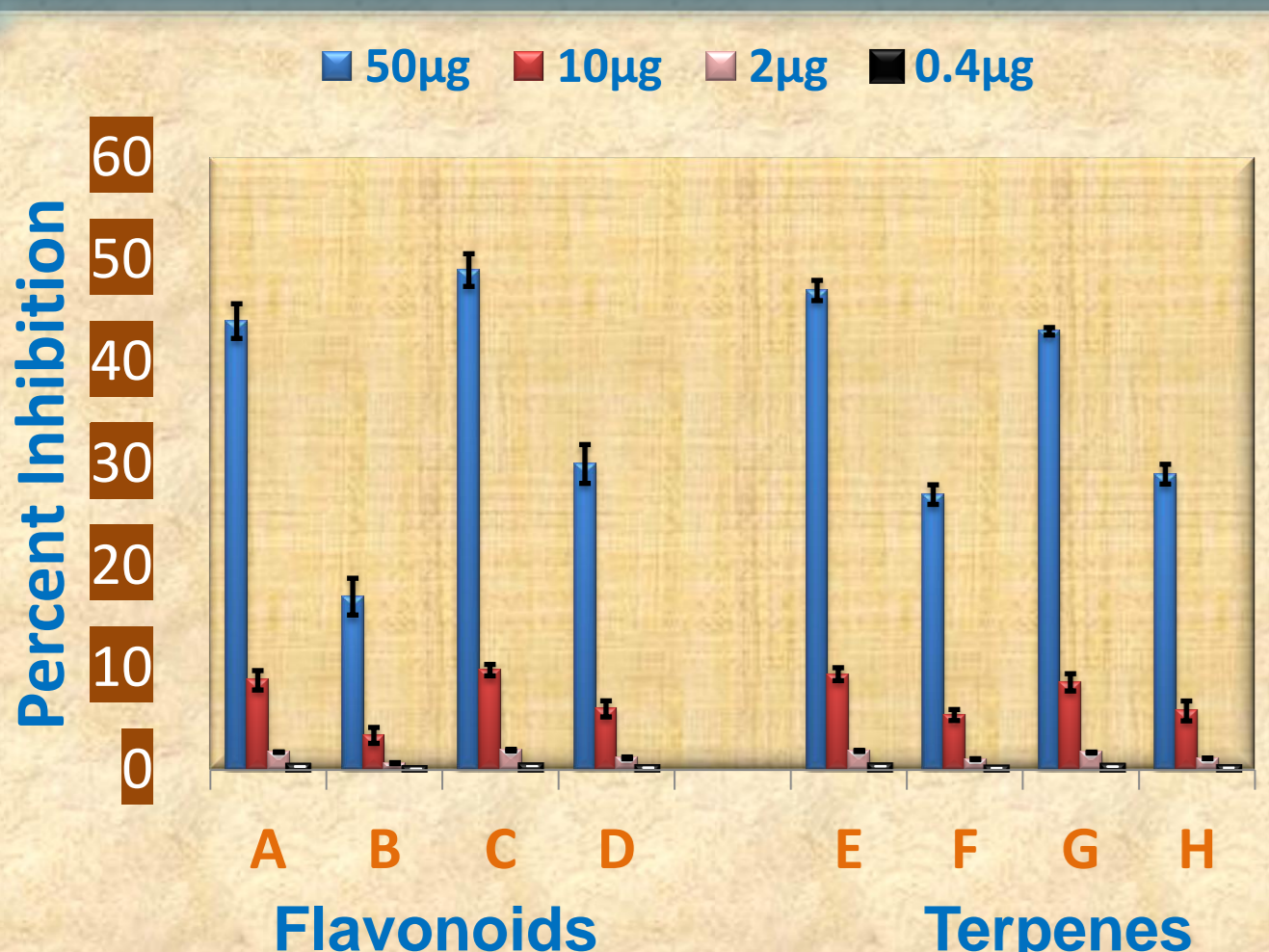


AIM OF THE STUDY

- To develop an improved, easy, reliable and cost-effective method for measuring the activity of ornithine decarboxylase utilizing small quantity of chemicals.
- Exploration of the phytochemicals as inhibitors of ornithine decarboxylase activity.
- Finding the correlation between free radical scavenging potential with NO inhibition capacity of phytomolecules.
- Understanding the specificity of ODC enzyme to pH, time and substrate concentration.



RESULTS

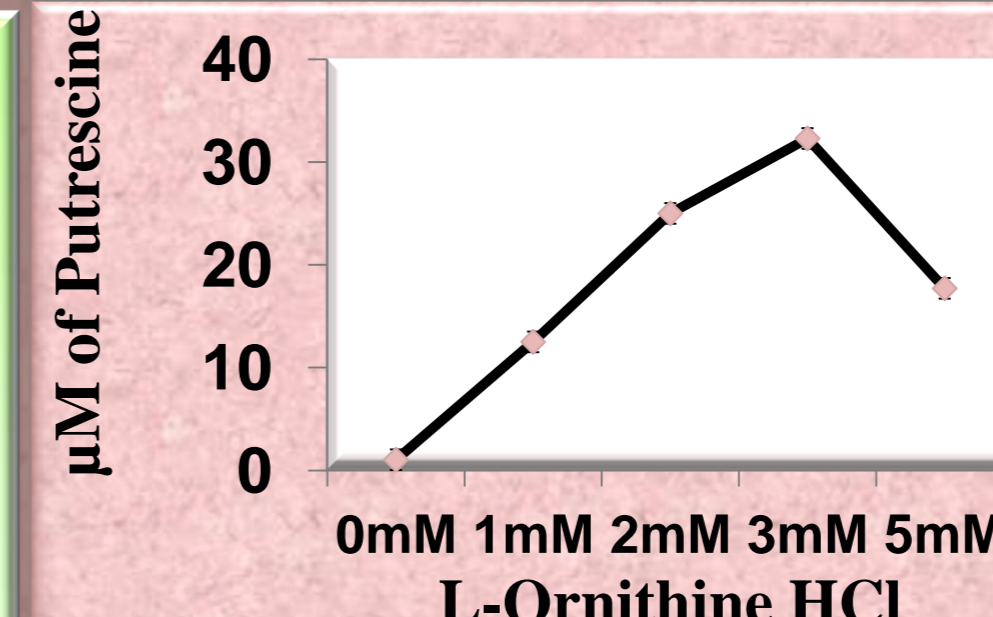
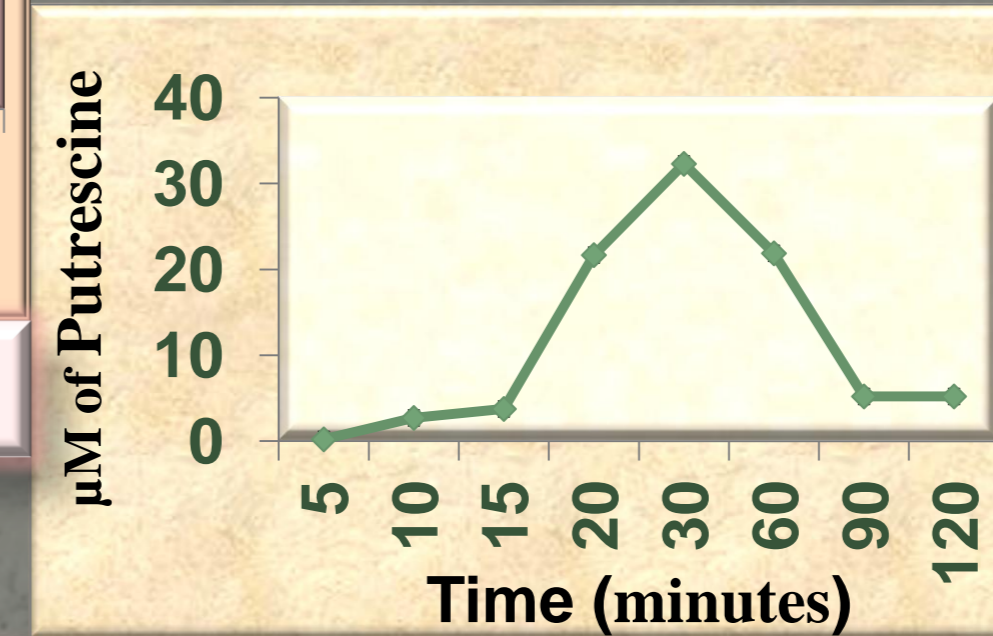
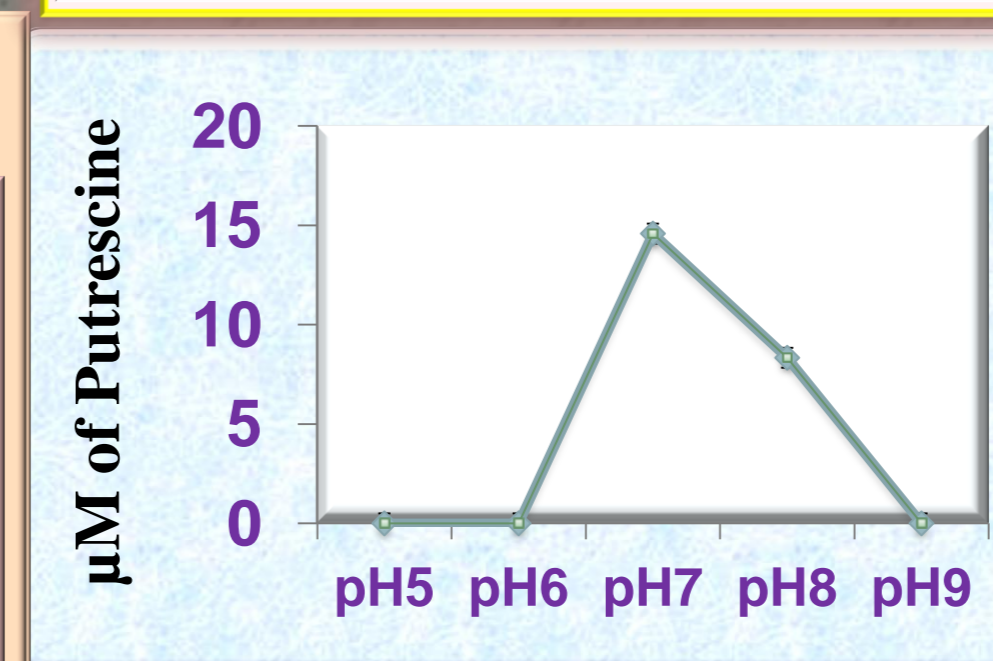


ODC inhibition assay

DPPH scavenging assay

NO scavenging assay

ODC, a highly inducible enzyme specific to pH, time & substrate concentration.



FUTURE PROSPECTS

- A great no. of hurdles still abound in the use of ODC inhibitors, like DFMO as endpoints for chemoprevention clinical trials.
- Simply, ODC inhibitors may be used to prevent or slow the rate of tumour re-growth between doses of therapy with radiation or other more toxic chemotherapeutic agents.
- Continuous progress in cancer drug development will move from traditional cancer clinical trial to biomarker-driven and hypothesis-testing trials.
- Also in near future some gaps in our knowledge of phytomolecules targeted cancer chemoprevention will close.

DISCUSSION

- ODC transform L-ornithine hydrochloride substrate to yellow coloured product putrescine soluble in pentanol.
- Some phytochemicals were found to inhibit enzyme activity in a concentration dependent manner (0.4-50µg/mL).
- Molecules having phenolic group and lactone rings in their structure are better inhibitors. Comparatively flavonoids are better free radical scavengers.
- A positive correlation was observed among the nitric oxide and DPPH inhibition (p<0.01)
- To act as inhibitor of ODC enzyme, phytochemical should interact in some way with the enzyme to prevent it from working in the normal manner.

ACKNOWLEDGEMENT

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