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General Information

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Other Defense Agencies, Defense Advanced Research Projects Agency, Contracts Management Office, 3701 North Fairfax Drive, Arlington, VA, 22203-1714

Description

PART II
 DEFENSE SCIENCES RESEARCH AND TECHNOLOGY
 SOL: BAA05-19
 POC: Dr. Brett Giroir, DARPA/DSO
 DUE: February 7, 2006
 FAX: (571) 218-4553
 WEB: <http://www.darpa.mil/baa/>
 E-MAIL: BAA05-19@darpa.mil

PROGRAM OBJECTIVES, SCOPE AND FUNDING

The mission of the Defense Advanced Research Projects Agency's (DARPA) Defense Sciences Office (DSO) is to identify and pursue the most promising technologies within a broad spectrum of the science and engineering research communities and to develop those technologies into important, radically new military capabilities. In addition, DSO is looking for research ideas and areas that might lead to innovations in science and engineering. To this end, DSO is soliciting proposals for advanced research and development in a variety of enabling technical areas as described below.

Proposals may be either basic or applied research. However, in all cases, proposers should demonstrate that their proposed effort is aimed at high-risk/high-payoff technologies that have the potential for making, in the 5-10 year timeframe, revolutionary rather than

incremental improvements to national security, including emerging threats and operational challenges. Proposals that are not within the topical areas described below may be considered out of scope and not evaluated. Likewise, proposals that are the integration of technologies or systems development will also be considered out of scope and will not be evaluated.

Multiple awards are anticipated. The amount of resources made available to this BAA will depend on the quality of the proposals received and the availability of funds. While there is no specific requirement for cost and duration of the proposed effort, it is recommended that proposers include a Phase I of 12 to 18 months in length that addresses the most critical issues on the path to success. This BAA constitutes the entire solicitation for this effort. No Proposer Information Pamphlet or other additional information will be published, nor will a formal request for proposal, or other solicitation, regarding this research and development be issued. Requests for same will be disregarded.

TECHNICAL TOPIC AREAS OF INTEREST TO DSO

This section describes the general technical interests of DSO. Please note that while the topics are organized by traditional disciplines, interdisciplinary proposals are encouraged. Regardless of the technical area, the ultimate success of a proposal is based on the specific technical idea(s) advanced within these areas and especially the uniqueness of the proposed approach. Consequently, proposing within one of these topic areas is not sufficient to make a compelling case for funding. For this reason, white papers are strongly suggested before submitting a full proposal. (See below)

New Materials, Materials Concepts, Materials Processing and Devices:

Specific areas of interest include, but are not limited to:

- Demonstrations of multifunctional (structure + function) materials;
- Demonstrations of smart materials and structures; Novel approaches for manufacturing and self-assembly of materials and structures;
- Engineered materials and material systems with designed structure and morphology (e.g., meta-materials);
- Novel electronic and optical materials;
- Materials and enabling technologies for power generation and energy storage at all scales;
- Materials and enabling technologies for directed energy systems;
- Digitally driven manufacturing processes that control properties within components with spatially controlled composition, crystal texture, or macrostructure;
- Materials and enabling technologies for efficient propulsion in all environments including space;
- Materials and devices for urban combat;
- Materials for ultra lightweight protection from blast and non-lethal weapons;
- Novel approaches to non-destructive evaluation, property/life prediction and related technologies;
- Materials and enabling technologies for controlling quantum and non-equilibrium behavior (e.g., atom interferometers; slowing, storing, and processing of light; quantum computation and communication, etc.);
- Materials and rapid screening technologies for molecular-based memory

and computing;
Lightweight or thin film materials with near zero coefficient of thermal expansion;
Biomaterials and biomimetic materials, including adaptive/malleable systems; and Self-healing, -sensing and -adapting materials.

Advanced Mathematics: Application and development of advanced mathematics for applications of interest to the Department of Defense (DoD):

Specific areas of interest include, but are not limited to:

Dimensionality reduction, error propagation, and uncertainty management in databases, models, and experiments;
Modeling of materials, physics, and biology;
Tools to predict the performance of complex systems across a variety of application domains (e.g., physics, biology, and sociology);
Adaptive sensing, waveform design, and scheduling;
Methods for the design of experiments that minimize the number of experiments and that maximize information for coupled non-linear systems;
Representation and analysis of large and/or disparate data sets;
Computational geometry and topology;
Electromagnetic modeling and simulation;
Quantum information science including quantum games and their potential applications;
Signal and image processing; and
New applications of traditionally pure mathematics.

Defense Against Weapons of Mass Destruction: Technologies to render biological, chemical, nuclear, or radiation attacks against the U.S. military harmless:

Specific areas of interest include, but are not limited to:

Unique approaches for pre-symptomatic diagnosis of disease and health;
Novel approaches for external protection including decontamination of materials and equipment;
Medical countermeasures against both known and unknown pathogens and infectious diseases;
Remote detection/characterization of biological substances;
Accelerated manufacture of biologics, including vaccines and immune modifiers;
Medical countermeasures against radiation exposure; and
Rapid, non-invasive determination of radiation exposure.

Applications of Biology to Defense Applications:

Specific areas of interest include, but are not limited to:

Biological approaches for maintaining the warfighter's performance, capabilities and medical survival in the face of harsh battlefield conditions;
Biological approaches for minimizing the after-effects of battle injuries, including neurotrauma from penetrating and non-penetrating injuries as well as faster recuperation from battlefield injury and wounds;
Approaches for maintaining the general health of deployed troops;

Bio-inspired systems;
Biomolecular motors and devices;
Biological approaches to the growth of materials and devices;
Understanding the human effects of non-lethal weapons;
Micro/nano-scale technologies for non-invasive assessment of health (e.g., vital signs, blood chemistry);
Technologies to enable remote interrogation and control of biological systems at the system/organ/tissue/cellular/molecular scales;
Investigation of the interactions between physical forces, material and biology (e.g., interface of biology with magnetics);
Novel mathematical and computational approaches to characterizing and simulating complex biological processes;
New technologies to drastically reduce the logistics burden of medical treatment in the field;
Advanced signal processing techniques for the decoding of neural signals in real time, specifically those associated with operationally relevant cognitive events, including target detection, errors, and other decision-making processes; and
Novel interface and sensor designs for interacting with the central (cortical and subcortical structures) and peripheral nervous systems, with a particular emphasis on non-invasive and/or non-contact approaches.

Novel Technologies to Improve the Human Consequences of Transformation:

Specific areas of interest include, but are not limited to:

New approaches for training individuals and teams, including embedded training and simulation;
Understanding and improving team performance; and
Understanding and improving individual performance and individual and group behavior.

Special Focus Areas

From time to time, DARPA will publish addenda to this BAA that will highlight particular areas of interest. It is highly recommended that potential proposers look periodically for these updates. Addenda will have deadlines for submission of white papers and proposals that are different from the deadline in this BAA. Under Addenda, the technical content for a submission as well as the overall structure of the proposed effort may also differ. DARPA will not establish a distribution list for automatic distribution of these addenda. Any specific instructions or criteria in a published addendum will take precedence over this BAA in response to that addendum only.

Other Technical Areas

Ideas outside of the advertised focus areas will be considered in scope only if the proposers can demonstrate that they have the potential for radical improvement to national security and are within the technical interests of the office. Proposals that integrate existing technologies or products into systems generally do not fall within the purview of DSO and are likely to be rejected.

WHITE PAPER SUBMISSIONS

Before proposers put together a full proposal, it is highly recommended (though not required) that they submit a white paper in response to the BAA. This white paper should clearly state the uniqueness of the idea presented in the context of existing state of the art in the technical area of interest. Demonstrating that the proposer has a clear understanding of the state of the art and that their proposed effort will make significant improvements therein is essential for a successful proposal. The white paper should also describe the proposed approach and explain why it is unique. Further, the proposer should demonstrate an understanding of the payoff of the technical idea, especially in terms of how it might make a difference to Defense capabilities. Key milestones expected in the effort should be described. Also, a brief discussion of the technical expertise of the proposed principal investigator and other key team members should be provided. Finally, an estimate of the program costs and duration should be included. White papers should not be longer than 8 pages; however, shorter white papers that can cover the content above are strongly encouraged.

Procedures have been put in place that will help proposers to rapidly determine the applicability of their proposal to DARPA/DSO and to help develop promising ideas into formal proposals with a reasonably high probability of funding. Proposers may recommend a program manager to review their proposals based on prior discussions and/or information on the DSO web site.

A website <http://www.sainc.com/dso0519/> has been set up to facilitate the submission of white papers. This site will allow proposers to fill in contact information and upload a white paper document in either Word or PDF format. It will provide a method by which proposers can track their submissions. White paper submissions may also be made by attachment to an e-mail sent to BAA05-19@darpa.mil (Word 97 or higher is recommended). Embedded text and Postscript are also acceptable. Note: if the website is not used then the body of the e-mail and the attachment must include name, mailing address, phone number, and fax number of the proposer. If this information is not contained in the body, the e-mail will be returned for inclusion of that information. (If proposers choose not to use e-mail, U.S. mail may be used. White papers will not be accepted by way of facsimile transmissions.) Within two weeks of receipt of the white paper, the proposer will be informed of receipt of the white paper, provided a log number and given both a technical and administrative point of contact. The formal recommendation about whether a formal proposal is recommended will be made as soon as possible. However, the exact time for response will depend on a variety of circumstances, including the number of white papers received. **Please note, this recommendation and any additional feedback provided is for the benefit of the proposer and following these recommendations is not a guarantee that the full proposal will be funded.** All full proposal submissions will be evaluated regardless of the disposition of the white paper.

Point of Contact

Brett Giroir, Deputy Director, DSO, Phone (571) 218-4224, Fax (571) 218-4553, Email bgiroir@darpa.mil

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PROPOSAL SUBMISSION AND DEADLINES

Proposals may be submitted and received at any time until the final proposal deadline of 4:00 PM EST February 7, 2006. Proposals will be evaluated against the criteria set forth in this solicitation, and an offeror will be notified either that: (1) the proposal has been selected for funding, or (2) the proposal has not been selected for funding. Proposers may elect to have their proposal withdrawn from consideration at any time during the evaluation process. If a formal request is not made, DARPA will assume that continued evaluation is desired. One copy only of proposals that are not selected for funding will be retained for administrative purposes.

The Government reserves the right to select for award all, some, or none of the proposals received in response to this announcement, including those that do not strictly adhere to the division of technical

and cost sections. The Government also reserves the right to fund proposals in phases with options for continued work at the end of one or more of the phases. Proposals identified for funding may result in a procurement contract, grant, cooperative agreement, or "Other Transaction," depending upon the nature of the work proposed, the required degree of interaction between parties, and other factors. The offeror must submit a separate list of all technical data or computer software that will be furnished to the Government with other than unlimited rights (see DFARS Part 227).

FORMAT AND CONTENT OF FULL PROPOSAL

The descriptions contained in this section are to help proposers ensure that proposals have sufficiently detailed information to be evaluated. Proposals not conforming to the instructions of this section may not, at the discretion of the Government, be evaluated. Full proposals shall consist of two volumes, technical and cost. A website <http://www.sainc.com/dso0519> has been established to facilitate the submission of full proposals electronically. This site will allow proposers to fill in contact information and upload a full proposal created with the requirements listed below in either Word or PDF format. Note: if the website is not used, please use the U.S. mail system or the BAA e-mail account. If submitting via e-mail, the body of the e-mail and the attachment must include name, mailing address, phone number, and fax of the proposer. If this information is not contained in the body, the e-mail will be returned for inclusion of that information. If offerors choose to submit by U.S. mail, they should submit one (1) original and three (3) copies of the full proposal to the address shown below. Proposals will not be accepted by way of facsimile transmissions. Both volumes should be included as a single document when uploading to the website.

Volume 1: Technical.

The technical volume is limited to a maximum of 30 pages including all figures, references, tables, charts, cover sheet, and appendices and consists of the following sections:

- a) Executive Summary (two pages or less);
- b) Technical section that clearly describes the innovation of the work to be accomplished, specific metrics for the effort, the risks to achieving those metrics and approaches for mitigation of those risks. All milestones should be clearly delineated, especially those early (12 to 18 months) milestones that are critical to demonstration of the concept or approach. Supporting rationale for performance enhancements should be included. The perceived need for this research and the potential impact on the DoD should be described, and a Statement of Work (SOW) that summarizes critical tasks to be accomplished should be presented;
- c) Time-phased schedule-milestone chart;
- d) Summary of relevant prior work;
- e) Brief description of applicable facilities and equipment;
- f) Short resumes of key individuals. The level of effort and specific roles and qualifications of key individuals should be included. If the team is large (greater than 3 separate entities), a management plan for coordination of the effort should also be included; and
- g) Current and pending support (award title, amount, period of performance, and degree of overlap with this proposal).

Proposers are cautioned not to submit supporting material (articles, CDs, etc.) as these will not be accepted and will not be used in evaluation of the proposal.

Volume 2: Cost.

The cost volume shall contain the following:

a) Cover sheet to include: (1) BAA number; (2) Technical area; (3) Lead organization submitting proposal; (4) Type of business, selected among the following categories: "LARGE BUSINESS," "SMALL DISADVANTAGED BUSINESS," "WOMAN OWNED BUSINESS," "SERVICE DISABLED VETERAN OWNED," "OTHER SMALL BUSINESS," "HBCU," "MI," "OTHER EDUCATIONAL," or "OTHER NONPROFIT"; (5)

Contractor's reference number (if any); (6) Other team members (if applicable) and type of business for each; (7) Proposal title; (8) Technical point of contact to include: salutation, last name, first name, street address, city, state, zip code, telephone, fax (if available), electronic mail (if available); (9) Administrative point of contact to include: salutation, last name, first name, street address, city, state, zip code, telephone, fax (if available), and electronic mail (if available); (10) Award instrument requested: cost-plus-fixed-fee (CPFF); cost-contract--no fee; cost sharing contract--no fee; or other type of procurement contract (specify), grant, cooperative agreement, or other transaction; (11) Place(s) and period(s) of performance; (12) Total proposed cost separated by basic award and option(s) (if any); (13) Name, address, and telephone number of the offeror's cognizant Defense Contract Management Agency (DCMA) administration office or Office of Naval Research; (14) Name, address, and telephone number of the offeror's cognizant Defense Contract Audit Agency (DCAA) audit office; (15) Date proposal was prepared, (16) DUNS, TIN, CAGE CODE; and (17) All subcontractors proposal backup documentation to include items 1-16 above, as applicable and available.

b) Detailed cost breakdown to include: (1) total program cost broken down by major cost items (direct labor, subcontracts, materials, travel, other direct costs, overhead charges, etc.), and (2) an itemization of major subcontracts (labor, travel, materials and other direct costs) and equipment purchases. Where the effort consists of multiple portions that could reasonably be partitioned for purposes of funding, these should be identified as options with separate cost estimates for each.

c) Supporting cost and pricing information in sufficient detail to substantiate the summary cost estimates in b) above. Include a description of the method used to estimate costs and supporting documentation. Note: "cost or pricing data" as defined in the Federal Acquisition Regulation (FAR) Subpart 2.101 shall be required if the offeror's proposal is for a procurement contract award of \$550,000 or greater unless the offeror requests an exception from the requirement to submit cost or pricing data. "Cost or pricing data" are not required if the offeror proposes an award instrument other than a procurement contract (e.g., a grant, cooperative agreement, or other transaction). The requirements for submission of "cost or pricing data" are specified in FAR Subpart 15.403-4 (see <http://www.arnet.gov/far>).

OTHER RELEVANT INFORMATION FOR PROPOSAL SUBMISSION

Teaming and Team Composition

Teaming is encouraged, especially when interdisciplinary approaches to a problem are required.

Proposals may include, or be led by, foreign firms and/or personnel provided all export control laws and U.S. national security requirements are adhered to in the conduct of the effort and that the work relating to the foreign firm or personnel is unclassified. The onus of understanding and complying with export control rests with the proposer, not the Government.

Small Disadvantaged Businesses, Historically Black Colleges and Universities (HBCUs), and Minority Institutions (MIs) are encouraged to

submit proposals and to join others in submitting proposals. Awards made under this BAA are subject to the provisions of the FAR Subpart 9.5, Organizational Conflicts of Interest. Consequently, all offerors and proposed subcontractors must, therefore, affirm whether they are providing scientific, engineering and technical assistance (SETA) or similar support to any DARPA technical office(s) through an active contract or subcontract. All affirmations must state which office(s) the offeror supports, and identify the prime contract numbers. Affirmations should be furnished at the time of proposal submission. All facts relevant to the existence or potential existence of organizational conflicts of interest, as that term is defined at FAR 9.501, must be disclosed. The disclosure shall include a description of the action the offeror has taken or proposes to take to avoid, neutralize or mitigate such conflict.

Technology Transition

Proposers are strongly encouraged to engage commercial and military end-users and commercial manufacturers from the program inception. The engagement of these communities also helps ensure that the various technologies being developed will be commercially viable (cost effective, manufacturability, etc.) and available to the military. Thus, proposals are strongly encouraged to include/involve the user-community that intends to bring the technology to practice as a result of this research. This relationship encourages the participation of researchers, end-users and manufacturers as collective contributors to the technology definition, implementation, and performance evaluation.

Proprietary Information

All proprietary information should be marked on both the white paper and the full proposal. It is the policy of DARPA to treat all proposals as competitive information and to disclose their contents only for the purpose of evaluation. Standard proprietary disclaimers notwithstanding, proposals may be reviewed by non-Government technical experts who have signed a nondisclosure agreement with DARPA, unless the specific phrase "TO BE REVIEWED BY GOVERNMENT EMPLOYEES ONLY" appears on the cover sheet. In any case, personnel under exclusive contract with DARPA who have completed the appropriate nondisclosure agreements will handle the proposals for administrative purposes.

Security

Proposals and white papers may contain classified information or data (up to the level of Top Secret/SCI). HOWEVER, DO NOT SEND CLASSIFIED WHITE PAPERS OR FULL PROPOSALS BY EMAIL OR VIA ONLINE SUBMISSION SYSTEMS. Offerors that intend to include classified information or data in their proposals should contact DARPA security at the address identified in this BAA (or alternatively, the point-of-contact for this BAA) for guidance and direction in advance of proposal preparation. Offerors must have existing approved capabilities (personnel and facilities) to perform research and development at the classification level they propose.

Guidance for Classified Information and Data

The Government anticipates that proposals submitted under a BAA will be unclassified. In the event that a proposer chooses to submit a classified proposal, the following information is applicable. Security Classification guidance on DD Form 254 will not be provided at this time since DARPA is soliciting ideas only. After reviewing the incoming proposals, if a determination is made that the award

instrument may result in access to classified information, a DD Form 254 will be issued and attached as part of the award. Proposers choosing to submit a classified proposal must first receive permission from the Original Classification Authority to use their information in applying to this BAA. An applicable classification guide should be submitted to ensure that the proposal is protected appropriately. For instructions on submitting Classified White Papers or Full Proposals, contact Security & Intelligence Directorate (SID) Classification Management at (571) 218-4841.

Research Involving Human Use

Proposals selected for funding are required to comply with provisions of the Common Rule (32 CFR 219) on the protection of human subjects in research (<http://www.dtic.mil/biosys/downloads/32cfr219.pdf>) and the DoD Directive 3216.2

(<http://www.dtic.mil/whs/directives/corres/html2/d32162x.htm>). All proposals that involve the use of human subjects are required to include documentation of their ability to follow Federal guidelines for the protection of human subjects. This includes, but is not limited to, protocol approval mechanisms, approved Institutional Review Boards (IRB), and Federal Wide Assurances. These requirements are based on expected human use issues sometime during the entire length of the proposed effort.

For proposals involving "greater than minimal risk" to human subjects within the first year of the project, performers must provide evidence of protocol submission to a federally approved IRB at the time of final proposal submission to DARPA. For proposals that are forecasted to involve "greater than minimal risk" after the first year, a discussion on how and when the proposer will comply with submission to a federally approved IRB needs to be provided in the submission. More information on applicable federal regulations can be found at the Department of Health and Human Services Office of Human Research Protections website (<http://www.dhhs.gov/ohrp/>).

EVALUATION CRITERIA

The following evaluation criteria are listed in order of decreasing importance. Proposals that are deemed unsatisfactory in Scientific and Technical Merit will not be evaluated further.

Scientific and Technical Merit of the Proposal

Proposers must demonstrate that their proposal is innovative and unique, that the technical approach is sound, that they have an understanding of critical technical issues and risk, and that they have a plan for mitigation of those risks. A significant improvement in capability or understanding above the state of the art must be demonstrated. All milestones must be clearly and quantitatively described.

Value to Defense

Proposers must demonstrate the potential of successful research to radically change military capability or improve national security with a clear statement of the goals of their program and a quantitative comparison with existing technology.

Capability of the Personnel and Facilities to Perform the Proposed Effort

Proposers must demonstrate that their team has the necessary background and experience to perform this project. The balance of the technical capabilities of the team must match that required in the program plan. The relevant experience of key personnel must be sufficient to provide confidence that the proposers can accomplish their

objectives. Proposers must demonstrate that the combined facilities of the team are sufficient to accomplish the objectives of the proposal.

Cost Realism

Costs of the proposal must be reasonable and provide a high value to the Government.

ADMINISTRATION

Address for Submission of White Papers or Full Proposals (Except Classified Proposals):

DARPA/DSO, ATTN: BAA05-19
3701 North Fairfax Drive
Arlington, VA 22203-1714

Web address for White Paper and Full Proposal Submission:

<http://www.sainc.com/dso0519/>

Fax: (571) 218-4553 (Addressed to: DARPA/DSO, BAA05-19)

Electronic Mail: BAA05-19@darpa.mil

This announcement may be retrieved via the WWW at URL

<http://www.darpa.mil/baa/>.

Point of Contact

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Quercetin and Blood Oxidative Stress During Ultra-Marathon Running

M. Hudson, J. Quindry, S. McAnulty, P. Hosick, C. Dumke, L. McAnulty, D. Nieman. Appalachian State University, Dept of Health, Leisure, and Exercise



Abstract

Previous research indicates that prolonged exercise bouts result in blood oxidative stress. We investigated the efficacy of oral quercetin supplementation, a compound with known antioxidant properties, as a potential countermeasure against blood oxidative stress during ultra-marathon exercise. In double blind fashion, 63 subjects received either oral quercetin (250 mg, 4x/day; 1000 mg/day total) or placebo 3-weeks prior to and during the Western States 100 mile trail run. Blood draws before and immediately following (quercetin finishers n=18, placebo finishers n=21) the event was analyzed for markers of oxidative stress. Results show that in response to the ultra-marathon challenge, aqueous phase antioxidant capacity (ferric reducing ability of plasma, FRAP) was similarly elevated in runners from both quercetin and placebo treatments and likely reflects significant increases in plasma urate levels. Alternately, trolox equivalent antioxidant capacity (TEAC) was not altered by exercise. Quercetin supplementation did not significantly influence pre-to-post-exercise TEAC levels based on a significance level of $p < 0.05$. These findings indicate that oral quercetin supplementation does not appear to alter the lipid or aqueous phase antioxidant capacity of the blood plasma. Accordingly, quercetin supplementation would not be expected to prevent blood oxidative damage during an ultra-marathon event.

Intro

- Previously, blood oxidative stress has been observed following ultra-marathon running.
- Ongoing research efforts seek efficacious antioxidant counter therapies for activity-related ox-stress.
- Quercetin, a polyphenolic compound of grapes, is a beneficial intervention in other exercise models.
- The purpose of this study was to investigate the efficacy of quercetin as a potential countermeasure to oxidative stress during ultra-marathon running.

Methods



Results

	Quercetin	Placebo
Males	n=19	n=22
Female	n=15	n=19
Height (cm)	173.3 ± 2.3	177.1 ± 2.1
Weight (kg)	68.3 ± 2.5	74.4 ± 2.3
Years Running	12.6 ± 2.2	13.4 ± 1.6
Miles/Week	51.2 ± 2.9	46.8 ± 4.2
Ultra Marathons	38.7 ± 10.07	38.9 ± 5.81
Finish Time (hours)	26.4 ± 0.6	27.5 ± 0.6

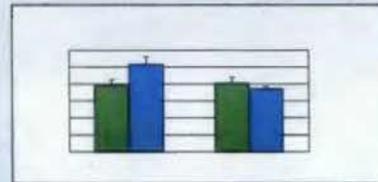


Figure 1. Mass Spectrometry analysis revealed plasma F2-isoprostanes did not differ between quercetin and placebo (pre or post-race), and further, was not affected by ultra-marathon running (interaction effect pre-race, 0.103, post-race $p=0.600$, time effect, $p=0.027$). Values are means ± SEM



Figure 2. ELISA (Zentix Technology, Dunedin, New Zealand) measurements of plasma protein carbonyls did not differ between quercetin and placebo, and was not affected by ultra-marathon running (interaction effect, $p=0.709$, time effect, $p=0.783$). Values are means ± SEM

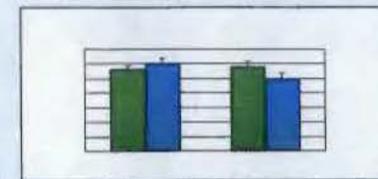


Figure 3. Spectrophotometric analysis of Trolox-Equivalent Antioxidant Capacity (TEAC) did not differ between quercetin and placebo, and was not affected by ultra-marathon running (interaction effect, $p=0.178$, time effect $p=0.289$). Values are means ± SEM



Figure 4. Spectrophotometric analysis of the ferric reducing ability of plasma (FRAP) was significantly affected by ultra-marathon running, but did not differ between quercetin and placebo (interaction effect, $p=0.695$, time effect, $p<0.001$). Values are means ± SEM

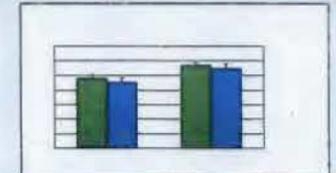


Figure 5. Spectrophotometric analysis of uric acid did not differ between quercetin and placebo, but was significantly affected by ultra-marathon running (interaction effect, $p=0.629$, time effect, $p=0.027$). Values are means ± SEM

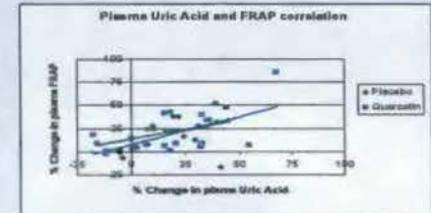


Figure 6. Positive correlations were observed between plasma uric acid and ferric reducing ability of plasma (FRAP). This finding was similar between quercetin and placebo.

Conclusions

- Protein carbonyls, F2-isoprostanes, and trolox equivalent antioxidant capacity (TEAC) were not altered by exercise.
- Aqueous phase antioxidant capacity (ferric reducing ability of plasma, FRAP) was similarly elevated in both quercetin and placebo treatments.
- A positive correlation between plasma uric acid and ferric reducing ability of plasma (FRAP) was observed suggesting that the increased plasma antioxidant capacity may be due to purine metabolism in skeletal muscle.
- Oral quercetin supplementation did not alter the antioxidant capacity of the blood plasma.
- Oral quercetin supplementation would not be expected to prevent blood oxidative damage during ultra-marathon running

Partially supported by a grant from the Defense Advanced Research Projects Agency (DARPA) and the Army Research Office (ARO), award number W911NF-06-0014



TECHNOLOGY DRIVEN. **WARFIGHTER FOCUSED.**

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

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US Army Natick Soldier RD&E Center

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Nutraceutical / Bioactive Food Compounds



Military Nutrition and Performance Divisions, USARIEM

- 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

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Quercetin is the most common flavonoid



Quercetin Content¹ of Commonly Consumed Fruits and Vegetables

Food	Level (mg/kg fresh edible wt)	Food	Level (mg/kg fresh edible wt)
Onion	347	Lettuce	1.4
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.

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Quercetin and Performance

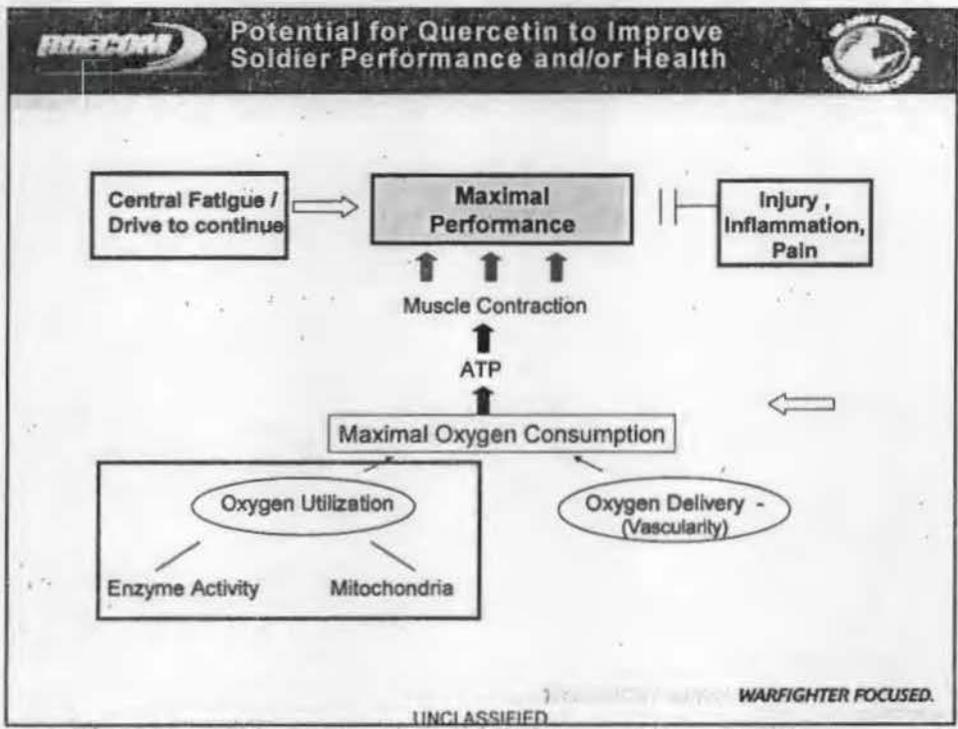


Animal studies have shown some unique and potentially remarkable affects of Quercetin with as little as 7 days of pre-treatment

- 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

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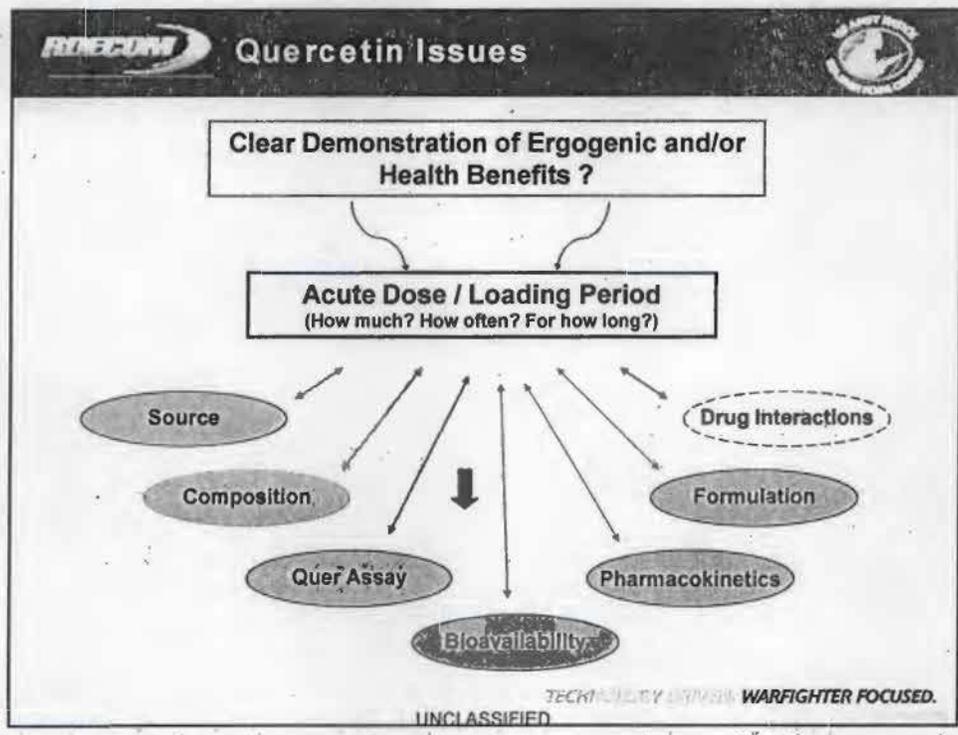
PRIMECOW Quercetin is being "highly marketed" and "pushed" 



Basic Questions:

- Is it safe?
- What dose (how much for how long)?

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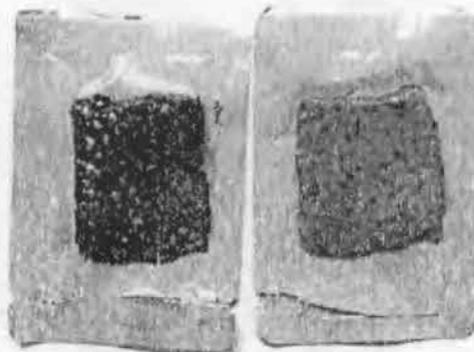


Peak Performance Ration Components



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

Control



Added 500 mg
Quercetin

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"Tasking"



- 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*

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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.)

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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.

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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

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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"

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AIBS Panel Report
received 31 Oct 2008



- 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

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AIBS Panel Report
received 31 Oct 2008



- 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

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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



For a bioactive substance in candidate carrier food component/item

