

MITOCHONDRIA AS PHARMACOLOGICAL TARGETS FOR PHARMACOLOGICAL AND TOXICOLOGICAL EVALUATION OF MEDICINAL PLANT EXTRACTS

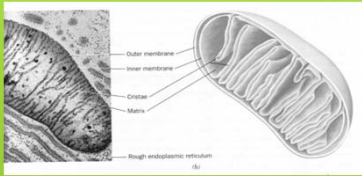
Augustine Ocloo, PhD

Senior Lecturer

Department of Biochemistry, Cell and Molecular Biology,
Faculty of Science, University of Ghana, Legon

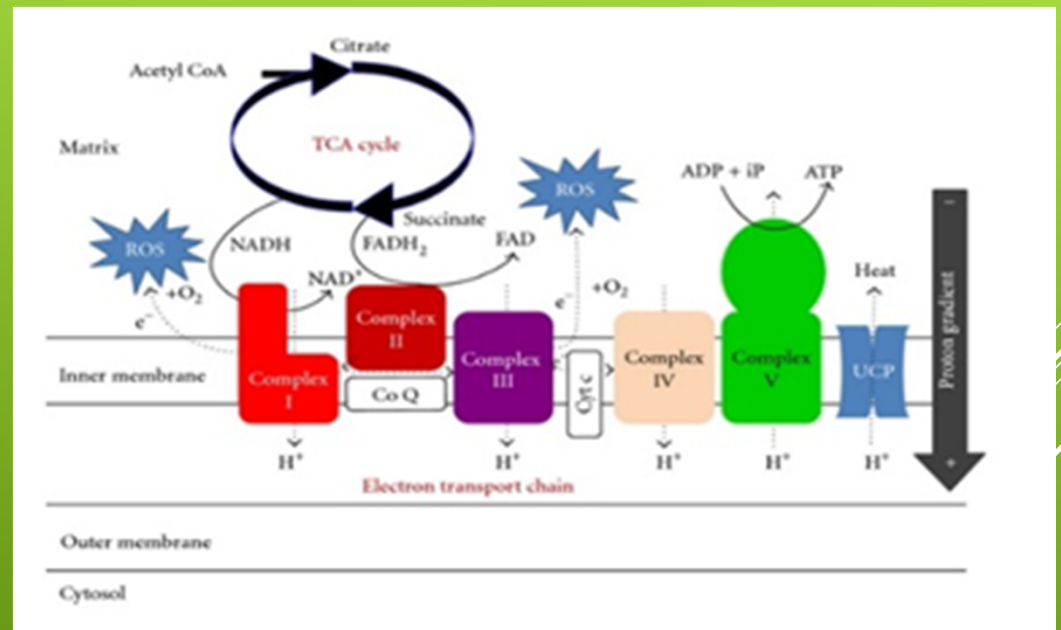
Collaborator: Andrew J. Murray

Department of Physiology, Development and
Neuroscience, Cambridge



THE MITOCHONDRIA ARE UNIQUE CELLULAR ORGANELLES

- ▶ Their unique structure and function make them important targets for xenobiotics
 - ▶ Inner membrane rich in cardiolipin
 - ▶ Alkaline interior
 - ▶ Presence of DNA
- ▶ Are sensitive to many compounds
- ▶ Primary or secondary targets



MITOCHONDRIA RESPONSIBLE FOR UNEXPECTED ADVERSE OR BENEFICIAL EFFECTS OF DRUGS

- ▶ Why do nearly 1 million people taking cholesterol-lowering statins often experience muscle cramps?
- ▶ Why is it that in the rare case when a diabetic takes medication for intestinal worms, his/her glucose levels improve?
- ▶ Is there any scientific basis for the purported health effects of green tea?

<http://news.harvard.edu/gazette/story/2008/02/hms-broad-institute-team-works-to-better-understand-mitochondria>

BENEFITS OF TARGETING MITOCHONDRIA IN NATURAL PRODUCT RESEARCH

- ▶ Discovery and development of: anti-ageing; anti-diabetic; anti-cancer; anti-obesity plant pharmaceuticals
- ▶ Management for many neurodegenerative diseases
- ▶ **Compounds that improve mitochondrial function can be good candidate for managing OXOPHOS diseases**
- ▶ Understand the mechanism of action of many herbal products
- ▶ Unearth long term toxic effects

RESEARCH QUESTION

- ▶ Are there phytochemicals in Ghana's medicinal plants that interfere with mitochondrial function?

AUG. 2013 – FEB. 2014: PDN, UNIVERSITY OF CAMBRIDGE

▶ Main Activities

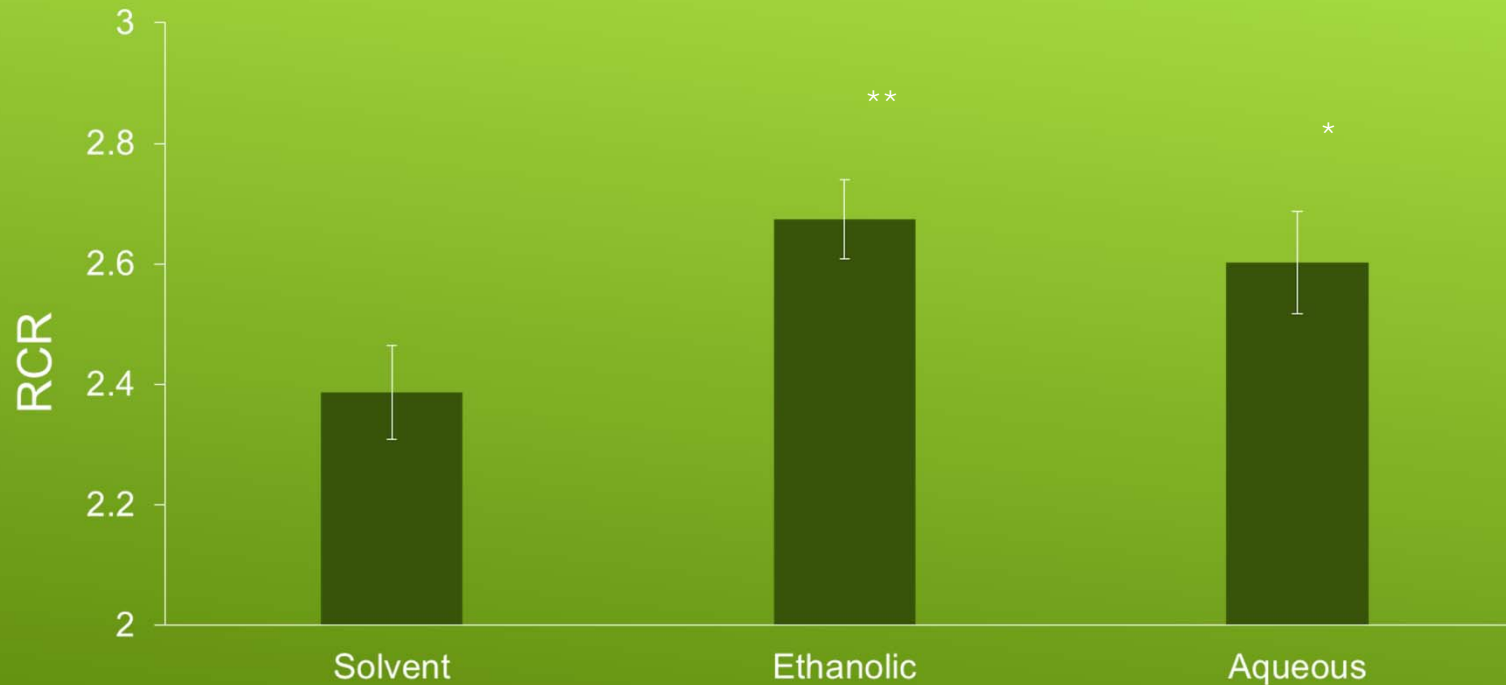
- ▶ Set up Clark type oxygen electrode
- ▶ Analysed selected plant extracts and isolated compounds
- ▶ Attended conferences and seminars
- ▶ Made presentations



ANALYSIS OF EFFECT OF PLANT EXTRACTS ON MITOCHONDRIAL FUNCTION USING CLARK TYPE OXYGEN ELECTRODE SET UP (STRATHKELVIN)

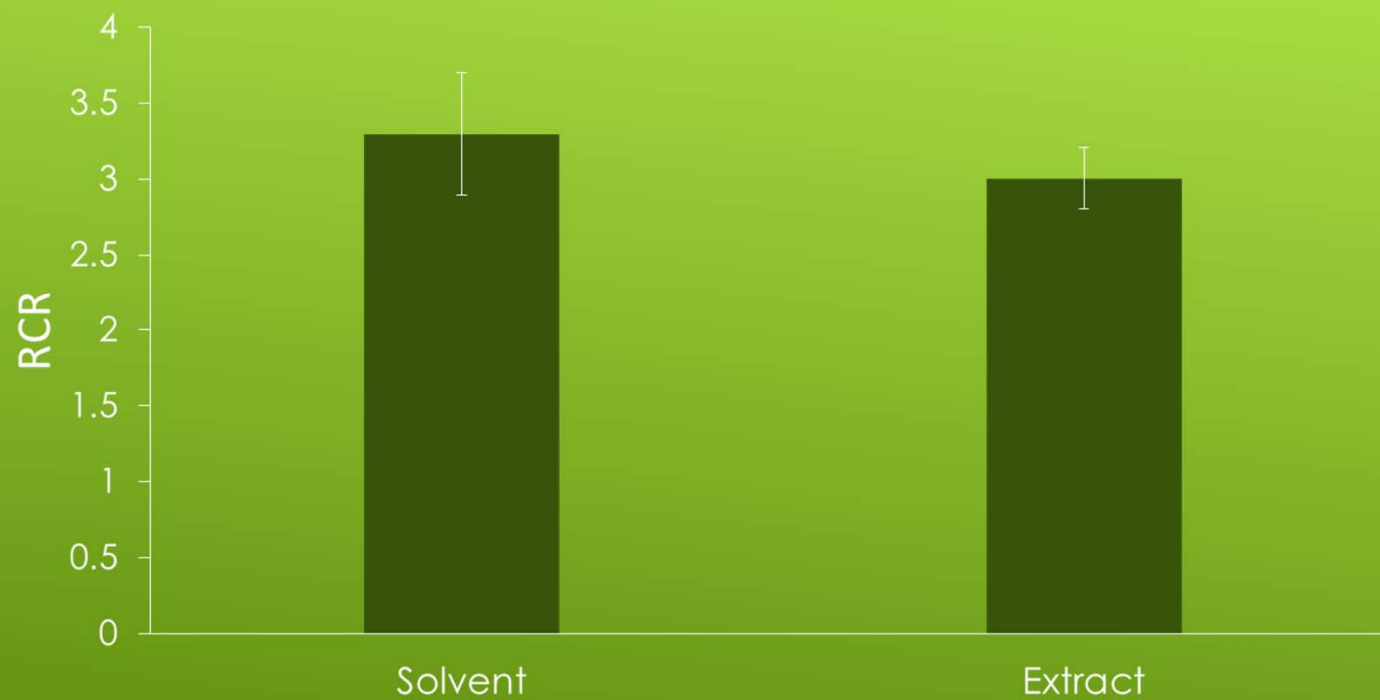


Effect of Ethanolic and Aqueous extracts of *T. officinale* (Dandelion) leaves



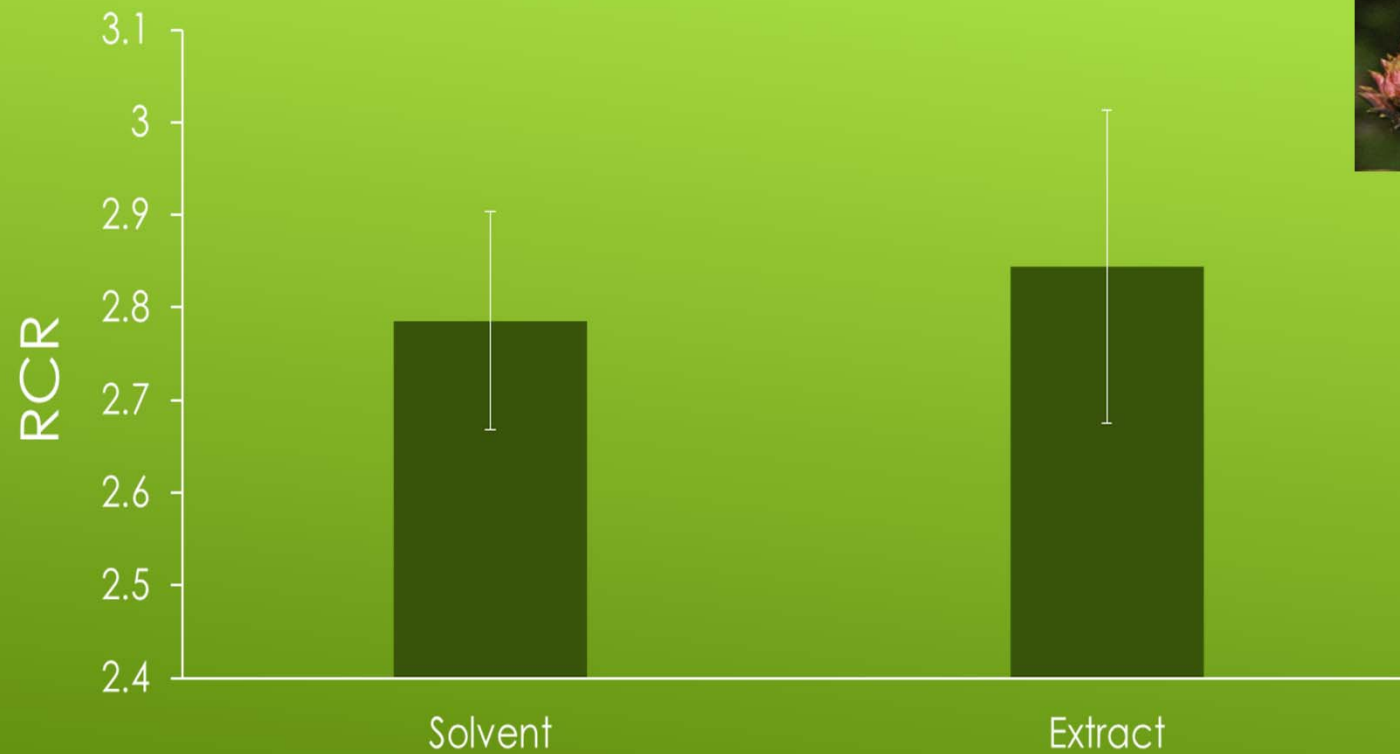
50 µg/ml; n = 7, 1 µl water; **p = 0.009, *p = 0.05

Crude ethanolic extract from *Paullinia pinnata* stem



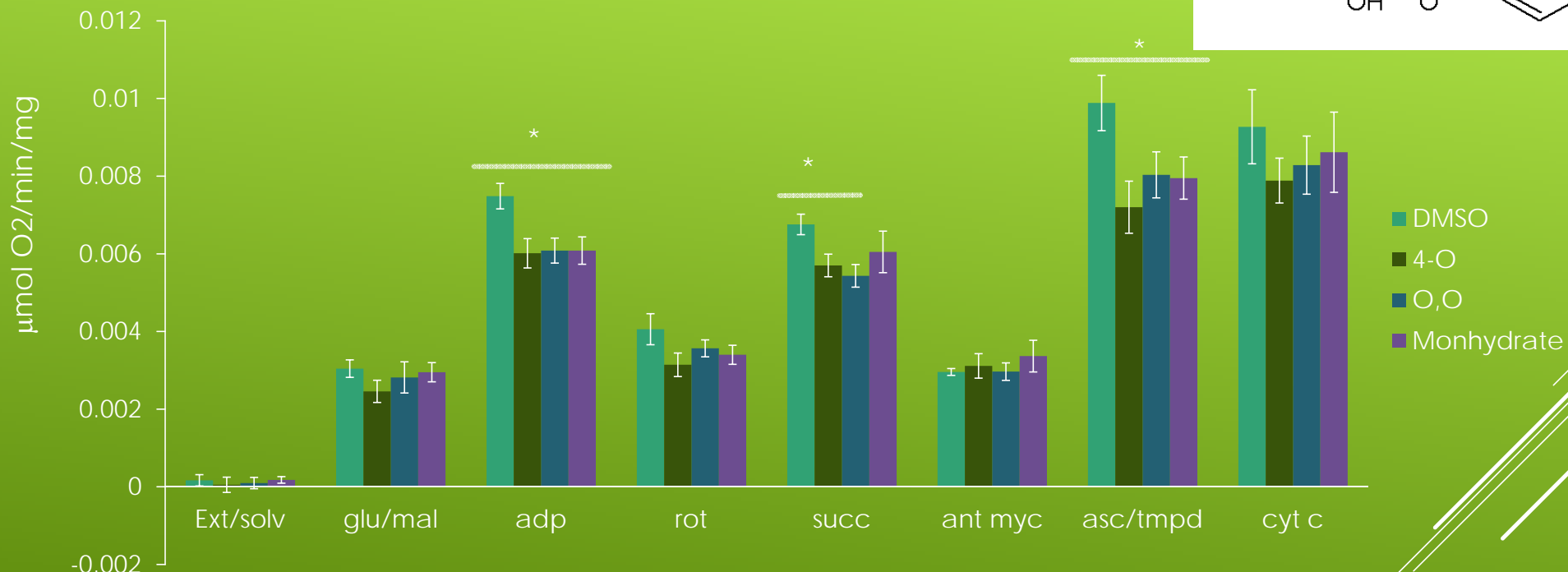
66 mg/ml of extract, 1 ml 25% ethanol; n = 5; *p = 0.02

Crude extract from *T. sanguinea* plant



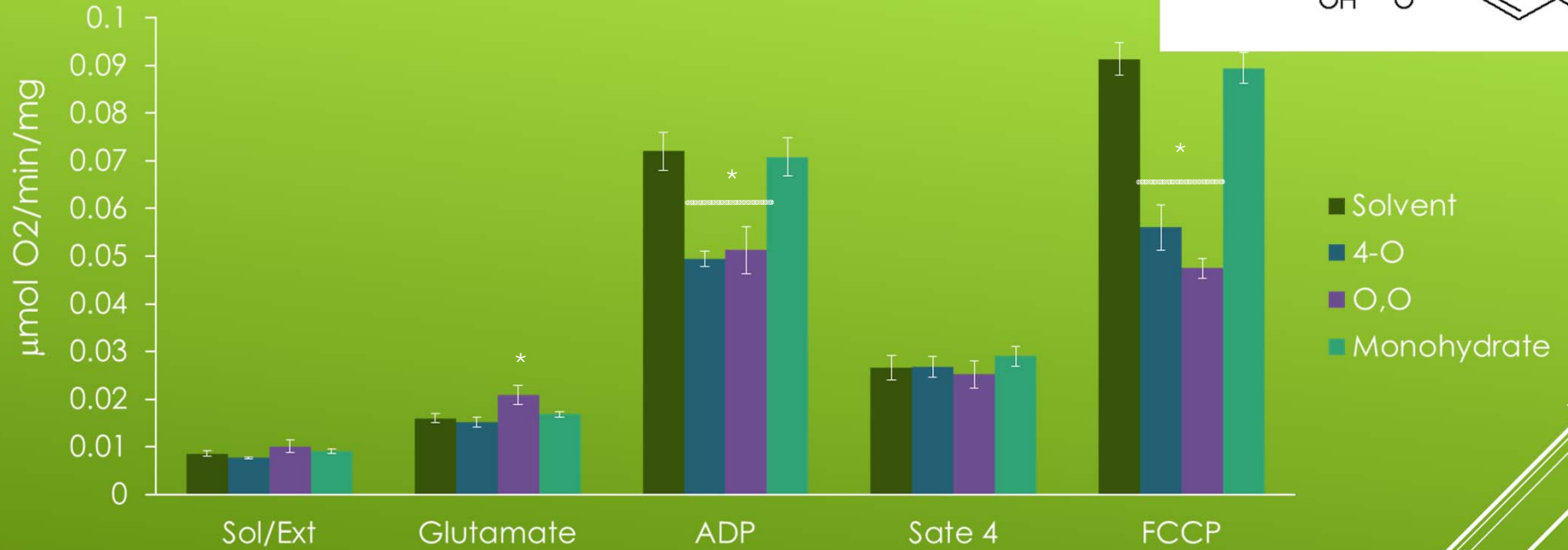
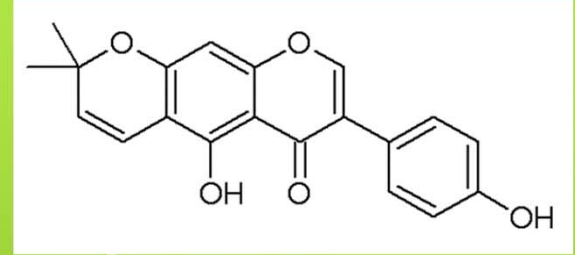
50 mg/ml of extract, 1 ml water; n = 4; *p = 0.02

Alpinumisoflavones from *Milletia thonningii*



35 $\mu\text{g/ml}$ of compounds, 0.5 μl DMSO; n = 4: 4-O is 4-O-methylalpinumisoflavone; O,O is O,O-dimethylalpinumisoflavone

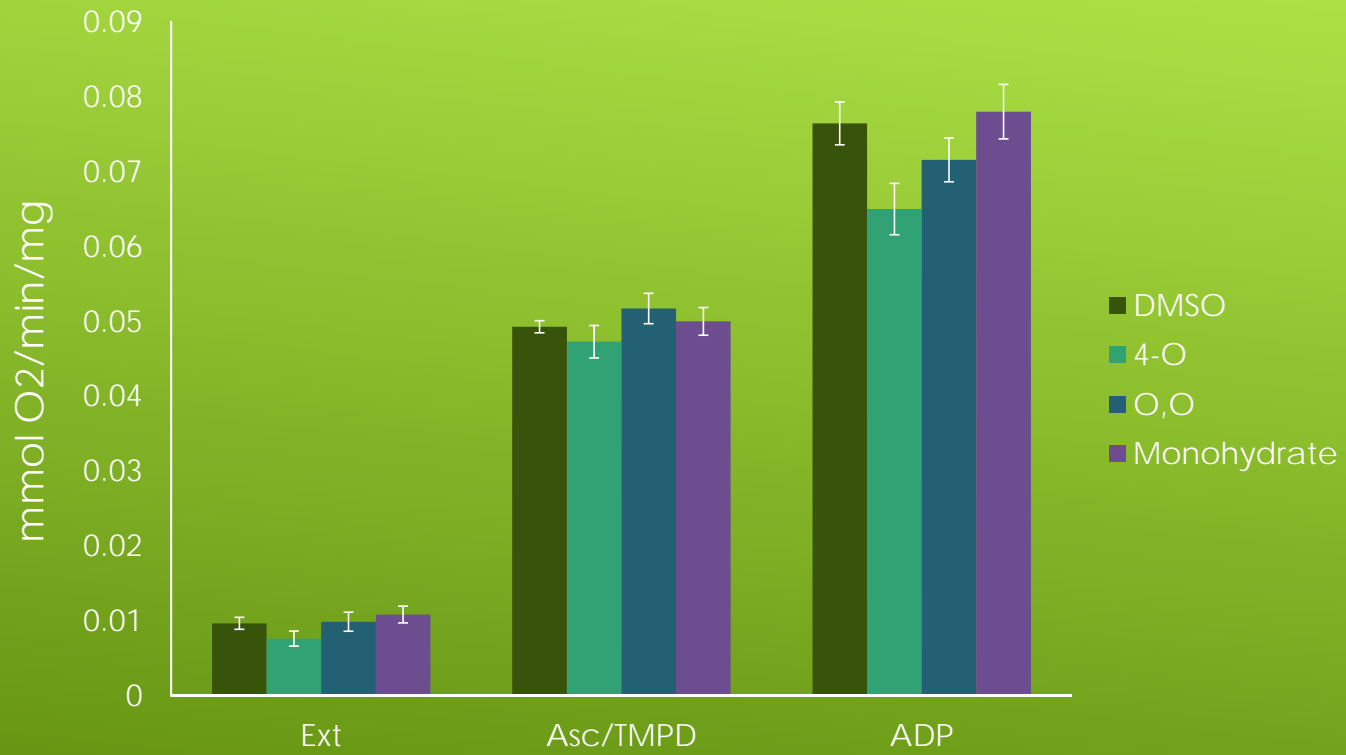
Effect on isolated rat liver mitochondria



35 $\mu\text{g/ml}$ of compounds, 0.5 μl DMSO; n = 4: 4-O is 4-O-methylalpinumisoflavone; O,O is O,O-dimethylalpinumisoflavone



35 $\mu\text{g}/\text{ml}$ of compounds, 0.5 μl DMSO; n = 3: 4-O is 4-O-methylalpinumisoflavone; O,O is O,O-dimethylalpinumisoflavone



SUMMARY

- ▶ The extracts generally increased RCR
- ▶ Alpinumisoflavones (O-4 and O,O) decreased complex I respiration
- ▶ Methanolic extract of *Paullinia pinnata* decreased complex II activity

MANUSCRIPTS

- ▶ An *in situ* study of the effect of extracts of *T. officinale*, *P. pinnata* and *T. sanguinea* on mitochondrial function in mouse heart (Submitted to J. H. S. M. P)
- ▶ Inhibition of mitochondrial respiratory chain activity by O, O-dimethylalpinumisoflavone and its derivative 4-O-methylalpinumisoflavone (Preparing)

- ▶ Life Member of the Mitochondrial Physiology Society, Austria



SEPT. 2013: MIP CONFERENCE (OBERGURGL, AUSTRIA)



NOV. 2013: CAPREx RESEARCH SHOWCASE PRESENTATION

18



08-10 APRIL, 2014: THE ENERGY WITHIN: WORKSHOP ON SKILLS IN MITOCHONDRIAL RESEARCH, UG, LEGON

COMMENTS FROM PARTICIPANTS

- ▶ The workshop was generally very educative.
- ▶ I learned and saw how to use respirometer for the first time.
- ▶ The workshop has given me insights to future research in mitochondrial function.
- ▶ The practical session was very useful.
- ▶ The workshop should be expanded for more people to participate.
- ▶ Congratulations to the organisers.

IN SUMMARY

- ▶ Assembled fully functional oxygen electrode
- ▶ Attended an international conference
- ▶ Submitted a manuscript

FUTURE GOALS

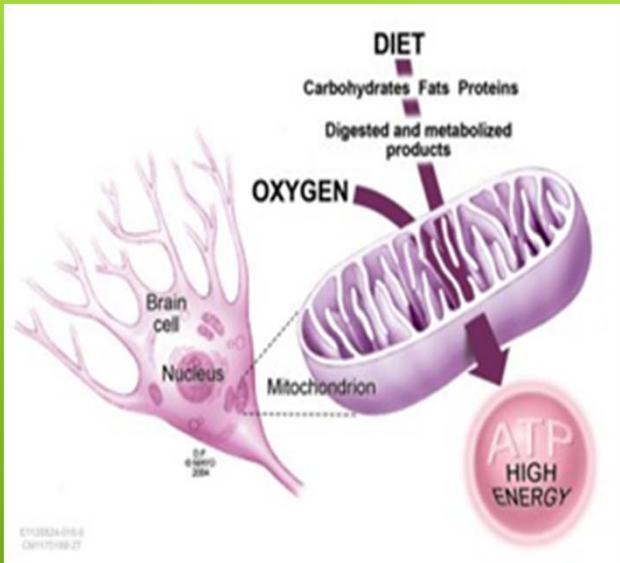
- ▶ Conduct *in vivo* study on the effect of extracts of selected medicinal plants on mitochondrial function
- ▶ Submit a proposal on “effective diagnosis of mitochondrial disorders and investigation of effect of herbal products on mitochondria function”

ACKNOWLEDGEMENT

▶ Collaborators

- ▶ Dr. Andrew J. Murray (PDN, Cambridge)
- ▶ Prof. L. K. N. Okine (BCMB, UG)
- ▶ Dr. A. A. Appiah (CPMR, Mampong)
- ▶ Dr. A. A. Sittie (CPMR, Mampong)
- ▶ Dr. J. P. Adjimani (BCMB, UG)
- ▶ Dr. Regina Appiah-Oppong (NMIMR, UG)
- ▶ Prof. R. Kingsford-Adaboh (Chem. UG)
- ▶ Dr. Mary A. Chama (Chem. UG)





THANK YOU