# Caper (*Capparis spinosa* L.)*:* An updated review on its phytochemistry, nutritional value, traditional uses, and therapeutic potential

**Table 1S**. *In vitro* antibacterial and antifungal effects of Caper extracts.

| Bacteria | Plant part | Extract | Method | Key results | References |
|---|---|---|---|---|---|
| *Escherichia coli* | Stem | Ethanolic (80%) | Microbroth dilution | MIC=12,5 mg/mL | (1) |
| | | Aqueous | | MIC=25 mg/mL | |
| | Leaves | Ethanolic (80%) | | MIC=6,25 mg/mL | |
| | | Aqueous | | MIC=6,25 mg/ mL | |
| | flowers fruits | Ethanolic (75%) (phenols) | Microbroth dilution | MIC=50 mg/mL, IZ=19 mm<br>MIC=50 mg/mL, IZ=15 mm | (2) |
| | Roots | Aqueous | Disc diffusion | 6.50, 8.75, 10.34, 12.20, 13.42, 14.76 mm corresponding respectively to the concentrations 0.5, 1, 1.5, 2, 4, 6 mg/disc | (3) |
| | | Methanolic (70%) | | 8.76, 10.45, 12.18, 14.56, 15.20, 16.56 mm corresponding respectively to the concentrations 0.5, 1, 1.5, 2, 4, 6 mg/disc | |
| | | Ethanolic (70%) | | 9.20, 11.78, 13.85, 15.20, 17.36, 18.36 mm corresponding respectively to the concentrations 0.5, 1, 1.5, 2, 4, 6 mg/disc | |
| | | Ethyl acetate (70%) | | 9.86, 13.30, 14.88, 17.40, 18.54, 19.72 corresponding respectively to the following crude extract 0.5, 1, 1.5, 2, 4, 6 mg/disc | |
| | Leaves | Petroleum ether (subsequently fractioned and gave to 2 compounds) | Broth microdilution | MIC compound 1= 100mg/mL<br>MIC compound 2= 100 mg/mL | (4) |
| | Flower buds | Methanolic | Disc diffusion | IZ= 21 mm | (5) |
| | Leaves | Ethanolic extract 80% | Agar diffusion method | NT | (6) |
| | | Chloroform fraction | | Inactive | |
| | | Ethyl acetate fraction | | IZ= 18.7 mm at 100 µl/disc<br>IZ= 16.9 mm 50 µl/disc<br>IZ= 14.9 mm at 25 µl/disc | |
| | | N-butanol fraction | | IZ= 16.3 mm at 100 µl/disc | |

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|---|---|---|---|---|---|
| | | | | IZ= 12.9 mm at 50 µl/disc<br>IZ= 9.9 mm at 25 µl/disc<br>MIC= 12.5 mg/mL | |
| | Flowers buds | 10% decoctate | Microdilution method | MIC= 66.66 mg/mlL | (7) |
| | | | | MBC= NA | |
| | | Ethanolic | | MIC= 10,26 mg/mL | |
| | | | | MBC= 41,04 mg/mL | |
| | fruits | 10% decoctate | | MIC= 41.66 mg/mL | |
| | | | | MBC= 66.66 mg/mL | |
| | | Ethanolic | | MIC=6.25 mg/mL | |
| | | | | MBC= 8.33 mg/mL | |
| | fruits | Copper nanoparticles from aqueous extract | Broth microdilution | MBC=10 mg/mL | (8) |
| | Stems | Methanolic 80% | Disc diffusion<br><br>- Resazurin microtitre-plate assay | IZ=17.9 mm, MIC= 184.6 µg/mL | (9) |
| | | Ethanol 80% | | IZ= 13.2 mm, MIC=236.2 µg/mL | |
| | | Acetone 80% | | IZ=18.6 mm, MIC= 278.9 µg/mL | |
| | roots | Methanolic 80% | | IZ=23.9 mm, MIC=142.6 µg/mL | |
| | | Ethanol 80% | | IZ=19.2mm, MIC=194.1 µg/mL | |
| | | Acetone 80% | | IZ=16.7mm, MIC= 229.6 µg/mL | |
| | fruits | Methanolic 80% | | IZ=20.9mm, MIC=253.2 µg/mL | |
| | | Ethanol 80% | | IZ=15.2 mm, MIC=266.7 µg/mL | |
| | | Acetone 80% | | IZ=16.7 mm, MIC=306.9 µg/mL | |
| | Shoots | Methanolic (80%) | | IZ= 21.9 mm, MIC= NA µg/mL | |
| | | Ethanol (80%) | | IZ= 13.7 mm MIC= NA µg/mL | |
| | | Acetone (80%) | | IZ=14.5 mm MIC= NA µg/mL | |
| | Flowers | Methanolic 80% | | IZ=26.5 mm MIC= 181.2 µg/mL | |
| | | Ethanol 80% | | IZ=18.2 mm MIC=215.6 µg/mL | |
| | | Acetone 80% | | IZ= 21.6mm MIC=224.0 µg/mL | |
| | leaves | Acetone | Agar-well diffusion | IZ= 11mm | (10) |
| | | Ethyl acetate | | IZ= 13mm | |
| | | Boiled water | | IZ= 11mm | |
| *Staphylococcus aureus* | Stem | Ethanolic (80%) | Microbroth dilution | MIC=25 mg/mL | (1) |
| | | Aqueous | | MIC=25 mg/mL | |
| | Leaves | Ethanolic (80%) | | MIC=12,5 mg/mL | |
| | | Aqueous | | MIC=12,5 mg/mL | |
| | flowers fruits | Ethanolic (75%) (phenols) | Microbroth dilution | MIC=50 mg/mL IZ=14 mm<br>MIC=50 mg/mL IZ=12 mm | (2) |

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|---|---|---|---|---|
| Twigs | Methanolic (85%) | disc diffusion | -IZ= 25.12, 21.15, 15.17, 10.23 mm corresponding respectively to the dilutions of 1 g/ml, 1, ½, ¼ ⅛ | (11) |
| Flower | | | IZ= 20.22, 15.55, 10.22, 8.75 mm corresponding respectively to the dilutions of 1 g/ml, 1, ½, ¼, ⅛ | |
| Fruits | | | IZ= 17.12, 12.50, 10.13, 7.75 mm corresponding respectively to the dilutions of 1 g/ml, 1, ½, ¼, ⅛ | |
| Leaves | | | IZ= 22.02, 15.50, 10.13, 8.78 mm corresponding respectively to the dilutions of 1 g/ml, 1, ½, ¼, ⅛ | |
| Roots | | | IZ= 11.83, 11.42, 9.83, 7.11 mm corresponding respectively to the dilutions of 1 g/ml, 1, ½, ¼, ⅛ | |
| Leaves | Petroleum ether (subsequently fractioned and gave to 2 compounds) | Broth microdilution | MIC compound 1= 100 mg/mL<br>MIC compound 2= 200 mg/mL | (4) |
| Flower buds | Methanolic e | Disc diffusion | IZ= 22 mm | (5) |
| Leaves | Ethanolic (80%) | Agar diffusion | NT | (6) |
| | Chloroform fraction | | Inactive | |
| | Ethyl acetate fraction | | IZ= 16.1 mm at 100 µl/disc<br>IZ= 14.6 mm 50 µl/disc<br>IZ= 14.9 mm at 25 µl/disc<br>MIC= 25mg/ml | |
| | N-butanol fraction | | IZ= 10.1 mm at 100 µl/disc<br>IZ= 9.1 mm at 50 µl/disc<br>MIC= 50 mg/mL | |
| fruits | Copper nanoparticles | Broth microdilution | MBC=5 mg/mL<br>MIC= 5 mg/mL | (8) |
| Stems | Methanolic 80% | - Disc diffusion<br><br>- Resazurin microtitre-plate assay | IZ=15.7 mm MIC= 145.2 µg/mL | (9) |
| | Ethanol 80% | | IZ= 11.1 mm MIC=189.1 µg/mL | |
| | Acetone 80% | | IZ=13.2 mm MIC= 256.7 µg/mL | |
| Roots | Methanolic 80% | | IZ=21.1 mm MIC=156.7 µg/mL | |
| | Ethanol 80% | | IZ=14.9 mm MIC=198.7 µg/mL | |
| | Acetone 80% | | IZ=15.6 mm MIC= 277.1 µg/mL | |
| fruits | Methanolic 80% | | IZ=17.7 mm MIC=110.9 µg/mL | |

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| | | Ethanol 80% | | IZ=11.9 mm MIC=125.6 µg/mL | |
| | | Acetone 80% | | IZ=12.6 mm MIC=272.7 µg/mL | |
| | Shoots | Methanolic 80% | | IZ= 21.0 mm MIC= NA µg/mL | |
| | | Ethanol 80% | | IZ= 17.9 mm MIC= NA µg/mL | |
| | | Acetone 80% | | IZ=11.1 mm MIC= NA µg/mL | |
| | Flowers | Methanolic 80% | | IZ=23.7 mm MIC= 122.1 µg/mL | |
| | | Ethanol 80% | | IZ=14.8 mm MIC=147.8 µg/mL | |
| | | Acetone 80% | | IZ= 12.1 mm MIC=266.7 µg/mL | |
| | leaves | Acetone | Agarwell diffusion | IZ= 19 mm | (10) |
| | | Ethanolic | | IZ= 15 mm | |
| | | Ethyl acetate | | IZ= 13 mm | |
| | | Petroleum ether | | IZ= 16 mm | |
| | | Methanolic | | IZ= 19 mm | |
| | | Boiled water | | IZ= 12 mm | |
| *Staphylococcus epidermidis* | Leaves | Petroleum ether (subsequently fractioned and gave to 2 compounds) | broth microdilution | MIC compound 1= 100mg/mL MIC compound 2= 200mg/mL | (4) |
| *Sarm (staphylococcus aureus resistant to methicillin)* | Stem | Ethanolic (80%) | microbroth dilution | MIC=6.25-12.5 mg/mL | (7) |
| | | Aqueous | | MIC=100 mg/mL | |
| | Leaves | Ethanolic (80%) | | MIC=12,5 mg/mL | |
| | | Aqueous | | MIC=50 mg/mL | |
| | Flowers buds | 10% decoctate | Microdilution | MIC= 66.66 mg/mL, MBC= NA | |
| | | Ethanolic | | MIC= 14.06 mg/mL, MBC= 36.04 mg/mL | |
| | fruits | 10% decoctate | | MIC= 33.33 mg/mL, MBC= NA | |
| | | Ethanolic | | MIC=8.33 mg/mL, MBC= 18.38 mg/mL | |
| | leaves | Acetone | Agarwell diffusion | IZ= 16 mm | (10) |
| | | Ethanolic | | IZ= 13 mm | |
| | | Ethyl acetate | | IZ= 18 mm | |
| | | Petroleum ether | | IZ= 15 mm | |
| | | Methanolic | | IZ= 13 mm | |
| | | Boiled water | | IZ= 15 mm | |
| *Sasm (staphylococcus aureus sensitive to methicillin)* | Flowers buds | 10% decoctate | Microdilution | MIC= 66.66 mg/mL, MBC= NA | (7) |
| | | Ethanolic | | MIC= 12.5 mg/mL, MBC= 40 mg/mL | |
| | fruits | 10% decoctate | | MIC= 33.33 mg/mL, MBC= NA | |
| | | Ethanolic | | MIC=21.62 mg/mL, MBC= 38.29 | |

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| | | | | mg/mL | |
| *Pseudomonus aeruginosa* | Flowers | Ethanolic (75%) (phenols) | microbroth dilution | MIC=50 mg/mL | (2) |
| | Fruits | | | MIC=50 mg/mL | |
| | Flower buds | Methanolic | Disc diffusion | IZ= 19 mm | (5) |
| | Leaves | Ethanolic 80% | Agar diffusion | NT | (6) |
| | | Chloroform fraction | | Inactive | |
| | | Ethyl acetate | | IZ= 18.1 mm at 100 µl/disc<br>IZ= 15.9 mm 50 µl/disc<br>IZ= 10.1 mm at 25 µl/disc<br>MIC= 25 mg/ml | |
| | | N-butanol fraction | | IZ= 14.9 mm at 100 µl/disc<br>IZ= 12.1 mm at 50 µl/disc<br>IZ= 10.1 mm at 25 µl/disc<br>IZ= 9.9 mm at 12.5 µl/disc<br>MIC= NA mg/ml | |
| | Flowers buds | Decoction | Microdilution method | MIC= NA | (7) |
| | | | | MBC= NA | |
| | | Ethanolic extract | | MIC= 12.76 mg/mL | |
| | | | | MBC= NA | |
| | fruits | Decoction | | MIC= 33.33 mg/mL | |
| | | | | MBC= NA | |
| | | Ethanolic extract | | MIC=NA | |
| | | | | MBC= NA | |
| | Aerial parts | Methanolic extract | Disc diffusion | IZ= 30 mm | (12) |
| | leaves | Ethyl acetate | Agar-well diffusion | IZ= 14 mm | (10) |
| *Klebsiella pneumonia* | Stem | Ethanolic (80%) | microbroth dilution | MIC=50 mg/mL | (1) |
| | | Aqueous | | MIC=100 mg/mL | |
| | Leaves | Ethanolic (80%) | | MIC=25 mg/mL | |
| | | Aqueous | | MIC=50 mg/mL | |
| | Leaves | Petroleum ether (subsequently fractioned and gave to 2 compounds) | broth microdilution | MIC compound 1= 50 mg/mL<br>MIC compound 2= 200mg/mL | (4) |
| | Flower buds | Methanolic | Disc diffusion | IZ= 16 mm | (5) |
| | Flowers buds | 10% decoctate | Microdilution | MIC= NA | (7) |
| | | | | MBC= NA | |
| | | Ethanolic | | MIC= 13.5 mg/mL | |
| | | | | MBC= 50 mg/mL | |

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| | fruits | 10% decoctate | | MIC= 55.55 mg/mL | |
| | | | | MBC= NA | |
| | | Ethanolic | | MIC= 32.44 mg/mL | |
| | | | | MBC= 86.5 mg/mL | |
| | fruits | Copper nanoparticules | Broth microdilution | MBC= 10 mg/mL | (8) |
| | | | | MIC= 10 mg/mL | |
| | leaves | Acetone | Agar-well diffusion | IZ= 12 mm | (10) |
| | | Ethanolic | | IZ= 17 mm | |
| | | Ethyl acetate | | IZ= 36 mm | |
| | | Petroleum ether | | IZ= 14 mm | |
| | | Methanolic | | IZ= 15 mm | |
| | | Boiled water | | IZ= 15 mm | |
| *Klebsiella oxytoca* | Flower buds | Methanolic | Disc diffusion | IZ= 19 mm | (5) |
| *Klebeslla sp* | flowers | Ethanolic (75%) (phenols) | microbroth dilution | MIC=50 mg/mL; IZ=20 mm | (2) |
| | fruits | | | MIC=50 mg/mL; IZ=15 mm | |
| *Bacillus subtilis* | flowers | -Ethanolic (75%) (phenols) | Microbroth dilution | MIC=50 mg/m; IZ=12 mm | (2) |
| | fruits | | | MIC=50 mg/mL; IZ=13 mm | |
| | Leaves | -Ethanolic 80% | Agar diffusion | NT | (6) |
| | | Chloroform | | IZ= 13.3 mm at 100 µl/disc<br>IZ= 10.3 mm 50 µl/disc<br>MIC= 25 mg/ml | |
| | | Ethyl acetate fraction | | IZ= 19.8 mm at 100 µl/disc<br>IZ= 18.2 mm at 50 µl/disc<br>IZ= 15.3 mm at 25 µl/disc<br>MIC= 25 mg/mL | |
| | | N-butanol fraction | | inactive | |
| | Stem | Methanolic 80% | - Disc diffusion<br>- Resazurin microtitre-plate assay. | IZ=26.8 mm MIC= 123.2 µg/mL | (9) |
| | | Ethanol 80% | | IZ= 19.2 mm MIC=159.7 µg/mL | |
| | | Acetone 80% | | IZ=13.7 mm MIC= 207.8 µg/mL | |
| | roots | Methanolic 80% | | IZ=21.7 mm MIC=157.8 µg/mL | |
| | | Ethanol 80% | | IZ=16.1 mm MIC=231.4 µg/mL | |
| | | Acetone 80% | | IZ=17.7 mm MIC= 282.6 µg/mL | |
| | fruits | Methanolic 80% | | IZ= 23.9 mm MIC=126.7 µg/mL | |
| | | Ethanol 80% | | IZ= 16.1 mm MIC=160.1 µg/mL | |
| | | Acetone 80% | | IZ=12.7 mm MIC=253.9 µg/mL | |
| | Shoots | Methanolic 80% | | IZ= 24.6 mm MIC= NA µg/mL | |

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| | | Ethanol 80% | | IZ= 19.9 mm MIC= NA µg/mL | |
| | | Acetone 80% | | IZ= 14.9 mm MIC= NA µg/mL | |
| | Flowers | Methanolic 80% | | IZ=17.6 mm MIC= 111.2 µg/mL | |
| | | Ethanol 80% | | IZ=19.7 mm MIC=175.6 µg/mL | |
| | | Acetone 80% | | IZ= 11.2 mm MIC=196.7 µg/mL | |
| *Acinetobacter* | Leaves | Ethanolic 95% | broth microdilution | MIC= 50ppm MBC= 25ppm | (13) |
| | Fruits | | | MIC= 25ppm MBC= 12.5ppm | |
| | Stems | | | MIC= 50ppm MBC= 50ppm | |
| | Leaves | Ethyl acetate | | MIC 50ppm MBC: 25ppm | |
| | Fruits | | | MIC= 12.5ppm MBC= 6.25ppm | |
| | Stems | | | MIC= 50ppm MBC= 25ppm | |
| *Acinetobacter baumannii* | Flower buds | Methanolic | Disc diffusion | IZ= 21 mm | (5) |
| | Aerial part | Methanolic | disc diffusion | IZ= 11 mm | (12) |
| *Salmonella Typhi* | Leaves | Petroleum ether (subsequently fractioned and gave to 2 compounds) | broth microdilution | MIC compound 1= 100 mg/mL MIC compound 2= 100mg/mL | (4) |
| *Enterobacter aerogenes* | Flower buds | Methanolic | Disc diffusion | IZ= 26 mm | (5) |
| *Listeria monocytogenes* | Flowers buds | 10% decoctate | Microdilution | MIC= 23.6 mg/mL, MBC= NA | (7) |
| | | Ethanolic | | MIC= 13.59 mg/mL, MBC= 42.8 mg/mL | |
| | Fruits | 10% decoctate | | MIC= 38.88 mg/mL, MBC= NA | |
| | | Ethanolic | | MIC= 1.73 mg/mL, MBC= 8.33 mg/mL | |
| *Pasteurella multocida* | Stems | Methanolic 80% | - Disc diffusion - Resazurin microtitre-plate assay | IZ=24,7 mm MIC= 126.7 µg/mL | (9) |
| | | Ethanol 80% | | IZ= 12.7 mm MIC=158.3 µg/mL | |
| | | Acetone 80% | | IZ=15.3 mm MIC= 246.7 µg/mL | |
| | Roots | Methanolic 80% | | IZ=20.4 mm MIC=207.9 µg/mL | |
| | | Ethanol 80% | | IZ=13.7 mm MIC=231.4 µg/mL | |
| | | Acetone 80% | | IZ=15.1 mm MIC= 264.8 µg/mL | |
| | Fruits | Methanolic 80% | | IZ= 24.9 mm MIC=120.1 µg/mL | |
| | | Ethanol 80% | | IZ= 17.7 mm MIC=176.7 µg/mL | |
| | | Acetone 80% | | IZ=12.1 mm MIC=234.9 µg/mL | |
| | Shoots | Methanolic 80% | | IZ= 23.6 mm MIC= NA µg/mL | |
| | | Ethanol 80% | | IZ= 16.9 mm MIC= NA µg/mL | |
| | | Acetone 80% | | IZ= 12.5 mm MIC= NA µg/mL | |
| | Flowers | Methanolic 80% | | IZ=20.7 mm, MIC= 146.7 µg/mL | |

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| | | Ethanol 80% | | IZ=15.9 mm, MIC=158.9 µg/mL | |
| | | Acetone 80% | | IZ= 14.7 mm, MIC=206.7 µg/mL | |
| *Enterococcus faecalis* | Flower buds | Methanolic | Disc diffusion | IZ= 22 mm | (5) |
| *Citrobacter freundii* | | | | IZ= 17 mm | |
| *Proteus mirabilis* | | | | IZ= 27 mm | |
| *Proteus vulgaris* | | | | IZ= 17 mm | |
| *Bacillus cereus* | Fruits | Aqueous (Copper nanoparticles) | Broth microdilution | MBC= 5 mg/mL, MIC= 5 mg/mL | (8) |
| *Enterococcus faecalis* | Leaves | Acetone | Agarwell diffusion | IZ= 14 mm | (10) |
| | | Ethanolic | | IZ= 17 mm | |
| | | Ethyl acetate | | IZ= 29 mm | |
| | | Petroleum ether | | IZ= 11 mm | |
| | | Methanolic | | IZ= 18 mm | |
| | | Boiled water | | IZ= 12 mm | |
| *Alcaligenes faecalis* | | Acetone | | IZ= 20 mm | |
| | | Ethanolic | | IZ= 21 mm | |
| | | Ethyl acetate | | IZ= 17 mm | |
| | | Petroleum ether | | IZ= 14 mm | |
| | | Methanolic | | IZ= 16 mm | |
| | | Boiled water | | IZ= 12 mm | |
| *Enterobacter cloacae* | | Acetone | | IZ= 17 mm | |
| | | Ethanolic | | IZ= 19 mm | |
| | | Ethyl acetate | | IZ= 19 mm | |
| | | Petroleum ether | | IZ= 13 mm | |
| | | Methanolic | | IZ= 14 mm | |
| | | Boiled water | | IZ= 16 mm | |
| **In vitro antifungal effects of Caper extracts.** | | | | | |
| **Fungi** | **Plant part** | **Extract** | **Method** | **Key results** | **References** |
| *Candida albicans* | Leaves | Ethyl acetate | Agar diffusion and microdilution | IZ= 10.2 – 16.8 mm<br>MIC= 25 mg/ml | (6) |
| | | N- Butanol | | IZ= 9.9-10 mm<br>MIC= 50 mg/mL | |
| | | Ethyl acetate | Microdilution | MIC ≤ 12.5 µg/mL | (10) |
| | | | Agar diffusion | IZ= 17 mm | |
| | | Ethanolic | Microdilution | MIC ≤ 12.5 µg/mL | |
| | | | Agar diffusion | IZ=19 mm | |
| | | Methanolic | Microdilution | MIC ≤ 12.5 µg/mL | |

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| | | | Agar diffusion | IZ= 14 mm | |
| | Fruits | Aqueous (Silver nanoparticles) | broth microdilution | MIC=2500µg/mL | (14) |
| *Aspergillus flavus.* | Twings | Methanolic (85%) | Agar diffusion | IZ= 8.43. 7.12. and 7.73 mm correspond respectively to the following concentrations 1g/mL; 500 mg/ mL; 250 mg/mL | (11) |
| *Candida glabrata* | Fruits | Aqueous (Silver nanoparticles) | broth microdilution | MIC= 5000µg/mL | (14) |
| | | | | MBC= 10000µg/mL | |
| *Kluyveromyces marxianus* | | | | MIC= 625µg/mL | |
| | | | | MBC= 156.25µg/mL | |
| *Fusarium moniliforme* | Leaves | Ethyl acetate | Agar well diffusion | IZ= 21 mm | (10) |
| *Trichoderma longibrachiatum* | | Ethyl acetate | | IZ=16 mm | |
| | | Boiled water | | IZ= 17 mm | |
| | | | | | |
| *Trichoderma viride* | | Ethyl acetate | | IZ= 19 mm | |
| *Penicillium aurantiacum* | | Ethyl acetate | | IZ=18 mm | |
| *Aspergillus niger* | | Methanolic | | IZ=16 mm | |
| *Rhizopus stolonifer* | | Ethyl acetate | | IZ=25 mm | |
| *Curvulariacl avata* | | Acetone | | IZ=12 mm | |
| | | Ethanolic | | IZ=17 mm | |
| | | Ethyl acetate | | IZ=25 mm | |
| | | Pet. Ether | | IZ=17 mm | |
| | | Methanolic | | IZ=15 mm | |
| | | Boiled water | | IZ=13 mm | |

IZ: Inhibition zone. MIC: Minimum inhibitory concentration. MBC: Minimum bactericidal concentration

**Table 2S.** *In vitro* antioxidants effects of Caper extracts.

| Plant part | Collection zone | Extraction method | Extract | Method | Key results | Reference |
|---|---|---|---|---|---|---|
| Leaves | Southern part of Iran (Ewaz of Fars province) | Percolation | Hydro-ethanolic | DPPH | $IC_{50}$=1.41 mg/ml | (15) |
| Fruits | | | | | $IC_{50}$= 1.56 mg/ml | |
| Buds | | | | | $IC_{50}$= 2.49 mg/ml | |
| Leaves | Jahrom city, Fars province, Iran | Maceration | Hydro-ethanolic 70% | DPPH | $IC_{50}$= = 3624 ppm | (16) |
| Fruits | | | | | $IC_{50}$= 21591 ppm | |
| Aerial part | Cholistan desert | Maceration | Methanolic | DPPH | 30.48± 0.37 mg TE/g extract | (17) |
| | | | | ABTS | 40.43 ± 3.33 mg TE/g extract | |
| | | | | FRAP | 47.13 mg TE/g extract | |
| | | | | CUPRAC | 86.64 mg TE/g extract | |
| | | | | Phosphomolybdenum assay | 6.73 mg TE/g extract | |
| | | | | Metal chelating power | 1.19 mg EDTA/g | |
| | | | Dichloromethane | DPPH | 6.24 TE/g extract | |
| | | | | ABTS | 23.64 mg TE/g extract g | |
| | | | | FRAP | 50.37 mg TE/g extract | |
| | | | | CUPRAC | 118.45 mg TE/g extract | |
| | | | | Phosphomolybdenum assay | 75.79 mg TE/g extract | |
| | | | | Metal chelating power | 2.51 mg EDTA/ | |
| Roots | | | Methanolic | DPPH | 28.45 mg TE/g extract | |
| | | | | ABTS | 40.55mg TE/g extract | |
| | | | | FRAP | 38.49 mg TE/g extract | |
| | | | | CUPRAC | 58.77 mg TE/g extract | |
| | | | | Phosphomolybdenum assay | NA mg TE/g extract | |
| | | | | Metal chelating power | 0.31 mg EDTA/g | |
| | | | Dichloromethane | DPPH | 16.06 mg TE/g extract | |
| | | | | ABTS | 33.68 mg TE/g extract | |
| | | | | FRAP | 42.82 mg TE/g extract | |
| | | | | CUPRAC | 96.89 mg TE/g extract | |
| | | | | Phosphomolybdenum assay | 13.56 mg TE/g extract | |

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|---|---|---|---|---|---|---|
| | | | | Metal chelating power | 1.41 mg EDTA/g | |
| Flower buds (small, medium and big), sprout and fruits | Mersin, Turkey | Not specified | Methanolic | DPPH | Antioxidant activity (%):<br>Bud (small)= 74.62 %<br>Bud (medium)= 76.65 %<br>Bud (big)= 72.21 %<br>Sprout=59.01 %<br>Fruit=50.51 % | (18) |
| Leaves | different regions in southern Tunisia | Maceration | Aqueous | DPPH | $IC_{50}$= 41.57 mg/mL | (19) |
| | | | | ABTS | 206.07 mg EAA/g DW | |
| | | | | FRAP | $EC_{50}$= 120.22 mg/mL | |
| | | Reflux | | DPPH | $IC_{50}$= 36.66 mg/mL | |
| | | | | ABTS | 179.68 mg EAA /g DW | |
| | | | | FRAP | $EC_{50}$= 89.91 mg/mL | |
| | | Ultrasonic assisted extraction. | | DPPH | $IC_{50}$= 40.20 mg/mL | |
| | | | | ABTS | 258.77 mg EAA /g DW | |
| | | | | FRAP | $EC_{50}$= 62.07 mg/mL | |
| Aerial parts | Botraba, Libya | Cold maceration | Methanolic (70%) | DPPH | % inhibition = 0.07 % | (20) |
| Fruit | Khuzestan Province, Iran | Electric mixer | Ethanolic (70%) | DPPH | $EC_{50}$=1.48 mg/mL | (21) |
| Roots | Anbarabad, Iran | Ultrasound | Ethanolic (70%) | DPPH | $IC_{50}$=79.28 µg/mg | (22) |
| | | | Aqueous | | $IC_{50}$= 90.09 µg/mg | |
| Flower buds | Alicante, Almería and Murcia, Spain | Sonication | Methanolic (80%) | DPPH | 1542.5 ± 180.4 mg Trolox/100 g FW | (23) |
| | | | | FRAP | 160.2 ± 17.0 mg Trolox/100 g FW | |
| | | | | ABTS | 192.7 ± 0.8 mg Trolox/100 g FW | |
| Leaves | Albaha, Saudi Arabia | Infusion | Ethanolic (80 %) | DPPH | $IC_{50}$= 0.0707 mg/mL, Activity % = 61.00 % | (24) |
| | | | n-Butanol | | $IC_{50}$= 0.043 mg/mL, Activity % = 68.55 % | |
| Fresh flower buds | Gaziantep province, Turkey | Magnetic stir | Methanolic (75%) | DPPH | 51.25 µM Trolox/kg | (25) |
| | | | | ABTS | 62.19 µM Trolox/kg | |
| Fermented flower buds | | | | DPPH | 21.41 µM Trolox/kg | |
| | | | | ABTS | 32.98 µM Trolox/kg | |
| Processed and fresh fruit | Fez, Morocco | Not mentioned | Acetone (80%) | DPPH | Processed buds $IC_{50}$=8.18 µg/ml<br>Small fresh buds $IC_{50}$=5.90 µg/ml | (26) |
| Leaves | Archipelago, Italy | Decoction for leaves | Methanolic 60% | DPPH | 38.82 mg TE/g extract | (27) |
| | | | | ABTS | 96.25 mg TE/g extract | |
| | | | | CUPRAC | 80.77 mg TE/g extract | |
| | | | | FRAP | 56.33 mg TE/g extract | |
| | | | | Phosphomolybdenum assay | 0.37 mmol TE/g extract | |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | Metal chelating power | 4.36 mg EDTAE/g extract | |
| Aerial parts | | Microwave extraction | | DPPH | 29.33 mg TE/g extract | |
| | | | | ABTS | 86.78 mg TE/g extract | |
| | | | | CUPRAC | 73.47 mg TE/g extract | |
| | | | | FRAP | 52.67 mg TE/g extract | |
| | | | | Phosphomolybdenum assay | 0.50 mmol TE/g extract | |
| | | | | Metal chelating power | 3.01 mg EDTAE/g extract | |
| | | Soxhlet extraction | | DPPH | 60.54 mg TE/g extract | |
| | | | | ABTS | 124.15 mg TE/g extract | |
| | | | | CUPRAC | 98.17 mg TE/g extract | |
| | | | | FRAP | 66.94 mg TE/g extract | |
| | | | | Phosphomolybdenum assay | 0.56 mmol TE/g extract | |
| | | | | Metal chelating power | 2.34 mg EDTAE/g extract | |
| Aerial parts | South Sinai region, Egypt | Soxhlet | Petroleum ether | DPPH | -DPPH activity: $EC_{50}$= 17.66 mg extract/ mg<br>Antioxidant efficiency AE= 0.056 | (28) |
| | | | | ABTS | Inhibition = 27.54% | |
| | | | | FIC | $IC_{50}$= 0.662 mg extract/ mL | |
| | | | | FRAP | 225.0 mmol Fe(II)/ mg extract | |
| Leaves, flowers, fruits, roots | Siliana, Tunisia | Maceration | Methanolic | TAC | Leaves 112.4 mg EAA / g of dry extract<br>Flowers 67.3 mg EAA / g of dry extract<br>Fruits 97 mg EAA / g of dry extract<br>Roots 175.7 mg EAA / g of dry extract. | (29) |
| | | | | DPPH | Leaves: $IC_{50}$ = 70.1 mg/L<br>Flowers: $IC_{50}$ = 137.1 mg/L<br>Fruits: $IC_{50}$ = 172.5 mg/L<br>Roots: $IC_{50}$ = 329 mg/L | |
| Leaves | Khuzestan, Iran | Maceration | -Ethanol 80%<br>-ethyl acetate<br>-chloroform | DPPH | Hydro-alcoholic: $IC_{50}$= 0.034891 mg/ml<br>Ethyl acetate: $IC_{50}$= 0.277039 mg/ml<br>Chloroform: $IC_{50}$= 0.0392 mg/ml | (30) |
| | | | | FRAP | Hydro-alcoholic 1.655187 mg/ml<br>Ethyl acetate 15.90301 mg/ml<br>Chloroform 3.908373 mg/ml | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Flower buds and fruits | Sidi Kacem, Morocco | Maceration | Ethanolic | DPPH | $IC_{50}$= 0.52 mg/ml for flower buds and 0.61 mg/ml for fruits. | (31) |
| | | Decoction | Aqueous | | IC50= 0.25 mg/ml for flower buds and 0.4 mg/ml for fruits. | |
| Fruit | Jaén, Spain | ultrasound-assisted solid-liquid extraction | Methanolic | DPPH | Fruits: 0.98 g TE/100 g extract<br>Laboratory fermented fruits: 1.08 g TE/100 g extract<br>Commercially fermented fruits: 1.48 g TE/100 g extract | (32) |
| | | | | ABTS | Fruits: 1.72 g TE/100 g extract<br>Laboratory fermented fruits: 1.92 g TE/100 g extract<br>Commercially fermented fruits: 2.21 g TE/100 g extract | |
| Leaves | Al Bayda city, Libya | Soxhlet | Methanolic | DPPH | $IC_{50}$ = 0.205 mg/ml | (33) |
| Seeds | South Sinai Governorate, Egypt | Soxhlet | Petroleum ether | DPPH | %= 152.40 % | (34) |
| Leaves | Gafsa, Tunisia | Not specified | Methanolic | DPPH | $EC_{50}$ = 43.031 ± 1.24 µg/ml | (35) |
| | | | | $H_2O_2$ | $EC_{50}$ = 81.21 ± 1.28 µg/ml | |
| Fruits | Not mentioned | Not specified | Methanol, ethanol, aqueous | DPPH | Ethanol: 38,8% as the highest activity. | (36) |
| Leaves | Kazeroon city, Iran | Reflux with deionized water | Polysaccharides | DPPH | DPPH activity % = 55% at 300 µg/mL | (37) |
| | | | | Hydroxyl (OH) scavenging activity | OH activity % = 64% at 300 µg/mL | |
| Aerial parts | Amman, Jordan | Infusion | Ethanolic (70%) | DPPH | $IC_{50}$= 76 µg/ml | (38) |
| | | | | FRAP | 0.5 absorbance is achieved at 5.59 mg/mL | |
| | | | Aqueous | DPPH | $IC_{50}$= 209 µg/ml | |
| | | | | FRAP | 0.5 absorbance is achieved at 13.0 mg/mL | |
| Leaves | Tunisia | Soxhlet | Ethanolic | DPPH | $IC_{50}$= 31.73 µg/ml | (39) |
| | | | | ABTS | $C_{50}$=34.02 µg/ml | |
| | | | Aqueous | DPPH | $IC_{50}$= 45.62 µg/ml | |
| | | | | ABTS | $IC_{50}$=38.32 µg/mL | |
| Not specified | Not indicated | Maceration | Ethanolic (80%) | DPPH | $IC_{50}$ = 7.41 µg/mL | (40) |
| | | | | ABTS | 3.15 TEAC | |
| Roots | Abu-graib, Iraq | reflux for aqueous extract | Aqueous | FRAP | 74.29% at 10 mg/mL | (41) |
| | | | | Chelating ability | 11.35% and 51.50% at 2 mg/mL and 10 mg/mL | |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | Maceration for ethanolic extract | Ethanolic (80%) | FRAP | Frap activity: 67.33% at 10 mg/mL | |
| | | | | Chelating ability | 9.02% and 35.21% 2 mg/mL and 10 mg/mL | |
| Fruits | Tunisia | Not specified | Methanolic | TAC | The highest activity is: 78.63 mg GAE/g dried residue | (42) |
| | | | | DPPH | The highest $IC_{50}$ is 126.5 µg/mL | |
| | | | | ABTS | ABTS activity: the highest ic50 is 74.82 µg/mL | |
| Not indicated | Gaziantep, Turkey | Sonication | Methanolic | FRAP | 145.07 µmol Trolox.100 g-1 dw | (43) |
| | | | | DPPH | $SC_{50}$= 0.32 mg. ml-1 | |

Trolox equivalent; EDTAE: EDTA equivalent; NA: not active, EAA: equivalents ascorbic acid, FRAP assay: Equivalent concentration 1 EC1) mmol/L FeSO4

**Table 3S**. Physicochemical parameters of caper phytoconstituents.

| | | Hydrogen bond | | | Lipinski | Ghose | Veber | Egan | Muegge |
|---|---|---|---|---|---|---|---|---|---|
| **Compound** | **MW** | **acceptors** | **donors** | **Consensus Log P** | | | **Violations** | | |
| **Alkaloids** | | | | | | | | | |
| 6 | 143.18 | 2 | 0 | -1.59 | 0 | 2 | 0 | 0 | 1 |
| 7 | 161.16 | 2 | 2 | 1.24 | 0 | 1 | 0 | 0 | 1 |
| 8 | 156.18 | 1 | 1 | 1.83 | 0 | 1 | 0 | 0 | 1 |
| 9 | 496.46 | 12 | 8 | -2.46 | 2 | 2 | 1 | 1 | 4 |
| 10 | 205.21 | 3 | 2 | 1.78 | 0 | 0 | 0 | 0 | 0 |
| 11 | 207.18 | 4 | 3 | 0.34 | 0 | 0 | 0 | 0 | 0 |
| 12 | 145.16 | 1 | 1 | 1.72 | 0 | 2 | 0 | 0 | 1 |
| 13 | 161.16 | 2 | 2 | 1.56 | 0 | 1 | 0 | 0 | 1 |
| 14 | 278.26 | 4 | 2 | 2.4 | 0 | 0 | 0 | 0 | 0 |
| 15 | 214.22 | 6 | 4 | -1.18 | 0 | 1 | 0 | 0 | 1 |
| 16 | 435.52 | 5 | 4 | 2.33 | 0 | 1 | 0 | 0 | 0 |
| 17 | 465.54 | 6 | 4 | 2.38 | 0 | 1 | 0 | 0 | 0 |
| 18 | 465.54 | 6 | 4 | 2.35 | 0 | 1 | 0 | 0 | 0 |
| 19 | 465.54 | 6 | 4 | 2.33 | 0 | 1 | 0 | 0 | 0 |
| 20 | 435.52 | 5 | 4 | 2.34 | 0 | 1 | 0 | 0 | 0 |
| 21 | 597.66 | 10 | 7 | 0.47 | 3 | 4 | 1 | 1 | 2 |
| **Glucosinolates** | | | | | | | | | |
| 22 | 597.66 | 10 | 7 | 0.47 | 3 | 4 | 1 | 1 | 2 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 23 | 448.47 | 10 | 6 | -0.3 | 2 | 0 | 1 | 1 | 2 |
| 24 | 478.49 | 11 | 5 | -0.08 | 1 | 0 | 1 | 1 | 2 |
| 25 | 478.49 | 11 | 6 | -0.29 | 2 | 0 | 1 | 1 | 3 |
| 26 | 464.47 | 11 | 7 | -0.89 | 2 | 0 | 1 | 1 | 3 |
| 27 | 221.28 | 2 | 1 | 2.23 | 0 | 0 | 0 | 0 | 0 |
| 28 | 280.37 | 3 | 1 | 1.83 | 0 | 0 | 0 | 0 | 0 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 29 | 333.34 | 10 | 5 | -1.61 | 0 | 1 | 1 | 1 | 1 |
| **Furans and pyrroles** | | | | | | | | | |
| 30 | 234.2 | 5 | 0 | 1.23 | 0 | 0 | 0 | 0 | 0 |
| 31 | 126.11 | 3 | 1 | 0.19 | 0 | 3 | 0 | 0 | 1 |
| 32 | 142.11 | 4 | 2 | 0.65 | 0 | 3 | 0 | 0 | 1 |
| 33 | 139.15 | 2 | 1 | 0.71 | 0 | 3 | 0 | 0 | 1 |
| 34 | 132.11 | 4 | 2 | -0.61 | 0 | 4 | 0 | 0 | 1 |
| 35 | 253.25 | 5 | 2 | -0.33 | 0 | 1 | 0 | 0 | 0 |
| 36 | 179.17 | 3 | 0 | 0.7 | 0 | 0 | 0 | 0 | 1 |
| 37 | 253.25 | 5 | 2 | -0.14 | 0 | 1 | 0 | 0 | 0 |
| 38 | 226.23 | 5 | 2 | -0.93 | 0 | 1 | 0 | 0 | 0 |
| 39 | 237.21 | 5 | 3 | -0.98 | 0 | 1 | 0 | 0 | 0 |
| **Flavonoids** | | | | | | | | | |
| 40 | 286.24 | 6 | 4 | 1.58 | 0 | 0 | 0 | 0 | 0 |
| 41 | 270.24 | 5 | 3 | 2.11 | 0 | 0 | 0 | 0 | 0 |
| 42 | 610.52 | 16 | 10 | -1.29 | 3 | 4 | 1 | 1 | 4 |
| 43 | 1205.04 | 31 | 19 | -2.63 | 3 | 4 | 2 | 1 | 6 |
| 44 | 600.53 | 12 | 6 | 3.5 | 3 | 2 | 1 | 1 | 5 |
| 45 | 300.26 | 6 | 3 | 2.11 | 0 | 0 | 0 | 0 | 0 |
| 46 | 286.28 | 5 | 2 | 2.25 | 0 | 0 | 0 | 0 | 0 |
| 47 | 448.38 | 11 | 7 | -0.25 | 2 | 0 | 1 | 1 | 3 |
| 48 | 316.26 | 7 | 4 | 1.65 | 0 | 0 | 0 | 0 | 0 |
| 49 | 772.66 | 21 | 13 | -3.18 | 3 | 4 | 1 | 1 | 5 |
| 50 | 610.52 | 16 | 10 | -1.27 | 3 | 4 | 1 | 1 | 4 |
| 51 | 566.51 | 10 | 4 | 4.34 | 1 | 3 | 1 | 1 | 2 |
| 52 | 566.51 | 10 | 4 | 4.39 | 1 | 3 | 1 | 1 | 2 |
| **Terpenoids** | | | | | | | | | |
| 53 | 224.3 | 3 | 2 | 1.46 | 0 | 0 | 0 | 0 | 0 |
| 54 | 386.44 | 8 | 5 | -0.02 | 0 | 1 | 0 | 1 | 0 |
| 55 | 402.44 | 9 | 6 | -1.06 | 1 | 1 | 1 | 1 | 2 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 56 | 386.44 | 8 | 5 | 0.01 | 0 | 1 | 0 | 1 | 0 |
| 57 | 416.42 | 10 | 6 | -0.88 | 1 | 1 | 1 | 1 | 2 |
| 58 | 402.44 | 9 | 5 | -0.56 | 0 | 1 | 1 | 1 | 1 |
| 59 | 240.3 | 4 | 2 | 0.94 | 0 | 0 | 0 | 0 | 0 |
| 60 | 280.32 | 5 | 2 | 0.94 | 0 | 0 | 0 | 0 | 0 |
| 61 | 248.27 | 6 | 4 | -0.53 | 0 | 1 | 0 | 0 | 0 |
| 62 | 194.18 | 6 | 4 | -1.39 | 0 | 1 | 0 | 0 | 1 |
| 63 | 414.71 | 1 | 1 | 7.26 | 1 | 3 | 0 | 1 | 2 |
| 64 | 576.85 | 6 | 4 | 5.49 | 1 | 4 | 0 | 0 | 1 |
| 65 | 843.31 | 7 | 3 | 11.39 | 2 | 4 | 1 | 1 | 3 |
| 66 | 430.71 | 2 | 1 | 8.29 | 1 | 3 | 1 | 1 | 1 |
| 67 | 462.7 | 4 | 1 | 6.52 | 0 | 3 | 1 | 1 | 1 |
| 68 | 180.16 | 6 | 6 | -2.81 | 1 | 2 | 0 | 0 | 3 |
| 69 | 172.18 | 4 | 0 | 0.62 | 0 | 0 | 0 | 0 | 1 |
| 70 | 186.16 | 3 | 0 | 2.21 | 0 | 0 | 0 | 0 | 1 |
| 71 | 186.16 | 3 | 0 | 2.12 | 0 | 0 | 0 | 0 | 1 |

**Table 4S**. Bioavailability Score, Fraction Csp3, topological polar surface area (TPSA), number of rotatable bonds (RB) and solubility (ESOL Log S) of caper phytoconstituents.

| Compounds | Bioavailability Score | Fraction Csp3 | RB | TPSA | ESOL Log S |
|---|---|---|---|---|---|
| **Alkaloids** | | | | | |
| 6 | 0.55 | 0.86 | 1 | 40.13 | -0.91 |
| 7 | 0.55 | 0 | 1 | 53.09 | -2.06 |
| 8 | 0.55 | 0.1 | 1 | 39.58 | -2.31 |
| 9 | 0.17 | 0.59 | 7 | 218.11 | -1.01 |
| 10 | 0.55 | 0.18 | 2 | 62.32 | -2.83 |
| 11 | 0.56 | 0.2 | 2 | 86.63 | -1.26 |
| 12 | 0.55 | 0 | 1 | 32.86 | -2.5 |
| 13 | 0.85 | 0 | 1 | 53.09 | -2.58 |
| 14 | 0.56 | 0 | 2 | 79.12 | -3.92 |
| 15 | 0.55 | 0.56 | 4 | 106.7 | 0.41 |
| 16 | 0.55 | 0.28 | 0 | 99.69 | -4.75 |
| 17 | 0.55 | 0.31 | 1 | 108.92 | -4.83 |
| 18 | 0.55 | 0.31 | 1 | 108.92 | -4.83 |
| 19 | 0.55 | 0.31 | 1 | 108.92 | -4.83 |
| 20 | 0.55 | 0.28 | 0 | 99.69 | -4.75 |
| 21 | 0.17 | 0.42 | 3 | 178.84 | -4.35 |
| **Glucosinolates** | | | | | |
| 22 | 0.17 | 0.42 | 3 | 178.84 | -4.35 |
| 23 | 0.11 | 0.44 | 7 | 215.58 | -2.33 |
| 24 | 0.11 | 0.47 | 8 | 213.95 | -2.66 |
| 25 | 0.11 | 0.47 | 8 | 224.81 | -2.42 |
| 26 | 0.11 | 0.44 | 7 | 235.81 | -2.2 |
| 27 | 0.55 | 0.18 | 3 | 67.39 | -2.93 |
| 28 | 0.55 | 0.33 | 2 | 101.29 | -2.8 |
| 29 | 0.11 | 0.88 | 5 | 199.79 | -0.44 |
| **Furans and pyrroles** | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| 30 | 0.55 | 0.17 | 6 | 69.65 | -1.87 |
| 31 | 0.55 | 0.17 | 2 | 50.44 | -0.54 |
| 32 | 0.85 | 0.17 | 1 | 70.67 | -1.72 |
| 33 | 0.55 | 0.29 | 3 | 42.09 | -0.99 |
| 34 | 0.55 | 0.8 | 1 | 66.76 | -0.05 |
| 35 | 0.55 | 0.58 | 1 | 80.92 | -0.66 |
| 36 | 0.55 | 0.33 | 1 | 48.3 | -1.48 |
| 37 | 0.55 | 0.58 | 2 | 80.92 | -0.94 |
| 38 | 0.55 | 0.7 | 3 | 86.71 | -0.14 |
| 39 | 0.55 | 0.3 | 3 | 114.43 | -0.54 |
| **Flavonoids** | | | | | |
| 40 | 0.55 | 0 | 1 | 111.13 | -3.31 |
| 41 | 0.55 | 0 | 1 | 90.9 | -3.94 |
| 42 | 0.17 | 0.44 | 6 | 269.43 | -3.3 |
| 43 | 0.17 | 0.44 | 12 | 518.63 | -5.4 |
| 44 | 0.17 | 0.06 | 4 | 200.26 | -7.42 |
| 45 | 0.55 | 0.06 | 2 | 100.13 | -3.9 |
| 46 | 0.55 | 0.19 | 2 | 75.99 | -3.7 |
| 47 | 0.17 | 0.29 | 4 | 190.28 | -3.18 |
| 48 | 0.55 | 0.06 | 2 | 120.36 | -3.36 |
| 49 | 0.17 | 0.55 | 9 | 348.58 | -2.69 |
| 50 | 0.17 | 0.44 | 6 | 269.43 | -3.3 |
| 51 | 0.55 | 0.06 | 5 | 159.8 | -7.17 |
| 52 | 0.55 | 0.06 | 5 | 159.8 | -7.17 |
| **Terpenoids and miscellaneous** | | | | | |
| 53 | 0.55 | 0.62 | 2 | 57.53 | -1.45 |
| 54 | 0.55 | 0.74 | 5 | 136.68 | -1.24 |
| 55 | 0.55 | 0.74 | 6 | 156.91 | -0.84 |
| 56 | 0.55 | 0.74 | 5 | 136.68 | -1.24 |
| 57 | 0.11 | 0.68 | 6 | 173.98 | -0.9 |

| | | | | | |
|---|---|---|---|---|---|
| 58 | 0.55 | 0.84 | 5 | 145.91 | -0.63 |
| 59 | 0.55 | 0.77 | 2 | 66.76 | -0.83 |
| 60 | 0.55 | 0.6 | 3 | 83.83 | -0.83 |
| 61 | 0.55 | 0.82 | 4 | 99.38 | -0.68 |
| 62 | 0.55 | 1 | 3 | 99.38 | 0.14 |
| 63 | 0.55 | 0.93 | 6 | 20.23 | -7.9 |
| 64 | 0.55 | 0.94 | 9 | 99.38 | -7.7 |
| 65 | 0.17 | 0.94 | 27 | 105.45 | -13.48 |
| 66 | 0.55 | 0.79 | 12 | 29.46 | -8.6 |
| 67 | 0.55 | 0.86 | 12 | 63.6 | -6.99 |
| 68 | 0.55 | 1 | 0 | 121.38 | 1.38 |
| 69 | 0.55 | 0.62 | 2 | 44.76 | -1.01 |
| 70 | 0.55 | 0 | 0 | 43.35 | -2.99 |
| 71 | 0.55 | 0 | 0 | 43.35 | -2.73 |

**Table 5S**. Pharmacokinetics behavior of caper phytoconstituents. Compounds number according to Figures 3, 4, 5 and 6 at the main text.

| Compounds | GI absorption | BBB permeant | Pgp substrate | CYP1A2 | CYP2C19 | CYP2C9 inhibitor | CYP2D6 | CYP3A4 | log Kp (cm/s) |
|---|---|---|---|---|---|---|---|---|---|
| **Alkaloids** | | | | | | | | | |
| 6 | Low | No | No | No | No | No | No | No | -6.89 |
| 7 | High | Yes | No | Yes | No | No | No | No | -6.46 |
| 8 | High | Yes | No | Yes | No | No | No | No | -6.12 |
| 9 | Low | No | No | No | No | No | No | No | -11.17 |
| 10 | High | Yes | No | No | No | No | No | No | -5.97 |
| 11 | High | No | No | No | No | No | No | No | -7.6 |
| 12 | High | Yes | No | Yes | No | No | No | No | -5.82 |
| 13 | High | Yes | No | Yes | No | No | No | No | -5.87 |
| 14 | High | No | No | Yes | No | No | Yes | No | -5.91 |
| 15 | High | No | No | Yes | No | No | No | No | -9.42 |
| 16 | High | No | Yes | No | No | No | No | Yes | -6.78 |
| 17 | High | No | Yes | No | No | Yes | No | No | -6.99 |
| 18 | High | No | Yes | No | No | No | No | No | -6.99 |
| 19 | High | No | Yes | No | No | No | No | No | -6.99 |
| 20 | High | No | Yes | No | No | No | No | Yes | -6.78 |
| 21 | Low | No | Yes | No | No | No | No | No | -9.05 |
| **Glucosinolates** | | | | | | | | | |
| 22 | Low | No | Yes | No | No | No | No | No | -9.05 |
| 23 | Low | No | No | No | No | No | No | No | -9.1 |
| 24 | Low | No | Yes | No | No | No | No | No | -9.03 |
| 25 | Low | No | Yes | No | No | No | No | No | -9.3 |
| 26 | Low | No | No | No | No | No | No | No | -9.45 |
| 27 | High | Yes | No | Yes | Yes | No | No | No | -6 |
| 28 | High | No | No | Yes | Yes | Yes | No | No | -6.77 |
| 29 | Low | No | Yes | No | No | No | No | No | -9.62 |
| **Furans and pyrroles** | | | | | | | | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 30 | High | Yes | No | Yes | No | No | No | No | -7.12 |
| 31 | High | No | No | No | No | No | No | No | -7.48 |
| 32 | High | No | No | No | No | No | No | No | -6.38 |
| 33 | High | Yes | No | No | No | No | No | No | -7.01 |
| 34 | High | No | No | No | No | No | No | No | -7.72 |
| 35 | High | No | No | No | No | No | No | No | -8.85 |
| 36 | High | Yes | No | No | No | No | No | No | -7.05 |
| 37 | High | No | No | No | No | No | No | No | -8.46 |
| 38 | Low | No | No | No | No | No | No | No | -8.7 |
| 39 | High | No | No | No | No | No | No | No | -8.64 |
| **Flavonoids** | | | | | | | | | |
| 40 | High | No | No | Yes | No | No | Yes | Yes | -6.7 |
| 41 | High | No | No | Yes | No | No | Yes | Yes | -5.8 |
| 42 | Low | No | Yes | No | No | No | No | No | -10.26 |
| 43 | Low | No | Yes | No | No | No | No | No | -15.23 |
| 44 | Low | No | No | No | No | Yes | No | No | -5.92 |
| 45 | High | No | No | Yes | No | No | Yes | Yes | -6.11 |
| 46 | High | Yes | No | Yes | Yes | No | No | Yes | -6.02 |
| 47 | Low | No | No | No | No | No | No | No | -8.52 |
| 48 | High | No | No | Yes | No | No | Yes | Yes | -6.9 |
| 49 | Low | No | Yes | No | No | No | No | No | -12.77 |
| 50 | Low | No | Yes | No | No | No | No | No | -10.26 |
| 51 | Low | No | No | No | No | Yes | No | No | -5.72 |
| 52 | Low | No | No | No | No | Yes | No | No | -5.72 |
| **Terpenoids and miscellaneous** | | | | | | | | | |
| 53 | High | Yes | No | No | No | No | No | No | -7.28 |
| 54 | Low | No | Yes | No | No | No | No | No | -9.4 |
| 55 | Low | No | No | No | No | No | No | No | -10 |
| 56 | Low | No | Yes | No | No | No | No | No | -9.4 |
| 57 | Low | No | No | No | No | No | No | No | -10.11 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 58 | Low | No | Yes | No | No | No | No | No | -10.3 |
| 59 | High | No | No | No | No | No | No | No | -8.18 |
| 60 | High | No | No | No | No | No | No | No | -8.18 |
| 61 | High | No | Yes | No | No | No | No | No | -8.3 |
| 62 | Low | No | No | No | No | No | No | No | -8.6 |
| 63 | Low | No | No | No | No | No | No | No | -2.2 |
| 64 | Low | No | No | No | No | No | No | No | -4.32 |
| 65 | Low | No | Yes | No | No | No | No | Yes | 0.04 |
| 66 | Low | No | Yes | No | No | No | No | No | -1.33 |
| 67 | Low | No | Yes | No | No | No | No | No | -3.41 |
| 68 | Low | No | Yes | No | No | No | No | No | -10.03 |
| 69 | High | Yes | No | No | No | No | No | No | -7.08 |
| 70 | High | Yes | No | Yes | No | No | No | No | -5.96 |
| 71 | High | Yes | No | Yes | No | No | No | No | -6.25 |

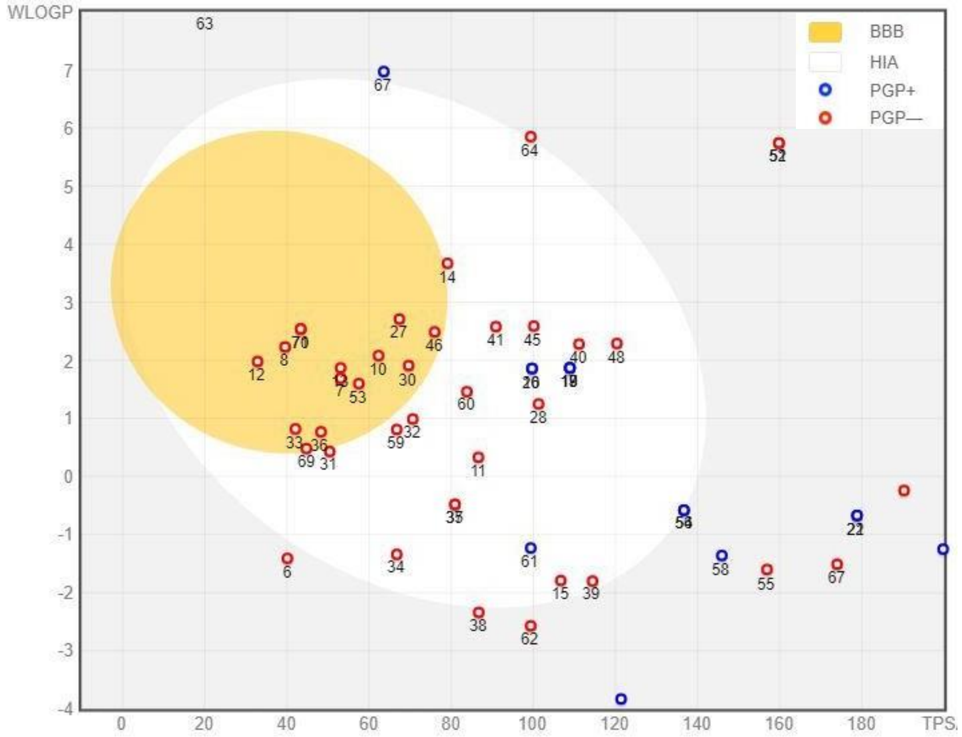


**Figure 1S**. Boiled-Egg of caper phytoconstituents highlighting that 14 compounds are able to cross the blood membrane barrier (BBB), 36 compounds passively absorbed by the gastrointestinal tract (HIA) and 45 compounds are not effluated from the central nervous system by the P-glycoprotein (PGP-), 12 compounds effluated from the central nervous system by the P-glycoprotein (PGP+), and 13 compounds are out of range. Compound numbers are from Table 1S.

**References**

1. Adwan GM, Omar GI. Evaluation of Antimicrobial activity and Genotoxic Potential of Capparis spinosa ( L .) Plant Extracts. Microbiology Research Journal International. 2021;31(1):48- 57.

2. Hameed AT, Zaidan DH, Dawd SM. The Phytochemical Constituent Of Capparis Spinosa L . And Phenolic Activity On Pathogenic Bacteria And Blood Parameters. Systematic Reviews in Pharmacy. 2021;12(1):1193- 8.

3. Kumari M. In vitro evaluation of antimicrobial activity of roots extracts of capparis spinosa l. and important medicinal plant. Indian Journal of Scientific Research. 2020;(2010).

4. Gaber A, Al-saudi THA, Muraih JK. Extracted chemical compounds from Capparis spinosa leaves and their antibacterial activity on pathogenic bacteria . Journal of Pharmaceutical Sciences and Research. 2019;11(2):603- 8.

5. Mickymaray S, Saleh M, Aboody A. medicina In Vitro Antioxidant and Bactericidal E ffi cacy of 15 Common Spices : Novel Therapeutics for Urinary Tract Infections ? 2019;

6. Fadlelmula AA, Alomari AALI. Phytochemical Study and Antimicrobial Activity of Two Medicinal plants from Al-Baha region of Saudi Arabia. Oriental journal of chemistry. 2019;35:1782- 8.

7. Ennacerie Fatima-Zahra RFF, Moukrad N, Ed-Dra A. Antibacterial synergistic effect of extracts of the organs of capparis spinosa and in combination with antibiotics. International journal of advanced research. 2017;5(9):1238- 47.

8. Ebrahimi K, Shiravand S, Mahmoudvand H. Biosynthesis of copper nanoparticles using aqueous extract of Capparis spinosa fruit and investigation of its antibacterial activity. Marmara Pharmaceutical Journal. 2017;21(4):866- 71.

9. Gull T, Sultana B, Bhatti IA, Jamil A. Antibacterial Potential of Capparis spinosa and Capparis decidua Extracts. International Jo urnal of agriculture & Biology. 2015;727- 33.

10. Sherif MM, El-Shiekh HH, Elaasser MM, Elbadry M. In vitro evaluation of antimicrobial and cytotoxic effects of Caper (Capparis spinosa). Journal of Applied Sciences Research. 2013;(January).

11. Benzidane N, Aichour R, Guettaf S, Laadel N, Khennouf S. Chemical investigation, the antibacterial and antifungal activity of different parts of Capparis spinosa extracts. Journal of Drug Delivery and Therapeutics. 2020;10(5):118- 25.

12. Abou-Zeid HM, Bidak LM, Goha YM. Phytochemical screening and antimicrobial activities of some wild medicinal plants of the western mediterranean coastal region, egypt. International journal of pharmaceutical sciences and research. 2014;5(7):3072- 80.

13. Saeidi S, Javadian E, Javadian F. Anti-microbial and Anti-biofilm activity of leaf fruit and stem Capparis spinose extract against Acinetobacter baumannii . 2019;30(3):501- 6.

14. Ebrahimi K, Madani M, Ashrafi B, Shiravand S, Sepahvand A. Antifungal Properties of Silver Nanoparticles Synthe- sized From. Research In Molecular Medicine. 2019;98(916):43- 50.

15. Assadi S, Shafiee SM, Erfani M, Akmali M. Antioxidative and antidiabetic effects of Capparis spinosa fruit extract on high-fat diet and low-dose streptozotocin-induced type 2 diabetic rats. Biomedicine and Pharmacotherapy. 2021;138(March):111391.

16. Khojasteh M, Ghani A, Ghani E. In vitro effects of Capparis spinosa L . extract on human sperm function , DNA fragmentation , and oxidative stress. Journal of Ethnopharmacology. 2021;269(March 2020):113702.

17. Saleem H, Khurshid U, Sarfraz M, Ahmad I, Alamri A, Anwar S, et al. Investigation into the biological properties, secondary metabolites composition, and toxicity of aerial and root parts of Capparis spinosa L.: An important medicinal food plant. Food and Chemical Toxicology. 1 sept 2021;155:112404.

18. Ghafoor K, Juhaimi F Al, Özcan MM, Uslu N, Babiker EE, Ahmed IAM. Bioactive properties and phenolic compounds in bud, sprout, and fruit of Capparis spp. plants. Journal of Food Processing and Preservation. 1 mars 2020;44(3):e14357.

19. Yahia Y, Benabderrahim MA, Tlili N, Hannachi H, Ayadi L, Elfalleh W. Comparison of Three Extraction Protocols for the Characterization of Caper ( Capparis spinosa L .) Leaf Extracts : Evaluation of Phenolic Acids and Flavonoids by Liquid Chromatography – Electrospray Ionization – Tandem Mass Spectrometry ( LC – ESI – MS ) . Analytical Letters. 2020;0(0):1- 12.

20. Elshibani F, Alamami A, Alshalmani S, Naili EA El. alpha-amylase inhibitory activities of Capparis spinosa L Estimation of phenolic content , flavonoid content , antioxidant properties and alpha-amylase inhibitory activities of Capparis spinosa L . Journal of pharmacognosy and phytochemistry. 2020;(January).

21. Hematian A, Nouri M, Dolatabad SS. Kashk with caper ( Capparis spinosa L . ) extract : quality during storage. Foods and Raw Materials. 2020;8(2):402- 10.

22. Safarzaei A, Sarhadi H, Haddad Khodaparast MH, Shahdadi F, Dashipour AR. Optimization of Aqueous and Alcoholic Extraction of Phenolic and Antioxidant Compounds From Caper (Capparis Spinosa L.) Roots Assisted by UltrasoundWaves. Zahedan Journal of Research in Medical Sciences. 22:2383- 894.

23. Grimalt M, Legua P, Hernández F, Amorós A, Almansa MS. Antioxidant Activity and Bioactive Compounds Contents in Different Stages of Flower Bud Development from Three Spanish Caper ( Capparis spinosa ) Cultivars. The Horticulture Journal. 2019;88(3):410- 9.

24. Fadlelmula AA, Alomari AA. Antioxidant Activity and Total Phenolic Contents of Dodonaea viscose and Capparis spinosa from Jebal Shuda in Albaha Area of Saudi Arabia. Asian Journal of Chemistry. 2019;31(January):445- 8.

25. Sonmezdag AS. Characterization of Aroma-Active Compounds , Phenolics , and Antioxidant Properties in Fresh and Fermented Capers ( Capparis spinosa ) by GC-MS-Olfactometry and LC-DAD-ESI-MS / MS. Journal of Food Science. 2019;84:2449- 57.

26. El amri N, Errachidi F, Bour A, Chabir R. Characterization of Moroccan raw and processed caper berries. Materials Today: Proceedings. 1 janv 2019;13:841-9.

27. Mollica A, Stefanucci A, Macedonio G, Locatelli M, Luisi G, Novellino E, et al. Chemical composition and biological activity of Capparis spinosa L . from Lipari Island. South African Journal of Botany. 2018;

28. El-shahaby OA, El-zayat MM, El-fattah GA, El-hefny MM. Evaluation of the biological activity of Capparis spinosa var . aegyptiaca essential oils and fatty constituents as Anticipated Antioxidant and Antimicrobial Agents. Progress in Chemical and Biochemical Research. 2019;2(4):211-21.

29. Rajhi I, Dhia MT Ben, Abderrabba M, Ayadi S. Phytochemical screening , in vitro antioxidant and antibacterial activities of methanolic extracts of Capparis Spionsa L . different parts from Tunisia. Journal of Materials and Environmental Sciences. 2019;2508(3):234-43.

30. Kalantari H, Foruozandeh H, Khodayar MJ, Siahpoosh A, Saki N, Kheradmand P. Antioxidant and hepatoprotective effects of Capparis spinosa L. fractions and Quercetin on tert-butyl hydroperoxide- induced acute liver damage in mice. Journal of Traditional and Complementary Medicine. 2018;8(1):120-7.

31. Ennacerie F z, Filali FR, Moukrad N, Bouidra M, Bentayeb A. Evaluation of the Antioxidant Activity and the Cytotoxicity of Extracts of Capparis spinosa. International Journal of Pharmaceutical Sciences and Drug Research. 2018;10(2):57-64.

32. Jiménez-López J, Ruiz-Medina A, Ortega-Barrales P, Llorent-Martínez EJ. Phytochemical profile and antioxidant activity of caper berries (Capparis spinosa L.): Evaluation of the influence of the fermentation process. Food Chemistry. 1 juin 2018;250:54-9.

33. Eltawaty S, Almagboul AZ, Mohammad AEH, Bufarwa SM. The potential antioxidant and hepatotoxicity of methanolic extract of leaves of libyan capparis spinosa subsp orientalis (duh.) jafri in rats. World Journal of Pharmaceutical Research. 2018;(October).

34. El-waseif M, Saed B. Using Egyptian Caper Seeds Oil ( Capparis spinosa L ) as a Natural Antioxidant to Improving Oxidative Stability of Frying Oils Using Egyptian Caper Seeds Oil ( Capparis spinosa L ) as a Natural Antioxidant. World Journal of Dairy & Food Sciences. 2018;(January).

35. Tlili N, Feriani A, Saadoui E, Nasri N, Khaldi A. Capparis spinosa leaves extract: Source of bioantioxidants with nephroprotective and hepatoprotective effects. Biomedicine and Pharmacotherapy. 2017;87:171-9.

36. Yarizade A, Niazi A, Kumleh HH. Investigation of Antiglycation and Antioxidant Potential of Some Antidiabetic Medicinal Plants. Journal of pharmaceutical sciences and research. 2017;2019(January 2018).

37. Mazarei F, Jooyandeh H, Noshad M, Hojjati M. Polysaccharide of caper (Capparis spinosa L.) Leaf: Extraction optimization, antioxidant potential and antimicrobial activity. International Journal of Biological Macromolecules. 1 févr 2017;95:224-31.

38. Dibas JI, Yaghi BM, Mansi IA, Mhaidat NM, Al-Abrouni KF. Biological and Chemical Sciences Screening for Cytotoxic and Antioxidant Activity of Selected Wild Plants at Shafa Badran, Amman, Jordan. Research Journal of Pharmaceutical. 2017;8(489):489-97.

39. Aichi-Yousfi H, Meddeb E, Rouissi W, Hamrouni, L, Rouz S, Rejeb MN, et al. Phenolic composition and antioxidant activity of aqueous and ethanolic leaf extracts of six Tunisian species of genus Capparis – Capparaceae. Industrial Crops and Products,. 92:218-26.

40. Mansour RB, Jilani IBH, Bouaziz M, Gargouri B, Elloumi N, Attia H, et al. Phenolic contents and antioxidant activity of ethanolic extract of Capparis spinosa. Cytotechnology. 2016;68(1):135-42.

41. Al-janabi NMS. Assay plant as natural antioxidant of capparis spinosa root bark. International Journal of Current Research In Chemistry and Pharmaceutical Sciences. 2015;2:62-8.

42. Tlili N, Mejri H, Anouer F, Saadaoui E. Phenolic profile and antioxidant activity of Capparis spinosa seeds harvested from different wild habitats. Industrial Crops & Products. 2015;76:930-5.

43. Aliyazicioglu R, Eyupoglu OE, Sahin H, Yildiz O, Baltas N. Phenolic components , antioxidant activity , and mineral analysis of Capparis spinosa L. African Journal of Biotechnology. 2013;12(47):6643-9.