



**TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.**

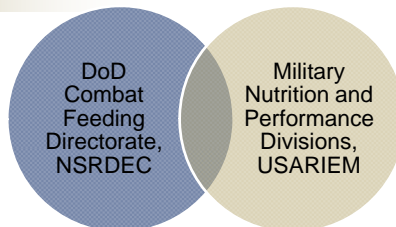
A case study of the proof of efficacy of a potential performance optimizing food ingredient, the flavonoid quercetin

C. Patrick Dunne, PhD  
Senior Advisor  
DoD Combat Feeding Directorate  
US Army Natick Soldier RD&E Center

UNCLASSIFIED



## Nutraceutical / Bioactive Food Compounds



- Long history of work in this area
- Currently examining a wide array of compounds for their affect on Soldier performance optimization
  - Muscadine extracts
  - Curcumin / turmeric
  - Cranberry extract
  - Quercetin, spun off from DARPA PSP program

**TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.**

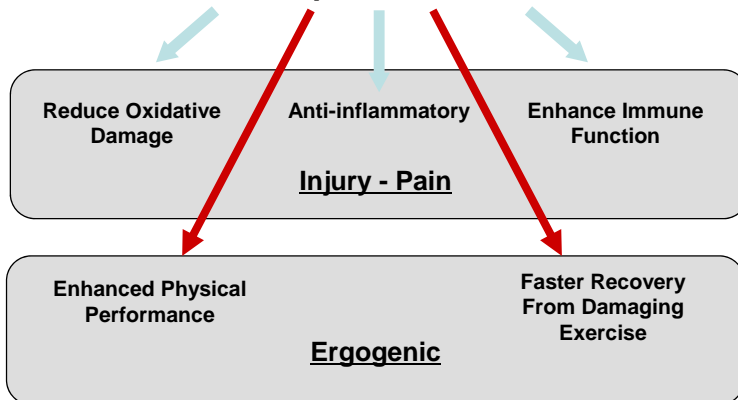
UNCLASSIFIED



## Bioactive Food Components and Maximal Exercise Performance



### Pathways for Improvement



TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.

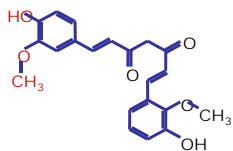
UNCLASSIFIED



## Phytochemicals for Performance Optimization



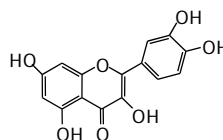
### Curcumin



CLEMSON UNIVERSITY

MUSC MEDICAL UNIVERSITY OF SOUTH CAROLINA

### Quercetin



TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.

UNCLASSIFIED



## Quercetin is the most common flavonoid



Quercetin Content <sup>1</sup> of Commonly Consumed Fruits and Vegetables			
Food	Level (mg/kg fresh edible wt)	Food	Level (mg/kg fresh edible wt)
Onion	347	Lettuce	14
Kale	110	Red currant	13
French bean	39	Grape, white	12
Apple	36	Strawberry	8.6
Broccoli	30	Turnip tops	7.3
Apricot	25	Broad bean	5.5
Grape, black	15	Endive	<1.3
Sweet cherry	15	Leek	<1

Day and Williamson (1999) 1 Expressed as the aglycone.

TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.

UNCLASSIFIED



## Quercetin and Performance



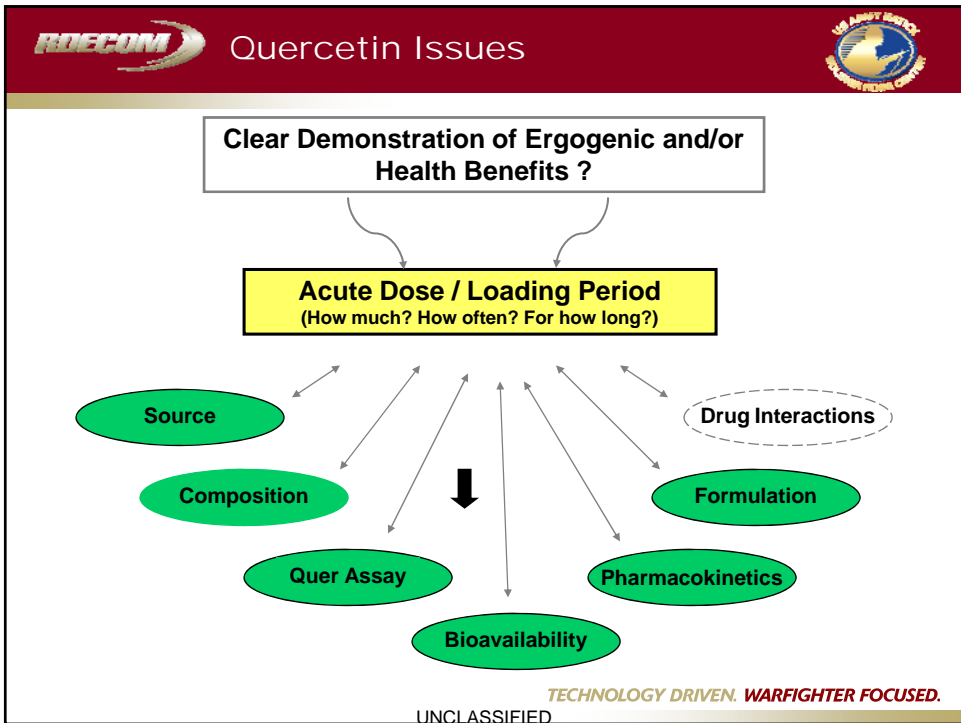
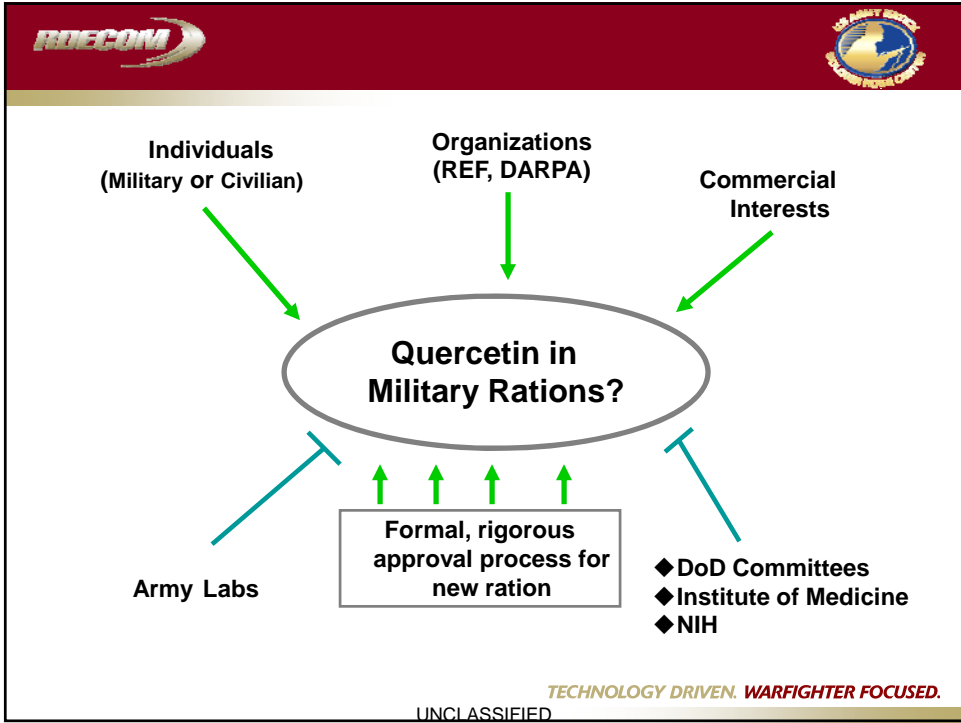
Animal studies have shown some unique and potentially remarkable affects of Quercetin with as little as 7 days of pre-treatment

- Increased mitochondria
- Increased mitochondrial enzymes (muscle & brain)
- Increased endurance capacity
- Decreased muscle inflammation (post-exercise)
- Potential improvement in immune function
- Little evidence on any cellular antioxidant functions

TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.

UNCLASSIFIED







Quercetin- fortified CranRaspberry Mini First  
Strike™ Bar used in efficacy studies

Control



Added 500 mg  
Quercetin

TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.

UNCLASSIFIED



- Briefing to BG P. Palmer, TRADOC (20 Jun 08)
- Resultant Requirement:

***"Bring together the researchers doing human Quercetin research and determine if there is evidence to support the immediate incorporation of Quercetin into or as part of the military ration."***

- Outcome:

***"Effects of Quercetin on Human Health, Physical and Cognitive Performance: Status of the Science"***

*September 22-23, 2008 Hosted by CFD and USARIEM;  
With American Institute of Biological Science (AIBS) review Panel*

TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.

UNCLASSIFIED



## Structure of the meeting



- AIBS Panel – American Institute of Biological Sciences, was convened by MRM – Military Operational Medicine
- Chair: Dr. W. Askew (Univ of Utah)
- Members:
  - Dr. M. Millard-Stafford (Georgia Tech)
  - Dr. P. Farrell (East Carolina Univ.)
  - Dr. S. Racette (Washington Univ.)
  - Dr. C-Y Chen (Tufts Univ.)

*TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.*

UNCLASSIFIED



## Structure of the meeting



Leading researchers working on Quercetin and performance or health from universities and the private sector were identified and invited to participate. Approximately 15 scientific presentations on various aspects of Quercetin were given. Followed by panel and audience questions.

A large number of attendees were invited as discussants. Institutions/entities represented included:

- DARPA, USDA nutrition researchers, NIH-Office of Dietary Supplements, DoD Military Nutrition Committee
- Quercegen Pharma LLC – CRADA partner
- Several major Universities - U South Carolina, Rutgers, UC-Davis, Clemson, Appalachian State, U Mass-Amherst, Pepperdine, U of Connecticut, U of Utah.

*TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.*

UNCLASSIFIED



## Critical Elements – Charge to panel



To justify the incorporation of Quercetin into the military ration, there must be:

- human data documenting the benefits
- information available on the dose & regimen
- documentation that the benefits are observed under operational conditions
- verification that there are no deleterious or untoward affects of Quercetin
- enough information known on the physiological mechanism(s) of action of Quercetin to predict the response of Quercetin over an extended period of time

*TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.*

UNCLASSIFIED



## AIBS Panel Report received 31 Oct 2008



- I. Quercetin should NOT be incorporated into the military ration at this time.
  - -the data in humans are inconsistent and not convincing
  - -no studies have evaluated Quercetin in the military operational setting
  - -lack of information on dose, loading period and/or delivery vehicle
  - -“dearth of consistent, corroboratory data...”
  - -“substantially more data must be published”
  - -“studies evaluating the effect on human health may show promise”

*TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.*

UNCLASSIFIED



- II. A large number (n=21) human studies on Quercetin's effect on performance and health are currently underway and will be completed within 9-12 months
- 7 studies will assess the affects on physical and/or cognitive performance
  - Comparable dosing (1000mg/day) is being used
  - 6 studies are addressing human health
  - Additional studies are examining bioavailability and pharmacokinetics

*TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.*

UNCLASSIFIED



- III. There are no data to indicate that prolonged (>6 months) use of Quercetin by soldiers is safe
- issue involves consumption of 5-10 times normal dietary intake of Quercetin
  - concern about military operational conditions that may influence any supplement's toxicity potential, such as sleep deprivation, negative energy balance, dehydration, etc.
  - Petition by Quercegen for FDA Generally Recognized as Safe (GRAS) affirmation for quercetin as a food ingredient at levels to 1 gm per day is still pending

*TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.*

UNCLASSIFIED



#### IV. Identifiable “Gap Areas”

- ability of Quercetin to improve performance in a military operational setting
- information on bioavailability and metabolism of Quercetin
- “very little is known about the physiological mechanism or the mechanisms of action of Quercetin”

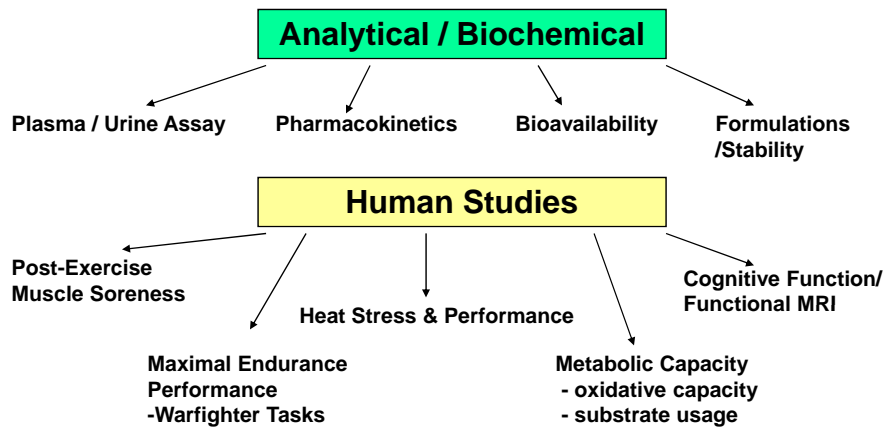
**Continued research in USARIEM and by CFD contractors is addressing these gap areas**

*TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.*

UNCLASSIFIED



For a bioactive substance in candidate carrier food component/item



*TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.*

UNCLASSIFIED