The Role of Antioxidants in Platelet Aggregation and their Stimulation of NK Cells Against Cancer Cells Line K562

Ioannis K. Toliopoulos*

Konstantinion Research Center of Molecular Medicine and Biotechnology, Non-Profit Foundation, Thessaloniki, Greece.


Keywords
Atherosclerosis, Cancer, Platelets, NKCs.

Atherosclerosis and cancer are two very common diseases that concern the global scientific community because of high lethal rate worldwide. Platelet aggregation is a process, which can be evaluated clinically and with laboratorial methods by measuring the platelet receptors [1]. On the other hand, the role of natural killer cells (NKCs, a population of Lymphocytes with shorter half-life compared to B and T cells) [2], which is the backbone of the immune system seemed to play a major role for the defense of the immune system against tumors. The major immunoregulatory role of these God given cells had been demonstrated especially when administered by plant extracts or vitamin supplements (antioxidants) in numerous in vitro as wells as in vivo scientific studies [3]. Recently, Huntington et al. reported a series of studies that clinically prove that NK cells are a key immune constituent in the protective antitumour immune, and provide an overview of the prognostic value of NK cell gene expression in 25 tumour types [2].

According to the process of platelet aggregation, it is well known that the major glycoprotein, which activated called GpIIb/IIIa, and it’s a platelet receptor. The formation of the so-called thrombus (coagulation) is the phenomenon of the binding of fibrinogen with GpIIb/IIIa receptor and other functionally activated receptors [1]. Several studies have been published in the past, and they have demonstrated that antiplatelet drugs have potential action in patients with conditions such as angiogenesis, tumor development, and metastasis [4]. Moreover, the past years, several studies have been performed and proved the stimulation of NKCs on tumor cells by administration of antioxidants both in vitro and in vivo [3,5].

The major issue for Platelet aggregation for evaluation and treatment of the associated diseases is the selection of the receptors. A wide variety of mobile transmembrane receptors covers the platelet membrane, including many integrins, leucine-rich repeated (LRR) receptors, G-protein coupled seven transmembrane receptors (GPCR) (PAR-1 and PAR-4 thrombin receptors, proteins belonging to the immunoglobulin superfamily (GP VI, FcyRIIA), C-type lectin receptors (P-selectin), tyrosine kinase receptors and and a miscellaneous of other types (CD63, CD36, P-selectin ligand 1, TNF receptor type, etc). However, the most important receptor in platelet aggregation is the GpIIb/IIa, which is at the forefront of recent research [6]. The basic methodology for platelet aggregation was fully described by Theocharis et al, and was induced by three different platelet stimulators (PAF, platelet activating factor, ADP, adenosine phosphate, ARA, arachidonic acid). In this study, three antioxidant substances (apigenin, genistein, quercetin) were demonstrated to inhibit platelet aggregation majory in PAF. All three flavonoids showed the same ability to decrease the number of GpIIb/IIa receptors per platelet [7]. Moreover, apigenin, genistein, and quercetin showed to decrease the production of TXA2 suggesting that each compound may act as an anti-inflammatory agent. Having as basal concept that TXA2 is crucial for every platelet aggregation agonist pathway, it is also demonstrated that flavonoid inhibiting effects are launched by the inhibition of TXA2 production [7]. Another antioxidant such as resveratrol showed in vitro anti-platelet properties, where it completely inhibited platelet aggregation at a concentration of 3 X 10^(-3) M, decreased TXB2 levels, and inhibited the expression of receptor GpIIb/IIa in non-stimulated platelets [1]. Also, Toliopoulos et al, in another study demonstrated the anti-platelet action of ascorbic acid with five stimulators and various concentrations, by evaluating in vitro its effectiveness in the receptor of GpIIb/IIa. The ascorbic acid in...
Table 1: The number of NK, NKT cells and their cytotoxicity in 15 end stage cancer patients before and after treatment with EMF at RF [7].

<table>
<thead>
<tr>
<th>No/SEX</th>
<th>Age</th>
<th>NK</th>
<th>NKT cells before treatment</th>
<th>%NK</th>
<th>NKT cells after treatment</th>
<th>Variation % of total NK cells after treatment</th>
<th>Cytotoxicity % of NK cells before treatment</th>
<th>Cytotoxicity % of NK cells after treatment</th>
<th>Variation in Cytotoxicity % of NK cells after treatment</th>
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<tr>
<td>1/F</td>
<td>38</td>
<td>15.7</td>
<td>21.13</td>
<td>6.22</td>
<td>13</td>
<td>14</td>
<td>12.5:1</td>
<td>25:1</td>
<td>50:1</td>
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<tr>
<td>2/F</td>
<td>92</td>
<td>5.54</td>
<td>10.16</td>
<td>20.43</td>
<td>161</td>
<td>3</td>
<td>89</td>
<td>43</td>
<td>59</td>
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<td>3/F</td>
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<td>19.25</td>
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<td>5</td>
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<td>5.45</td>
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<td>35</td>
<td>45</td>
<td>48</td>
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<td>5/F</td>
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<td>1.50</td>
<td>8.60</td>
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<td>100</td>
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<td>15</td>
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<td>10.62</td>
<td>15.46</td>
<td>1745</td>
<td>24</td>
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<tr>
<td>9/M</td>
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patients [9]. A recent encouraging detailed study by Lee et al. demonstrated the anticancer effects of resveratrol as antioxidant in vivo mediated by NK cell activation. Moreover, they proved that resveratrol appeared to activate NK cells most effectively among the substances tested and synergistically increased IFN-γ secretion and NK cell cytotoxicity with interleukin-2 (IL-2).10

Overall, it would be significant for most health professionals who care for the benefit of their patients who suffer from a variety of diseases such as cardiovascular, prothrombotic ones such as diabetes, sepsis, thrombocytopenia, sickle cell disease, and vasculitis (Behcet’s syndrome), to test them individually for platelet aggregation methodologies, and specifically for the activity of receptor GPIIb-IIIa, which can be specifically evaluated by flow cytometry even before the expression of the disease [10]. Therefore, individual evaluation of specific anti-platelet bioactive substances can be tested by activation of GPIIb-IIIa in relation to other markers (CD9, CD29, CD31, CD36, CD41, CD42a, CD42b, CD61, CD63, CD107a, CD154), and may contribute majorly in daily clinical practice in platelet immunology in both health and disease [11].

Nowadays Huntington et al reported that NK studies are targeted to specific cellular pathways, which can offer a significant value in evolvement of tumor progression, and evaluate cancer immunotherapy response [2]. In conclusion, cancer immunotherapy is a unique methodology, which can be performed by specialized doctors daily by stimulating NKCs and testing their functionality with different cancer cell lines of solid tumors. This can lead to the future of evaluation of clinical therapies and can include biological markers, which may include metabolism, multiplication, EMT (epithelial mesenchymal transition), metastasis, adhesion, and survival of the cancer cell [12]. All the above marker selection and can bring a new era in the specific diagnostic approach, which will absolutely will lead to the elongation of the life span and quality of life of the cancer patient.

References