Modifying Naturally Sourced Flavonoids for Increased Antioxidant Capacity and Antisickling Activity

1. Sickle Cell Disease

- Sickle Cell Disease (SCD) is a group of genetic blood disorders that primarily affects those of West African descent.
- This disease impacts hemoglobin, the protein that transports oxygen throughout the blood.
- It causes red blood cells to change from their normal, disc shape to a crescent, sickle shape.

Figure 1. What is Sickle Cell Disease (SCD)? Centers for Disease Control and Prevention.

- This study utilized mechanisms in two antisickling agents to investigate a method of treatment of SCD.

2. Antisickling Agents

- Sickling is caused by a lack of oxygen in Hb.
- Flavonoids are natural antioxidants that can prevent oxidative damage.
- Aldehydes are compounds that can bind to the sickle hemoglobin and strengthen its ability to take in oxygen, preventing sickling.
- The flavonoids Quercetin (Q), Galangin (G), Kaempferol (K), and Epigallocatechin gallate (E) were extracted from fruits and modified to have aldehydes on their structure.

Figure 2. Flavonoid Structure. Prepared by author.

Figure 3. Aldehyde Structure. Prepared by author.

3. Antioxidant Capacity

Table 1. Antioxidant Power Exhibited.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Originals [Fe$^{2+}$ μM]</th>
<th>Derivatives [Fe$^{2+}$ μM]</th>
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</thead>
<tbody>
<tr>
<td>ASC</td>
<td>1494.648</td>
<td>ASC 1494.648</td>
</tr>
<tr>
<td>Q</td>
<td>430.4281</td>
<td>Q-1 192.2006</td>
</tr>
<tr>
<td>G</td>
<td>1861.6208</td>
<td>G-1 2318.9415</td>
</tr>
<tr>
<td>K</td>
<td>2472.4771</td>
<td>K-1 1759.0529</td>
</tr>
<tr>
<td>E</td>
<td>2199.5413</td>
<td>E-1 5038.9972</td>
</tr>
</tbody>
</table>

- Compounds were tested for their ability to reduce Fe$^{3+}$ to Fe$^{2+}$ with a higher Fe$^{2+}$ concentration signifying a stronger reducing agent (antioxidant).
- All original flavonoids were strong antioxidants, stronger than Vitamin C.
- Some derivatives showed a large increase in antioxidant power, while others showed slight decreases.

4. Antisickling Activity

- Lag in sickling caused by flavonoids
- Q caused the longest delay, despite weak antioxidant strength

Figure 5. Sample Curve of 1mM Quercetin Derivative.

- Derivatives produced similar sample curves
- No increase in absorbance shows that they completely inhibited sickling over time frame

5. Conclusions

- Flavonoid modification was successful in producing stronger antisickling agents.
- Antioxidant power is not the sole indicator of antisickling ability.
- E and E-1 presented highest potential as both strong antioxidants and antisickling compounds.

References

All images and figures created by author unless otherwise noted.

Data & Statistics on Sickle Cell Disease | CDC. (2022, May 2). Centers for Disease Control and Prevention.

Mayo Clinic. (2022, March 9). Sickle cell anemia - Diagnosis and treatment - Mayo Clinic.