

**Table S1.** Orally administered cannabinoids evidences.

| Authors       | Year | Study Design              | Sample | Intervention                           | IOP lowering                  | Level | Strength | Grade    |
|---------------|------|---------------------------|--------|--|-------------------------------|-------|----------|----------|
| Hepler RS     | 1976 | Case-Control Study        | 120    | 5-10-20 mg delta-9-THC                 | 14-15%                        | 4     | IV       | Low      |
| Hepler RS     | 1976 | Case-Control Study        | 40     | 5-10-20 mg delta-9-THC                 | 23-18%                        | 4     | IV       | Low      |
| Newell FW     | 1979 | Prospective Study         | 18     | Nabilone 0.5 mg                        | 24-23%                        | 4     | IV       | Low      |
| Tiedeman JS   | 1981 | Randomized clinical trial | 37     | 5-10 mg BW29Y 4-8-12 mg BW146          | 10%                           | 2     | II       | Moderate |
| Flach AJ      | 2002 | Prospective study         | 9      | 10 mg to 80 mg oral delta-9-THC        | 10%                           | 4     | IV       | Very Low |
| Tomida I      | 2006 | Randomized clinical trial | 6      | 5 mg delta-9-THC, 20-40 mg cannabidiol | 16%                           | 2     | II       | Moderate |
| Plange N      | 2007 | Case series               | 8      | 7.5 mg Dronabinol                      | 27.9%                         | 4     | IV       | Very Low |
| Gagliano C    | 2011 | Randomized clinical trial | 42     | 300 mg palmitoyl-ethanolamide          | no significant effects on IOP | 2     | II       | Moderate |
| Pescosolido N | 2011 | Prospective Study         | 15     | 300 mg palmitoyl-ethanolamide          | no significant effects on IOP | 4     | IV       | Low      |
| Strobbe E     | 2013 | Randomized clinical trial | 40     | 300 mg palmitoyl-ethanolamide          | 23%                           | 2     | II       | Moderate |

POAG: primary open angle glaucoma, IOP intraocular pressure, THC Tetrahydrocannabinol.

**Table S2.** Inhaled cannabinoids evidences.

| Authors    | Year | Study Design       | Sample | Intervention                                      | IOP lowering              | Level | Strength | Grade    |
|------------|------|--------------------|--------|---|---------------------------|-------|----------|----------|
| Hepler RS  | 1971 | Case series        | 11     | 18 mg delta-9-THC cigarette                       | 24% IOP lowering          | 4     | IV       | Very Low |
| Flom MC    | 1975 | Case-Control Study | 15     | 12 mg delta-9-THC cigarette                       | 13% IOP lowering          | 4     | IV       | Low      |
| Hepler RS  | 1976 | Case-Control Study | 136    | 20-40-80 mg delta-9-THC cigarette                 | 17%-34% IOP lowering      | 4     | IV       | Low      |
| Hepler RS  | 1976 | Case-Control Study | 40     | 1-2-4% natural vs synthetic delta-9-THC cigarette | 15%-34% IOP lowering      | 4     | IV       | Low      |
| Merritt JC | 1980 | Case series        | 18     | 18 mg delta-9-THC cigarette                       | 14.5%- 23.4% IOP lowering | 4     | IV       | Low      |

POAG: primary open angle glaucoma, IOP intraocular pressure, THC Tetrahydrocannabinol.

**Table S3.** Topical cannabinoids evidences.

| Authors       | Year | Study Design              | Sample | Intervention                                    | IOP lowering                | Level | Strength | Grade    |
|---------------|------|---------------------------|--------|---|-----------------------------|-------|----------|----------|
| Merritt JC    | 1981 | Randomized clinical trial | 6      | 0.05-0.1% delta-9-THC eye drop                  | No significant IOP lowering | 2     | II       | Moderate |
| Merritt JC    | 1981 | Case series               | 8      | 0.01-0.05-0.1% delta-9-THC eye drop             | No significant IOP lowering | 4     | IV       | Very Low |
| Green K       | 1982 | Case-control study        | 16     | 1% delta-9-THC eye drop (single administration) | No significant IOP lowering | 4     | IV       | Low      |
| Jay WM        | 1983 | Case-control study        | 28     | 1% delta-9-THC eye drop (four times a day)      | 15±0.5% IOP lowering        | 4     | IV       | Low      |
| Porcella A    | 2001 | Case-control study        | 8      | 25-50 µg of WIN55212-2 eye drop                 | 23±0.9% IOP lowering        | 4     | IV       | Very Low |
| Pescosolido N | 2018 | Case series               | 5      | Bediol and topical Bedrocan eye drop            | No significant IOP lowering | 4     | IV       | Very Low |

POAG: primary open angle glaucoma, IOP: intraocular pressure, THC: Tetrahydrocannabinol.

**Table S4.** Intravenous cannabinoids evidences.

| Authors    | Year | Study Design       | Sample | Intervention                  | IOP lowering        | Level | Strength | Grade    |
|------------|------|--------------------|--------|-------------------------------|---------------------|-------|----------|----------|
| Purnell WD | 1975 | Case series        | 2      | 3.0-6.7 mg THC                | 42-62% IOP lowering | 4     | IV       | Very Low |
| Cooler P   | 1976 | Case-control study | 10     | 0.022-0.044 mg/Kg delta-9-THC | 29-37% IOP lowering | 4     | IV       | Very Low |

IOP: intraocular pressure, THC: Tetrahydrocannabinol.