Role of Lycopene and Long Chain n-3 Polyunsaturated Fatty Acid Supplements in Airway Inflammation

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A thesis submitted for the degree of Doctor of Philosophy

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STATEMENT OF ORIGINALITY

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............................................................

Ahmad Saedi
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List of abbreviations:

AA: arachidonic acid
AHR: airway hyper-responsiveness
BAL: bronchoalveolar lavage
BALF: bronco-alveolar-lavage fluid
BCDF: B cell differentiation factor
BHT: butylated hydroxytoluene
BMI: body mass index
COPD: chronic obstructive pulmonary disease
CRP: C-reactive protein
DHA: docosahexaenoic acid
DMSO: dimethylsulfoxide
DRI: dietary reference intake
EIA: exercise induced asthma
ELISA: enzyme linked immunosorbent assay
EPA: eicosapentaenoic
FCS/MEM: foetal calf serum/minimum essential medium
FEV₁: forced expiratory volume in 1 second
FVC: forced vital capacity
GC: gas chromatography
G-CSF: granulocyte colony stimulation factor
GINA: global initiative for asthma guidelines
GM-CSF: granulocyte-monocyte colony stimulation factor
GSHPx: glutathione peroxidise
HDL: high density lipoprotein
HPLC: high performance liquid chromatography
ICAM-1: intercellular adhesion molecule-1
ICS: inhaled corticosteroid (µg beclamethasone equivalent)
ICS: inhaled corticosteroids
IFN-γ: interferon-gamma
IgG: immunoglobulin G
IgM: immunoglobulin M
IL-1: interleukin-1
IL-2: interleukin-2
IL-3: interleukin-3
IL-4: interleukin-4
IL-5: interleukin-5
IL-6: interleukin-6
IL-8: interleukin-8
IL-12: interleukin-12
IL-17: interleukin-17
IP-10: interferon-gamma inducible protein-10
LCn-3PUFA: long chain n-3 polyunsaturated fatty acid
LDH: lactate dehydrogenase
LDL: low density lipoprotein
LPS: lipopolysaccharide
LTB: Leukotriene B
M-CSF: monocytes colony stimulation factor
MDA: malondialdehyde
MOI: multiplicity of infection (plaque forming unit (PFU)/the number of cells)
NF-κB: nuclear factor-κB
NO: nitric oxide
PEF: peak expiratory flow
PFU: plaque forming unit
PG: prostaglandin
PMN: polymorphonuclear
RDA: recommended dietary allowances
RER: relative expression ratio
ROS: reactive oxygen species
RT-PCR: reverse transcription polymerase chain reaction
RV: rhinovirus
SEM: standard error of mean
SOD: superoxide dismutase
TAC: total antioxidant capacity
TCID_{50}: tissue culture infective dose 50%
TDI: toluene diisocyanate
THF: tetrahydrofuran
TLR: toll-like receptor
TNF-α: tumour necrosis factor-α
TXA: thromboxane A
vRNA: viral ribonucleic acid
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Publications arising from this thesis:

Articles:


3. **Saedisomeolia A**, Wood LG, Garg ML, Gibson PG, Wark PAB. Supplementation of long chain n-3 polyunsaturated fatty acids increases the utilisation of lycopene in cultured airway epithelial cells. *Journal of Food Lipids* (Accepted 04/06/2008).

Abstracts:


Synopsis
In Western society, increased asthma prevalence over recent years has coincided with changes in dietary patterns, leading to the hypothesis that a Western diet increases susceptibility to asthma. Components of the diet that may be important are antioxidants (e.g. lycopene) and fatty acids. Lycopene and long chain n-3 polyunsaturated fatty acids (LCn-3PUFA) including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have anti-inflammatory effects. As asthma is a disease linked to oxidative stress and inflammation, it was hypothesised that these nutrients may have a beneficial effect individually, and may have a synergistic anti-inflammatory effect when used in combination. The aim was to examine the ability of lycopene and/or LCn-3PUFAs to protect against virus-induced inflammation, as rhinovirus infection is the primary cause of asthma exacerbation.

The results presented demonstrate that both lycopene and DHA (but not EPA) individually decreased the inflammatory response of airway epithelial cells infected with rhinovirus. The results also showed that DHA supplementation increased the utilization of lycopene by cells. Furthermore, lycopene reduced rhinovirus replication. A combination of lycopene and DHA also reduced the inflammatory response of cells to rhinovirus infection, however, no synergistic anti-inflammatory effect was apparent. It is concluded that consumption of foods containing lycopene and DHA may exhibit a beneficial effect on the inflammatory response to rhinovirus infection. This may have important clinical implications, as increased dietary intake of foods rich in these nutrients may lead to a reduction in the frequency and severity of asthma exacerbations.