DETERMINATION OF A LINK BETWEEN THE TAXONOMIC RELATIONSHIP OF CANADIAN MEDICINAL PLANTS AND THE EXHIBITED ANTIBIOTIC ACTIVITY OF THEIR CRUDE EXTRACTS

by

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ABSTRACT

Chemotaxonomy is effective in determining the expected chemical compounds found in extracts from different organisms. However, this is time-consuming and costly, as it is based on purified fractions of a chemical extract. Utilizing biological activity data of extracts and relating it to the taxonomic relationship of plants may be a more effective approach. The aim of this study was to determine if a link exists between the taxonomic relationship of plants and the exhibited antibiotic activity of their extracts. The antibiotic activity of methanolic extracts of 90 plants were evaluated against eight microorganisms. Bioactivity profiles were created and analyzed, using two separate methods. It was found that the lowest taxonomic level that correlated with the bioactivity profiles of the extracts was family.

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STATEMENT OF RESEARCH CONTRIBUTION

From 2010 to 2018, members of the Natural Products Research Group (NPRG), University of New Brunswick, Saint John, collected and extracted 90 Canadian medicinal plants, as well as tested the crude methanolic extracts' antibiotic activity against four test pathogens, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Candida albicans*, and *Escherichia coli*. Certain plant extracts had been tested against *Enteroccous faecium*, *Mycobacterium smegmatis* and *Mycobacterium tuberculosis.* The number of extracts tested varied for each organism. This data was made available to me in September 2018. I performed two hundred and twenty-nine bioassays using 90 Canadian medicinal plant extracts against *Enterococcus faecium*, *Saccharomyces cerevisiae*, *Mycobacterium smegmatis*, and *Mycobacterium tuberculosis* were performed, thorugh to the end of January 2019. Two different methods werte used to compile bioactivity profiles of the antibiotic activity exhibited by the 90 Canadian medicinal plant extracts giving a total of one hundred and eighty bioactivity profiles.

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List of Abbreviations and Symbols

ACS	American Chemical Society
ATCC	American type culture collection
AU	approximately unbiased
BP	bootstrap probability
ΔOD	change in optical density
DMSO	dimethyl sulfoxide
MDS	multidimensional scaling
MGIT	mycobacteria growth indicator tube
MRA	microplate resazurin assay
M1	method 1
M2	method 2
NPRG	Natural Products Research Group

1. Introduction

Natural products are chemical compounds produced by living organisms through their primary and/or secondary metabolisms.[1, 2] These compounds may exhibit biological activity, which means the chemical compounds can alter the chemical or physiological function of cells, tissues, organs or organisms.[1, 3, 4] An example of biologically active chemical is growth inhibition of the target cells.[1, 3, 4] Natural products have been isolated from a variety of sources: algae, microorganisms (endophytic fungi, bacteria, fungi, etc.), animals as well as plants.[3, 5] The growth inhibition caused by natural products is important in terms of drug discovery and agricultural applications because the biologically active natural products can be used to develop new antibiotic drugs or chemicals used to protect crops, among other uses.[6, 7] Historically, medicinal plants have been found to be prolific sources of natural products.[8, 9] This can be linked to the traditional use of these plants for their "medicinal properties" as utilized over time by many different cultures and groups.[10, 11] This led to the investigation of medicinal plants as a source of natural products and they were found to produce many different chemical compounds via their primary and secondary metabolic pathways.[8, 9] For this reason, plant extracts from Canadian medicinal plants were obtained by the Natural Products Research Group (NPRG), at the University of New Brunswick, Saint John.

Chemotaxonomy is a method of classifying chemicals found within organisms where profiles are built to relate to the taxonomic relationships of organisms.[16, 17, 18, 19] Chemotaxonomy, which is also known as chemosystematics, has been used to study organisms within the same families, classes, and orders.[12, 13, 14] In general, a large number of chemotaxonomic studies have shown that organisms that are taxonomically-related have similar

chemical profiles.[12, 13, 14] The concept that taxonomically-related organisms will exhibit similar chemical profiles was first introduced by Greshoff in 1909.[20] This concept was applied to plants as well.[12, 13, 14, 21] By utilizing the differentiation aspect of the technique, chemotaxonomy can be used to increase the likelihood of identifying novel chemistry, by first identifying which classes, families or orders of plants need further investigating.

Bioactivity profiling is a method used in the prioritization of libraries of biologically active chemicals, such as a natural products library.[22, 23] Bioacitvity profiling can also be used to reduce redundancy in the discovery of bioactive chemicals.[22, 23] From a natural products discovery perspective, redundancy in the discovery of chemicals is problematic, since known chemicals are re-isolated repeatedly, wasting resources in the process.[9] Redundancy occurs because of the limited building blocks available in the environment and the limited number of biosynthetic pathways.[24, 25, 26] Redundancy is undesirable due to the lack of efficiency; hence, the development of prioritization techniques is used to address this problem and try to improve it.

In trying to increase the discovery of novel chemistry, with potential biological activity, both chemotaxonomy and bioactivity profiling have been effective. [16, 17, 18, 19, 22, 23] They have enabled the prioritization of extract libraries and in turn contributed to the reduction of redundancy in natural products discovery. However, there may be a link between these two methods, since the biological activities exhibited by plant extracts will be related to the chemicals within them. The combination of these two techniques could be applied in attempt to increase the likelihood of extracts being identified as unique within chemical libraries. Using the biological activity exhibited by Canadian medicinal plants within the NPRG plant library could be used to determine which plants should be added to the library.

Hence, the objective of this study was to determine if there is a link between the taxonomic relationship of Canadian medicinal plants and the exhibited antibiotic activity of their crude extracts.

2. Materials and methods

2.1 General experimental procedures

The Natural Products Research Group's (NPRG; University of New Brunsiwck, Saint John) plant extract library consists of 90 Canadian medicinal plant extracts (see Table 1).

Table 1. Collection information for the NPRG plant library, including the scientific name of the plant collected, plant code, coordinates of collection location

Plant code	Plant	Collection coordinates	Voucher specimen code
BOEX-001	*Symplocarpus foetidus*	N 45° 26.324' W 65° 55.027'	NBM VP-37484
BOEX-002	*Nuphar lutea*	N 45° 18.376' W 66° 04.617'	NBM VP-37483
BOEX-003	*Empetrum nigrum*	N 45° 11.932' W 66° 13.803'	NBM VP-37479
BOEX-004	*Geum macrophyllum*	N 47° 37.489' W 67° 54.760'	NBM VP- 37480
BOEX-005	*Moneses uniflora*	N 45° 53.222' W 64° 52.888'	NBM VP- 37097
BOEX-006	*Sarracenia purpurea*	N 45° 11.988' W 66° 13.814'	NBM VP-39665
BOEX-007	*Acorus calamus*	N 45° 32.597' W 65° 50.340'	NBM VP- 37476
BOEX-008	*Rubus idaeus*	N 45° 18.556' W 66° 05.266'	n/a[2]
BOEX-009	*Acer spicatum*	N 47° 17.4' W 67° 52.8'	n/a[2]
BOEX-010	*Actaea rubra*	N 47° 16.2' W 67° 43.8'	n/a[2]
BOEX-011	*Rumex* sp.	N 47° 28.523' W 67° 40.437'	n/a[2]
BOEX-012	*Orthilia secunda*	N 47° 17.445' W 67° 52.192	NBM VP-37097
BOEX-013	*Sambucus racemosa*	N 47° 17.445' W 67° 52.8'	n/a[2]
BOEX-014	*Prunus pensylvanica*	N 45° 21.215' W 67° 14.023'	n/a[2]
BOEX-015	*Prunus virginiana*	N 45° 21.215' W 67° 14.023'	NBM VP- 40535
BOEX-016	*Rubus pubescens*	N 45° 18.447' W 66° 05.015'	n/a[2]
BOEX-017	*Viburnum lantanoides*	N 47° 16.2' W 67° 43.8'	n/a[2]
BOEX-018	*Corylus cornuta*	Unknown[1]	n/a[2]
BOEX-019	*Populus tremuloides*	N 45° 18.5294' W 66° 5.2994	NBM VP- 37484
BOEX-020	*Alnus viridis*	N 45° 18.455' W 66° 04.932'	NBM VP-40099
BOEX-021	*Scutellaria lateriflora*	N 45° 18.447' W 66° 05.015'	n/a[2]
BOEX-022	*Ranunculus* sp.	Unknown[1]	n/a[2]
BOEX-023	*Sorbus decora*	N 45° 18.455' W 66° 04.932'	NBM VP- 0533
BOEX-024	*Juniperus communis*	N 45° 18.453' W 66° 04.915'	NBM VP-37482
BOEX-025	*Maianthemum canadense*	N 45° 18.457' W 66° 04.913'	n/a[2]
BOEX-026	*Sambucus racemosa var. pubens*	N 45° 18.988' W 66° 05.154'	n/a[2]
BOEX-027	*Polypodium virginianum*	N 45° 18.377' W 66° 05.567'	n/a[2]
BOEX-028	*Daphne mezereum*	N 45° 18.402' W 66° 05.706'	n/a[2]
BOEX-029	*Arisaema triphyllum*	N 45° 18.402' W 66° 05.706'	n/a[2]
BOEX-030	*Aralia nudiclaulis*	N 45° 18.406' W 66° 05.486'	NBM VP-37477
BOEX-031	*Pyrola elliptica*	Unknown[1]	n/a[2]
BOEX-032	*Anaphalis margaritacea*	N 45° 22.129' W 66° 15.801'	n/a[2]
BOEX-033	*Abies balsamea*	N 45° 18.348' W 66° 05.296'	NBM VP-40096
BOEX-034	*Acer pensylvanicum*	N 45° 18.441' W 66° 05.304'	n/a[2]
BOEX-035	*Alnus incana*	N 45° 18.438' W 66° 05.277'	NBM VP- 40098
BOEX-036	*Betula alleghaniensis*	N 45° 18.438' W 66° 05.277'	n/a[2]
BOEX-037	*Cornus canadensis*	N 45° 18.439' W 66° 05.301'	n/a[2]

[1] Data for the collection coordinates were not available for some plants.

[2] These plants did not have voucher specimens submitted to the New Brunswick Museum Herbarium.

(Table 1 continued)

Plant code	Plant	Collection coordinates	Voucher specimen code
BOEX-038	*Crataegus* sp.	N 45° 18.432' W 66° 05.288'	n/a[2]
BOEX-039	*Hypericum perforatum*	N 45° 18.439' W 66° 05.267'	NBM VP-37566
BOEX-040	*Picea glauca*	N 45° 18.348' W 66° 05.296'	NBM VP-40102
BOEX-041	*Solanum dulcamara*	N 45° 18.438' W 66° 05.277'	n/a[2]
BOEX-042	*Spiraea alba*	N 45° 18.438' W 66° 05.277'	n/a[2]
BOEX-043	*Typha latifolia*	N 45° 18.439' W 66° 05.267'	n/a[2]
BOEX-044	*Vaccinium angustifolium*	N 45° 18.471' W 66° 05.317'	n/a[2]
BOEX-045	*Daucus carota*	N 45° 15.948' W 66° 12.393'	n/a[2]
BOEX-046	*Achillea millefolium*	N 45° 22.210' W 66° 15.714'	n/a[2]
BOEX-047	*Apocynum cannabinum*	N 45° 20.391' W 66° 13.158'	n/a[2]
BOEX-048	*Arisaema atrorubens*	N 45° 20.368' W 66° 13.132'	n/a[2]
BOEX-049	*Cornus sericea*	N 45° 22.210' W 66° 15.714'	n/a[2]
BOEX-050	*Iris versicolor*	N 45° 18.376' W 66° 04.617'	n/a[2]
BOEX-051	*Nymphaea odorata*	N 45° 18.376' W 66° 04.617'	n/a[2]
BOEX-052	*Pinus strobus*	N 45° 22.210' W 66° 15.714'	NBM VP-40534
BOEX-053	*Populus grandidentata*	N 45° 22.210' W 66° 15.714'	NBM VP-40103
BOEX-054	*Impatiens capensis*	N 45° 20.368' W 66° 13.132'	n/a[2]
BOEX-055	*Betula papyrifera*	N 45° 18.348' W 66° 05.296'	n/a[2]
BOEX-056	*Coptis trifolia*	N 45° 18.603' W 66° 05.104'	n/a[2]
BOEX-057	*Kalmia angustifalia*	N 45° 18.603' W 66° 05.104'	n/a[2]
BOEX-058	*Pteridium aquilinum*	N 45° 18.556' W 66° 05.266'	n/a[2]
BOEX-059	*Rumex crispus*	N 45° 18.694' W 66° 05.289'	n/a[2]
BOEX-060	*Scirpus microcarpus*	N 45° 18.556' W 66° 05.266'	n/a[2]
BOEX-061	*Tanacetum vulgare*	N 45° 18.394' W 66° 05.287'	n/a[2]
BOEX-062	*Cypripedium acaule*	N 45° 22.213' W 66° 15.719'	n/a[2]
BOEX-063	*Diervilla lonicera*	N 45° 22.213' W 66° 15.719'	n/a[2]
BOEX-064	*Gaultheria hispidula*	N 45° 21.923' W 66° 15.845'	n/a[2]
BOEX-065	*Mitchella repens*	N 45° 21.923' W 66° 15.845'	n/a[2]
BOEX-066	*Quercus rubra*	N 45° 22.032' W 66° 15.778'	NBM VP- 40104
BOEX-067	*Gaultheria procumbens*	N 45° 21.883' W 66° 15.913'	n/a[2]
BOEX-068	*Nemopanthus mucronatus*	N 45° 21.896' W 66° 15.924'	n/a[2]
BOEX-069	*Rubus hispidus*	N 45° 21.909' W 66° 15.886'	n/a[2]
BOEX-070	*Spiraea tomentosa*	N 45° 22.215' W 66° 15.714'	n/a[2]
BOEX-071	*Monotropa uniflora*	N 45° 21.926' W66° 15.925'	n/a[2]
BOEX-072	*Acer saccharum*	N 46° 01.498' W 67° 33.255'	n/a[2]
BOEX-073	*Angelica atropurpurea*	N 45° 18.534' W 67° 01.093'	n/a[2]
BOEX-074	*Berberis vulgaris*	N 45° 21.167' W 67° 13.975'	n/a[2]
BOEX-075	*Chelone glabra*	N 45° 01.766' W 67° 32.597'	n/a[2]
BOEX-076	*Sium suave*	N 45° 18.534' W 66° 01.093'	n/a[2]
BOEX-077	*Taxus canadensis*	N 46° 01.575' W 67° 33.071'	n/a[2]
BOEX-078	*Tsuga canadensis*	N 46° 01.498' W 67° 33.255'	NBM VP-40108

[1] Data for the collection coordinates were not available for some plants.

[2] These plants did not have voucher specimens submitted to the New Brunswick Museum Herbarium.

(Table 1 continued)

Plant code	Plant	Collection coordinates	Voucher specimen code
BOEX-079	*Fragaria virginiana*	N 45° 21.167' W 67° 13.975'	n/a[2]
BOEX-080	*Larix laricina*	N 45° 21.207' W67° 14.013'	NBM VP- 40101
BOEX-081	*Tilia americana*	N 45° 21.353' W 67° 14.141'	n/a[2]
BOEX-082	*Verbascum thapsus*	N 45° 22.298' W 67° 15.351'	n/a[2]
BOEX-083	*Chamerion angustifolium*	Unknown[1]	n/a[2]
BOEX-084	*Linnaea borealis*	N 45° 18.406' W 66° 05.486'	n/a[2]
BOEX-085	*Lycopodium* sp.	Unknown[1]	n/a[2]
BOEX-086	*Clintonia borealis*	Unknown[1]	n/a[2]
BOEX-087	*Chimaphila umbellata*	Unknown[1]	n/a[2]
BOEX-088	*Epifagus virginiana*	Unknown[1]	n/a[2]
BOEX-089	*Heracleum maximum*	N 45° 30.786' W 65° 53.959'	NBM VP- 37481
BOEX-090	*Actaea pachypoda*	N 46° 04.40' W 66° 03.19'	n/a[2]

[1] Data for the collection coordinates were not available for some plants.
[2] These plants did not have voucher specimens submitted to the New Brunswick Museum Herbarium.

2.2 Antibiotic activity testing

The antibiotic activity of the crude plant extracts was tested using eight micro-organisms: *Staphylococcus aureus* (ATCC 29213), *Enterococcus faecium* (ATCC 35667), *Candida albicans* (ATCC 14053), *Saccharomyces cerevisiae* (ATCC 9763), *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 10145), *Mycobacterium smegmatis* (ATCC 700084), and *Mycobacterium tuberculosis* H37Ra (ATCC 25177). A microplate resazurin assay and an optical density based microbroth dilution assay were utilized.

2.2.1 Microplate resazurin assay (MRA)

Plant crude extracts dissolved in sterile DMSO were tested in a microplate resazurin assay (MRA) against *Mycobacterium smegmatis* (ATCC 700084) at a concentration of 100 µg/mL. Samples, positive controls (1.25 µg/mL ciprofloxacin, 100 µL MGIT growth medium in 4% DMSO, and 100 µL of *M. smegmatis*), and negative controls (100 µL MGIT growth medium

in 4% DMSO and 100 µL of *M. smegmatis*), were all tested in triplicate as described by O'Neill et al.[27]

The solutions of crude plant extracts (100 µg/mL in 2% DMSO) were also evaluated using *Mycobacterium tuberculosis* H37Ra (ATCC 25177) as described in O'Neill et al.[27]

2.2.2 Antimicrobial susceptibility assay

Plant extracts dissolved in sterile DMSO were screened for antimicrobial activity against *Staphylococcus aureus* (ATCC 29213), *Enterococcus faecium* (ATCC 35667), *Candida albicans* (ATCC 14053), *Saccharomyces cerevisiae* (ATCC 9763), *Escherichia coli* (ATCC 25922), and *Pseudomonas aeruginosa* (ATCC 10145) at a concentration of 100 µg/mL, using a microbroth dilution antibiotic susceptibility assay, as described in Zhu et al.[28] Optical density values were collected before and after a 24-hour incubation period at 37 °C with a Molecular Devices Emax microplate reader with a 600 nm filter. The change in optical density (ΔOD) was calculated by subtracting the initial optical density from the final optical density for each corresponding well. The percentage inhibition of microbial growth was then defined as: [1 − (mean test or positive control optical density/mean negative control optical density)] × 100.

2.3 Data processing

2.3.1 Creation of bioactivity profiles for plant extracts

The percentage inhibition values against the eight test microorganisms obtained for each plant extract were compiled and subsequently normalized in two different ways, thus creating two data sets. The first data set [referred to as method 1 (M1)] was created using the following steps: all negative percentage inhibition values were converted to zero, the maximum percentage

inhibition value for an extract against the eight test pathogens was identified, and all percentage inhibition values were divided by the maximum value exhibited by the extract, to create a concentration independent ratio of activities between 0 and 1. The second data set [referred to as method 2 (M2)] was created as follows: the maximum percentage inhibition value (defined as the largest absolute value) for an extract against the eight test pathogens was identified and all percentage inhibition values for each extract were divided by the maximum value of that extract, to create a concentration independent ratio of activities between -1 and 1. These two data sets were then annotated using three different levels of taxonomy: class, order and family. The different levels of annotation of the two datasets were then imported into RStudio.[29]

2.4 Statistical analysis

2.4.1 Hierarchical clustering and multidimensional scaling

Within the R software, a distance matrix of the bioactivity profiles was created using Euclidean distances. Ward's method was utilized to perform the agglomerative hierarchical clustering on this matrix. This was done via the dendextend package.[30] The result of these analyses created eight dendrograms. The statistical term "k", which represents the number of clusters of a dendrogram, was determined using the NbClust package.[31] This package calculates the optimal k value using 26 different methods, and then determines the "true" optimal value, by comparing the number of times a value was suggested.[32] The value that was suggested most often was deemed the optimal value.[32] This was determined for both datasets M1 and M2. Using the pvclust package[33], the p-values for each node of two dendrograms (one corresponding to M1 and M2, respectively), were calculated using multiscale bootstrapping resampling [known as the approximately unbiased (AU) value], as well as normal bootstrap resampling [known as the

bootstrap probability (BP) value].[34] Due to the unbiased nature of the AU value, it has been found to be a better approximation than the BP value.[34] A multidimensional scaling (MDS) analysis was also performed on these datasets, to produce eight MDS plots. This analysis was again done using the distance matrices that were previously built using the dendextend package.[30]

3. Results & Discussion

Once the antibiotic activity of each plant extract was established, the data was compiled to create bioactivity profiles using two different methods (see Figures 1 and 2). This was to see if removing or including the growth promotion values found in the bioactivity profiles would have an effect in the clustering within the different taxonomic levels of the plants. These profiles were analyzed using hierarchical clustering and the number of clusters, a variable known as "k", was identified. This variable is not the same as the k-means calculation sometimes done within certain methods of hierarchical clustering. The value of "k" is arbitrary, though there exist calculations to determine which value may be the best given the specific dataset being analyzed (refer to section 2.4.1 for details on the method used for this study). MDS plots were also created alongside the dendrograms from the hierarchical clustering analysis.

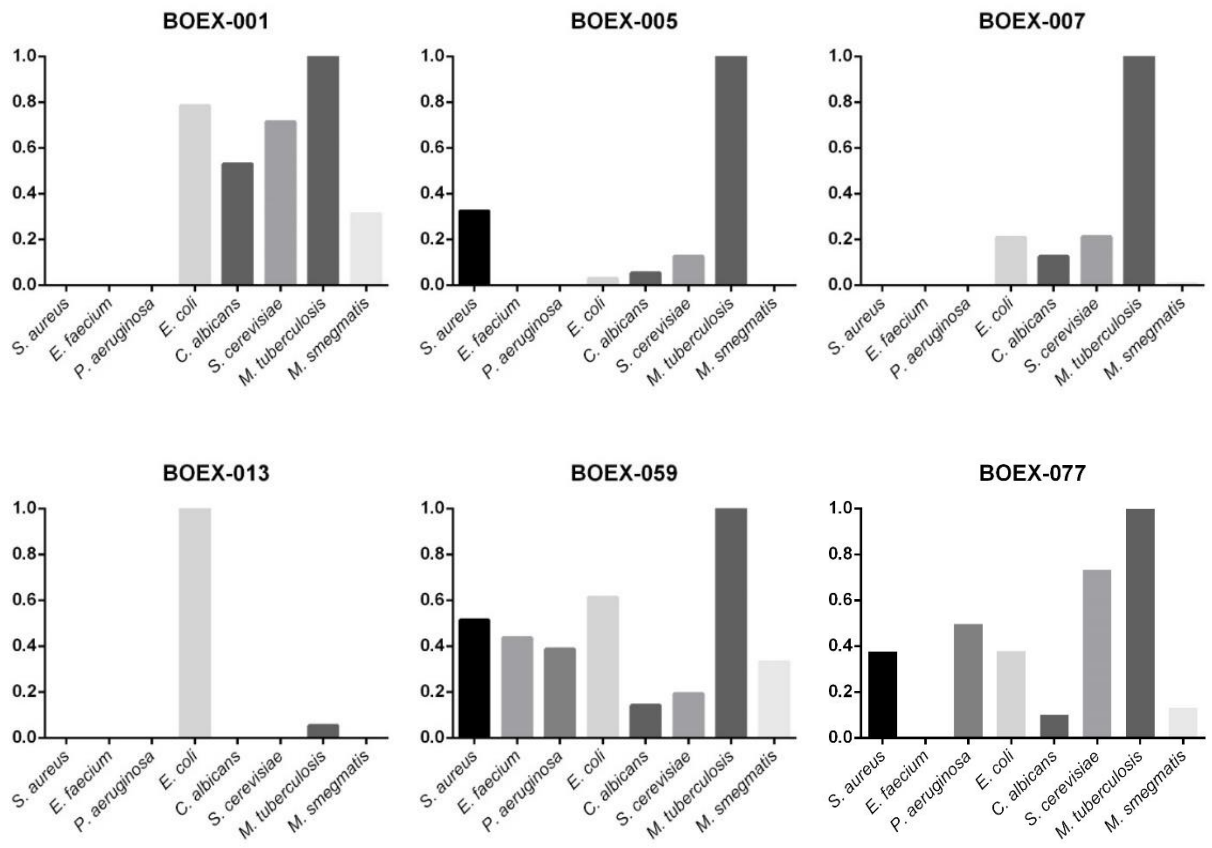

Figure 1. Examples of biological activity profiles which resulted from M1.

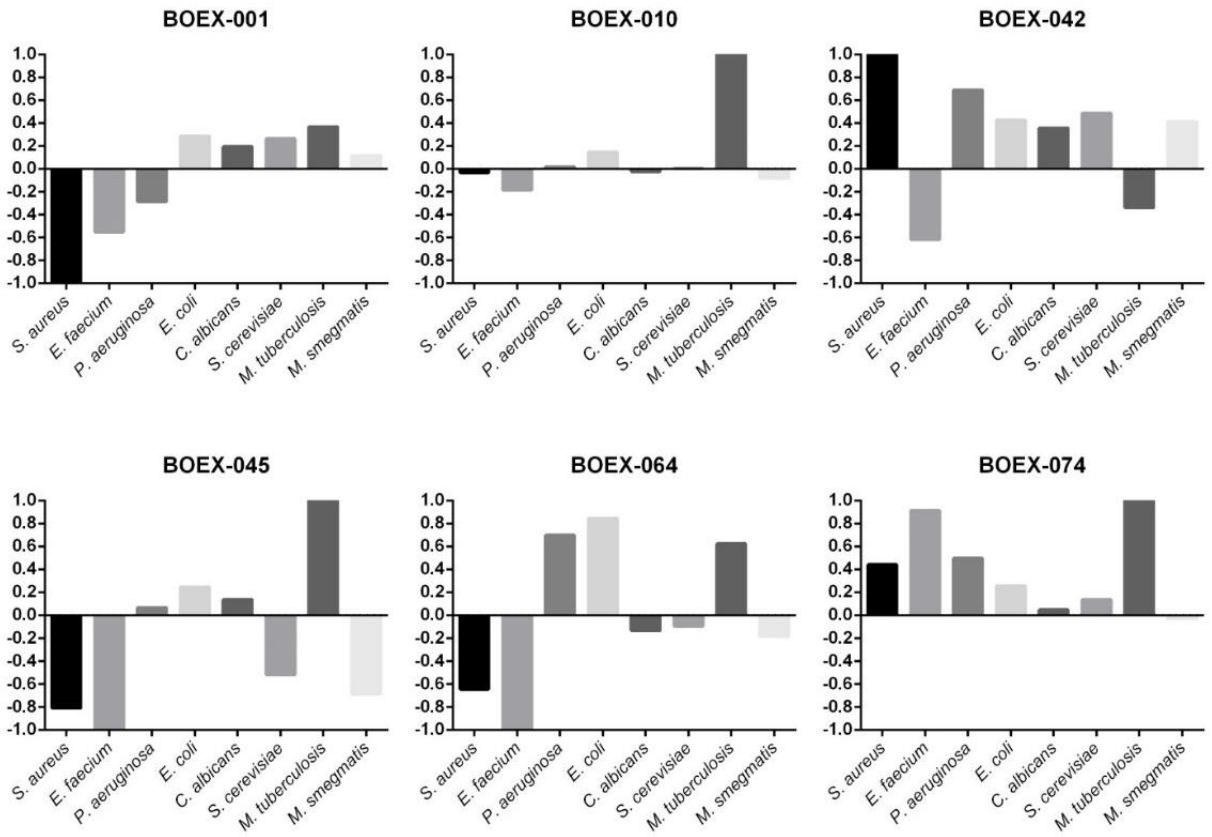

Figure 2. Examples of biological activity profiles which resulted from M2.

The bioactivity profiles yielded different results, as the incorporation of the growth promotion values affected the ratios exhibited in the M2 bioactivity profiles. The effectiveness of these two methods cannot be established on their own, and the use of the cluster patterns would be a more effective way of determining which of the two methods should be preferred. After the analysis of the bioactivity profiles within the context of hierarchical clustering, the clusters that were formed (given the calculated k value) were open to doubt. As a good example of the different patterns that will be discussed shortly, the following samples: BOEX-025, BOEX-027, BOEX-029, BOEX-031, BOEX-048, BOEX-071, BOEX-085, and BOEX-086 will be used (see Figure 3). As can be seen on the left-hand side in Figure 1, the shared antibiotic activity observed

is that of *S. cerevisiae*, where every selected plant's highest inhibition value is associated with its growth inhibition of *S. cerevisiae*. When looking at the right-hand side of Figure 3, this growth inhibition against *S. cerevisiae* is impacted by the growth promotion of *S. aureus*. In some cases, these values are equal and there is no change in the observed growth inhibition value of *S. cerevisiae*, while in other cases, the growth promotion value is double that of the growth inhibition, which caused the inhibition value to be halved in the bioactivity profile. This meant that, for the samples where the *S. cerevisiae* activity was halved, a different microorganism (in this case *S. aureus*) was now driving the clustering of the entire profile, which in turn meant that these samples would be clustering in a different section of the MDS plots and/or with different samples.

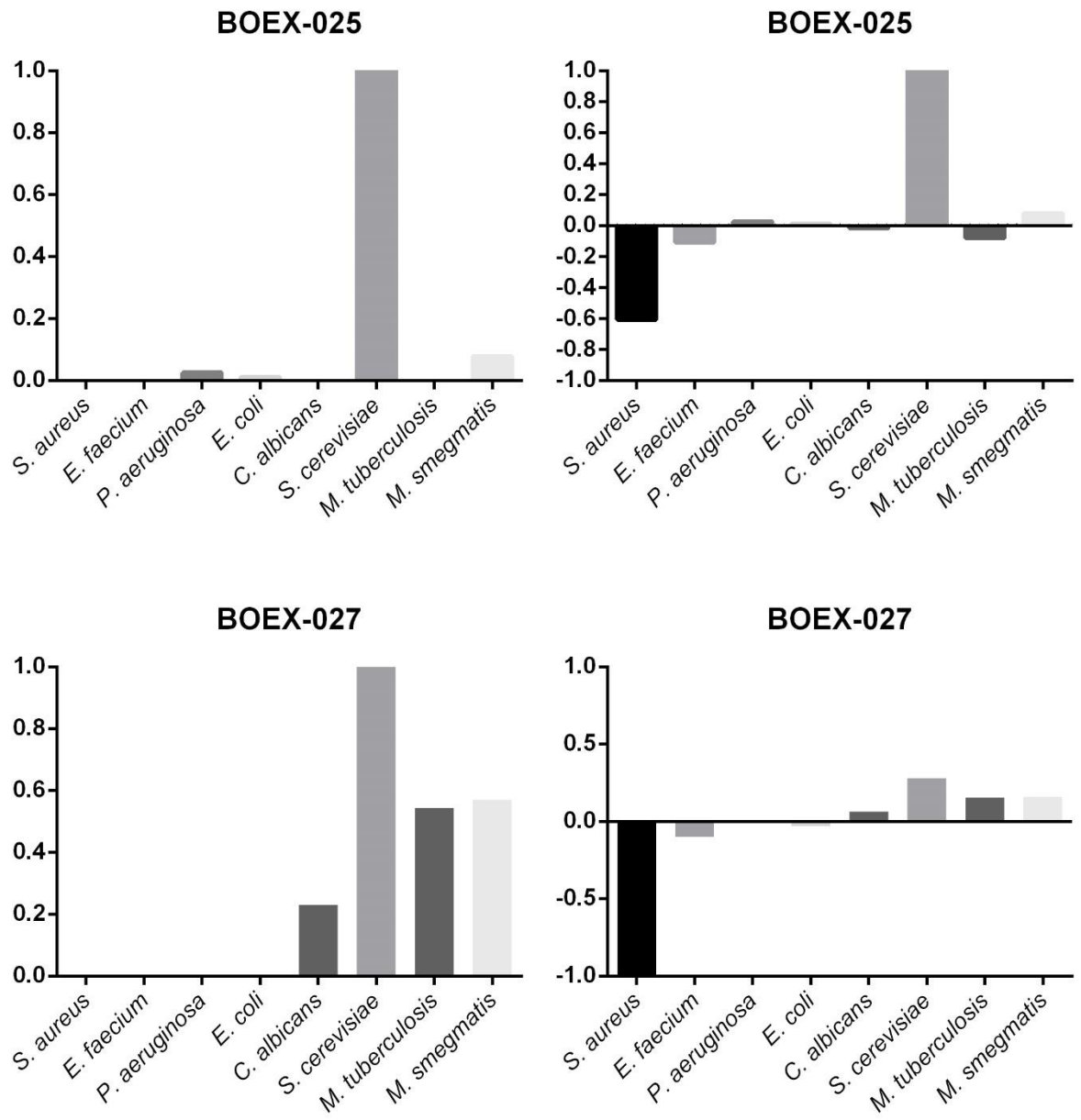

Figure 3. Select bioactivity profiles of antibiotic activity Canadian medicinal plants with method 1 on the left and method 2 on the right.

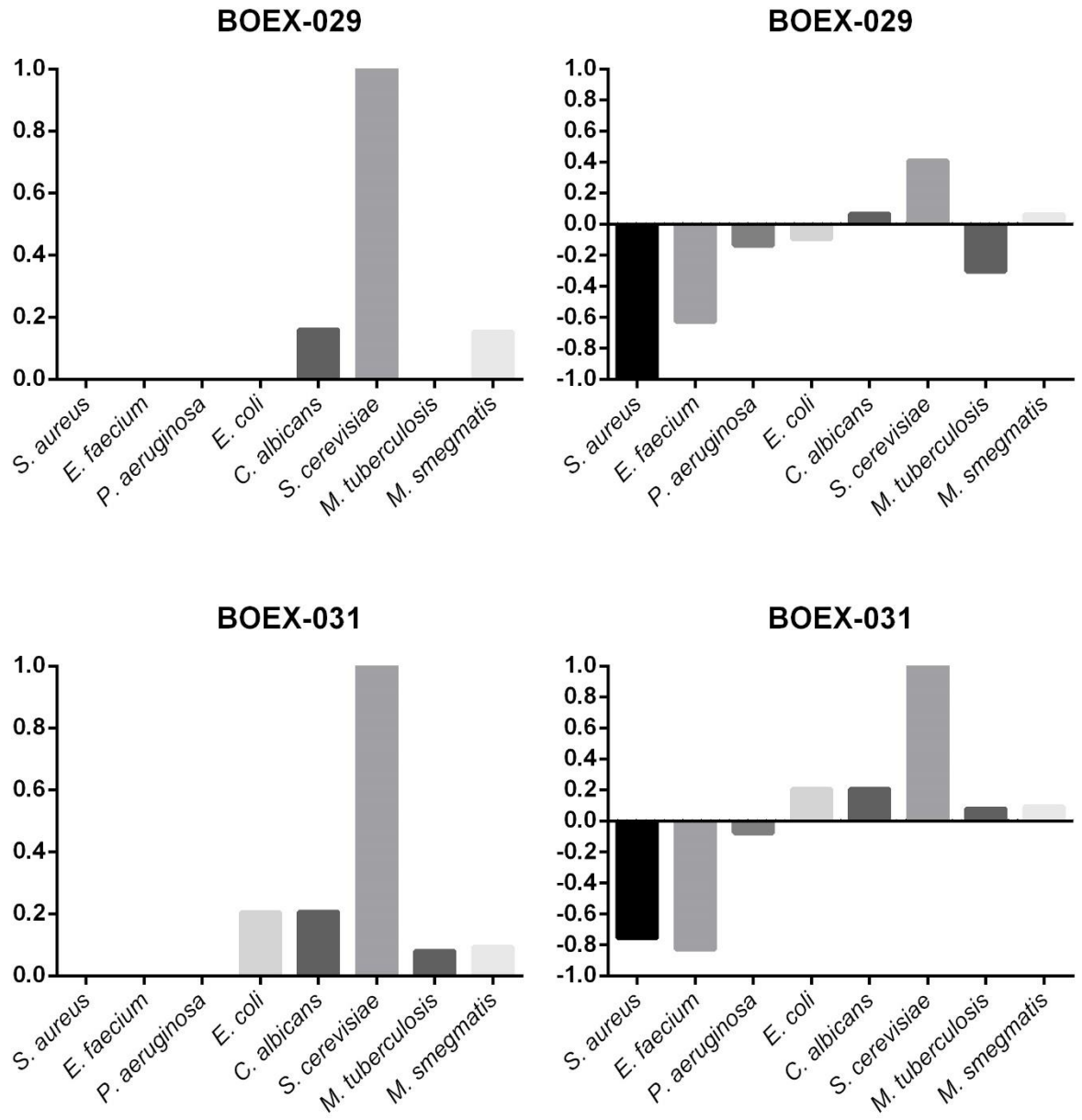

Figure 3. Select bioactivity profiles of antibiotic activity Canadian medicinal plants with method 1 on the left and method 2 on the right, continued.

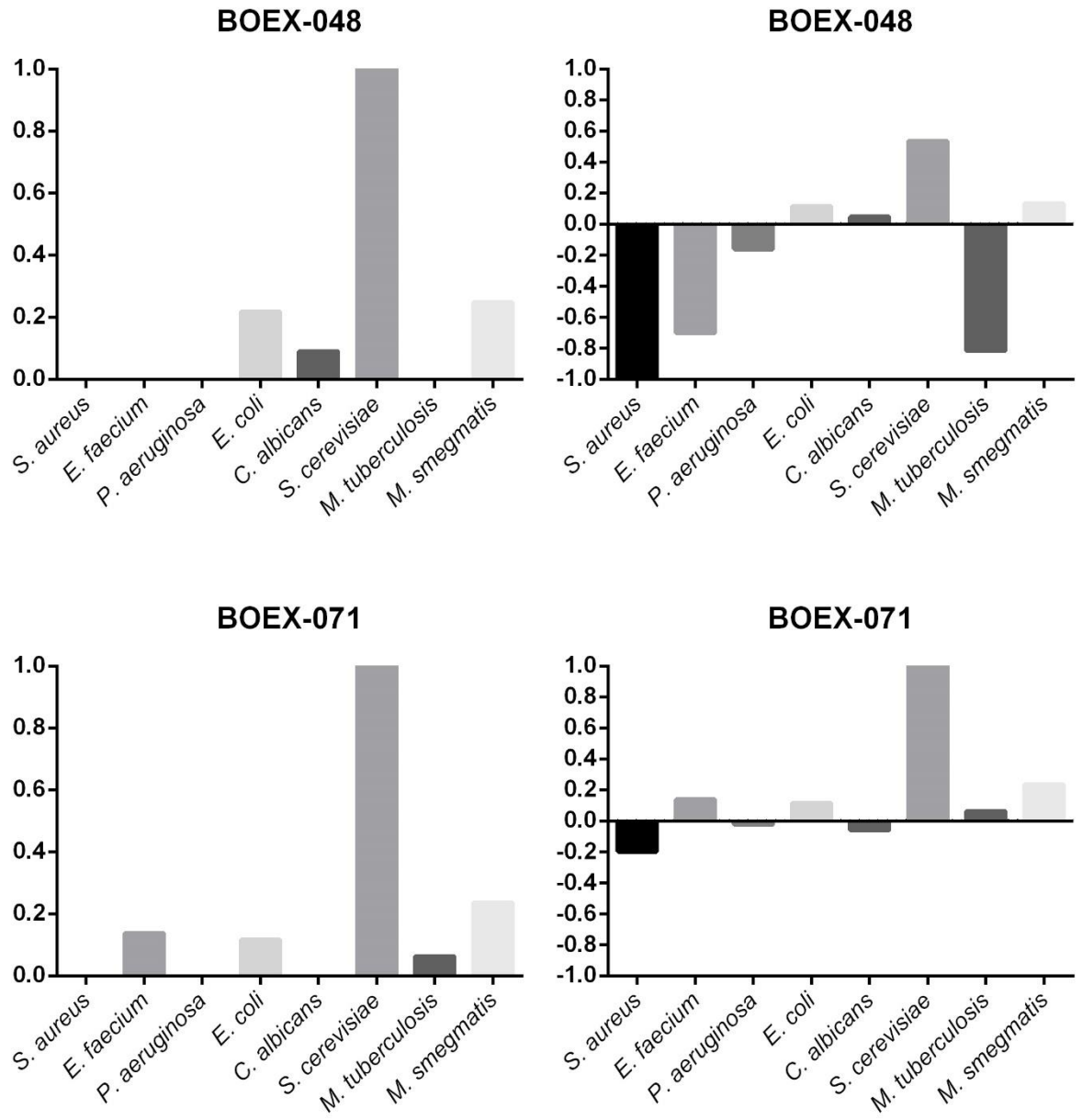

Figure 3. Select bioactivity profiles of antibiotic activity Canadian medicinal plants with method 1 on the left and method 2 on the right, continued.

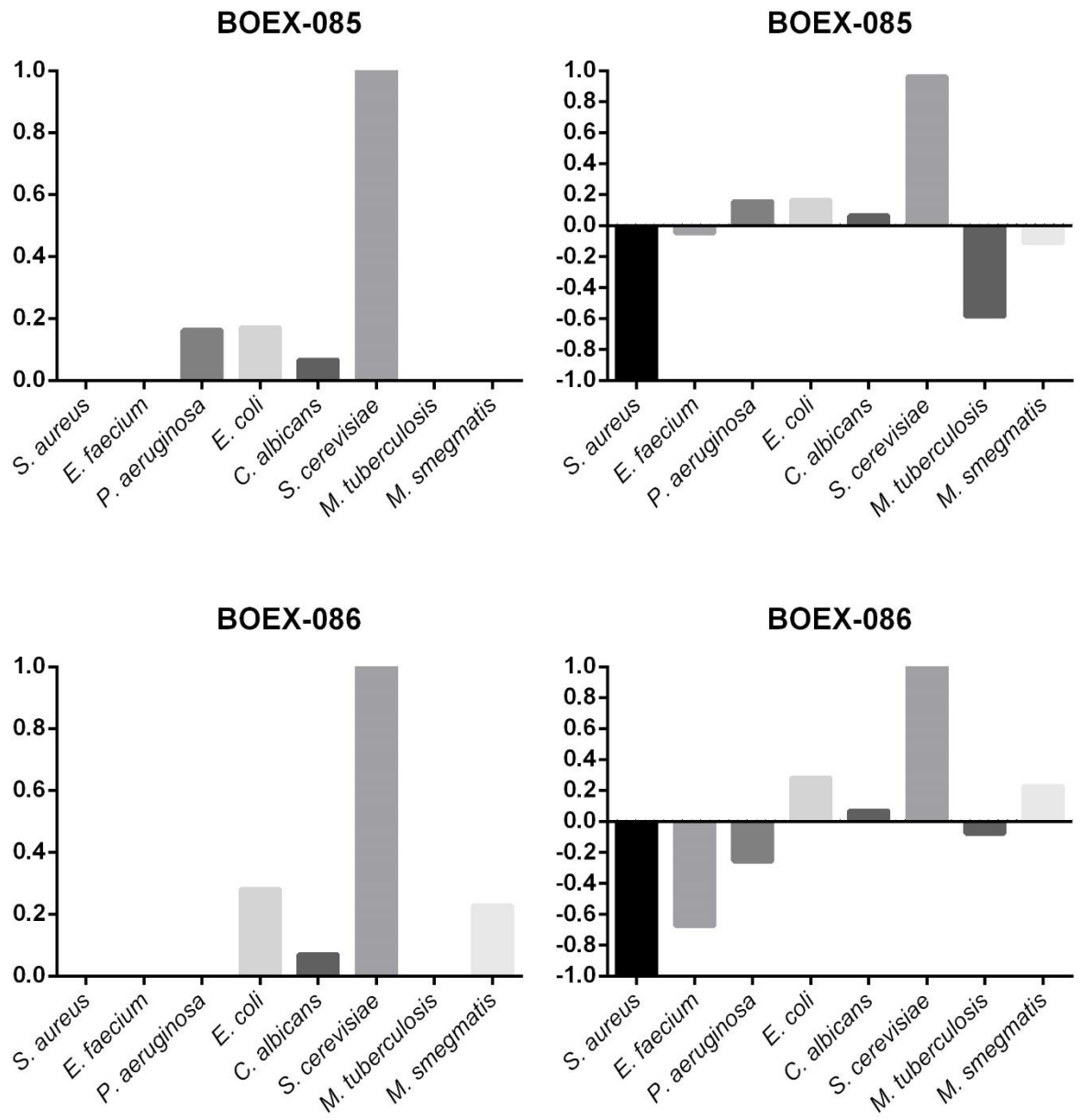

Figure 3. Select bioactivity profiles of antibiotic activity Canadian medicinal plants with method 1 on the left and method 2 on the right, continued.

When observing the cluster pattern in the output dendrogram using method 1 (Figure 4), all extracts of interest are clustered together. However, 21 other extracts are also included in this cluster. When observing the differences using method 2 (see Figure 5), the cluster includes exclusively the extracts of interest. The differences between the two methods led to the creation of MDS plots so that a comparison could be made to the already existing dendrograms.

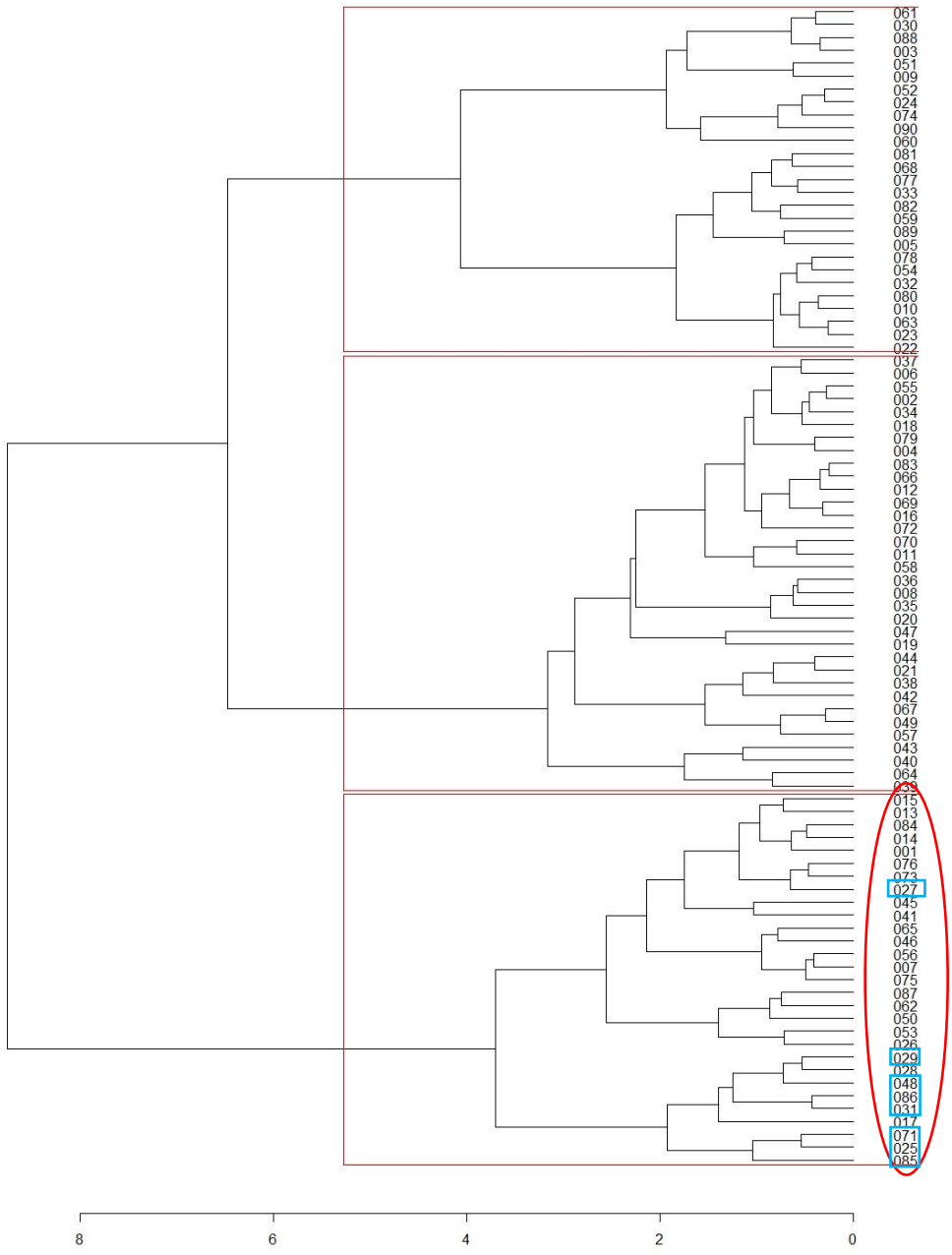

Figure 4. Hierarchical cluster analysis (Euclidean distance, Ward's method) of bioactivity profiles of Canadian medicinal plant extracts using the M1 dataset, where k was found to be seven, and the red circle is the cluster of interest, with the bioactivity profiles of interest in blue squares.

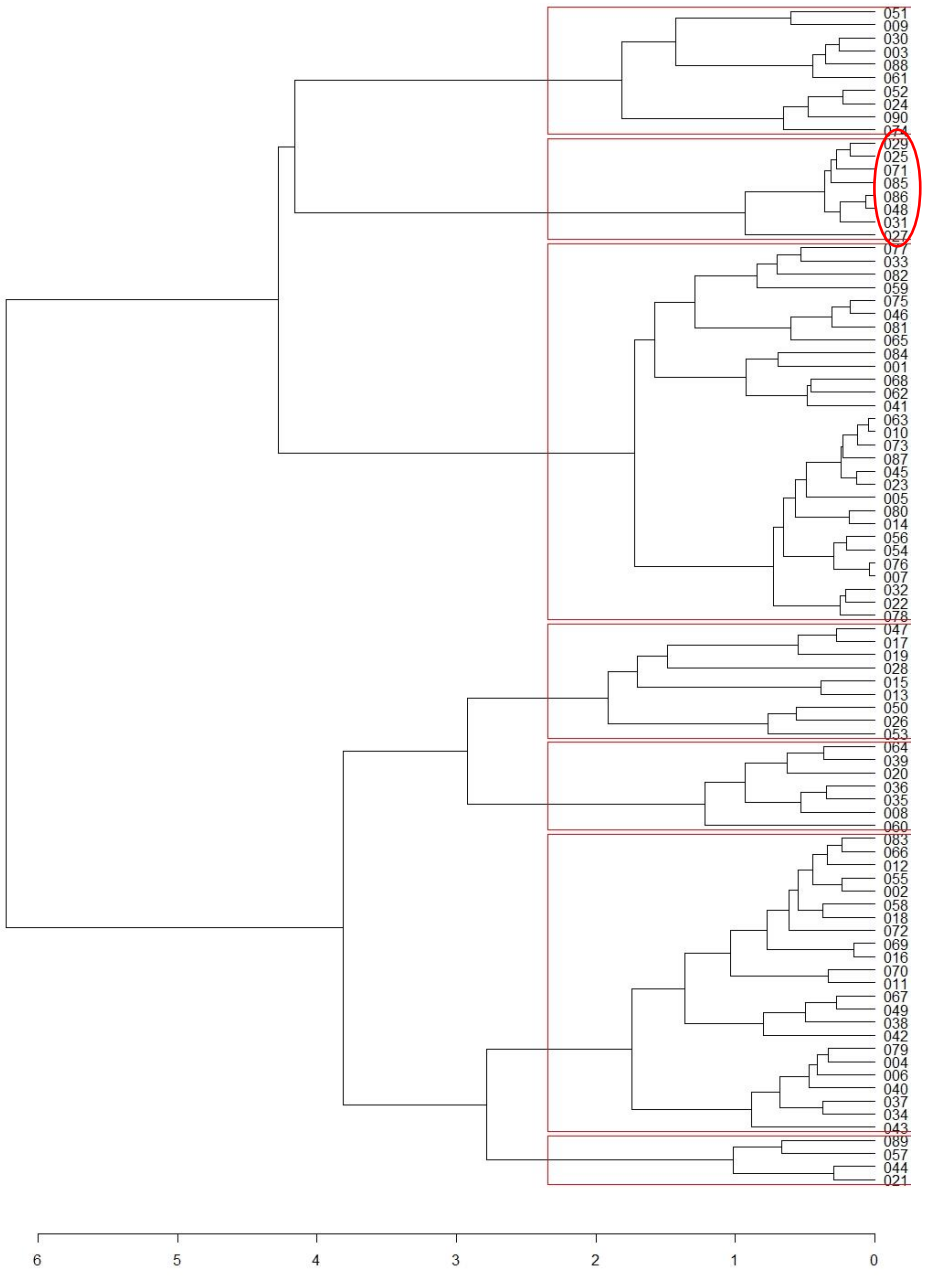

Figure 5. Hierarchical cluster analysis (Euclidean distance, Ward's method) of bioactivity profiles of Canadian medicinal plant extracts using the M2 dataset, where k was found to be seven, and the red circle is the cluster of interest.

Within these MDS plots, a lack of clustering is observed. As seen in Figure 6, only four of the eight extracts of interest are clustering together within the plot, BOEX-025 and BOEX-027 are clustering with a completely different group, and BOEX-048 as well as BOEX-071 are not clustering with any other plant extracts. This indicated that the dendrograms were not effective in determining which plants were clustering together. In Figure 7, there was also a difference in the clustering pattern as BOEX-027 was not clustering with the seven other extracts of interest; again, confirming the ineffectiveness of the dendrograms to exhibit the cluster patterns of the plants within the library. Once the effectiveness of the MDS plots was observed, there can be a focus on which method of creating bioactivity profiles is more effective. When comparing Figures 6 and 7, there is less clustering observed in the MDS plot based on bioactivity profiles built with both growth inhibition and growth promotion values. This indicates that M2 is more effective, as it can better distinguish the activity between different plant extracts, making it the preferred method. When looking at the clusters where the data was annotated by family, class or order, there is no apparent clustering pattern related to the relationship between the plants. Essentially, the cluster patterns are only based on the exhibited growth promotion and inhibition values. This is especially true in the case of the plants' class, as extracts in the same classes are clustering together and separately within the same MDS plot. This occurs when using both M1 and M2, though it is more prominent in M2. For the clustering patterns of the families and orders of the 90 Canadian medicinal plants, most families listed only have one plant within their category. This is because plants had previously been selected by other members of the NPRG, and the aim of this study was to apply a combined chemotaxonomic and bioactivity profiling method to the existing plant database. Since most of the data for these two taxonomic levels were affected, it may be beneficial to re-apply a similar analysis once the NPRG plant library has been

expanded, and this issue is less prevalent. It is possible that this issue is masking a pattern between the taxonomic relationship of plants and their antibiotic activity, however, no link is observed at this time.

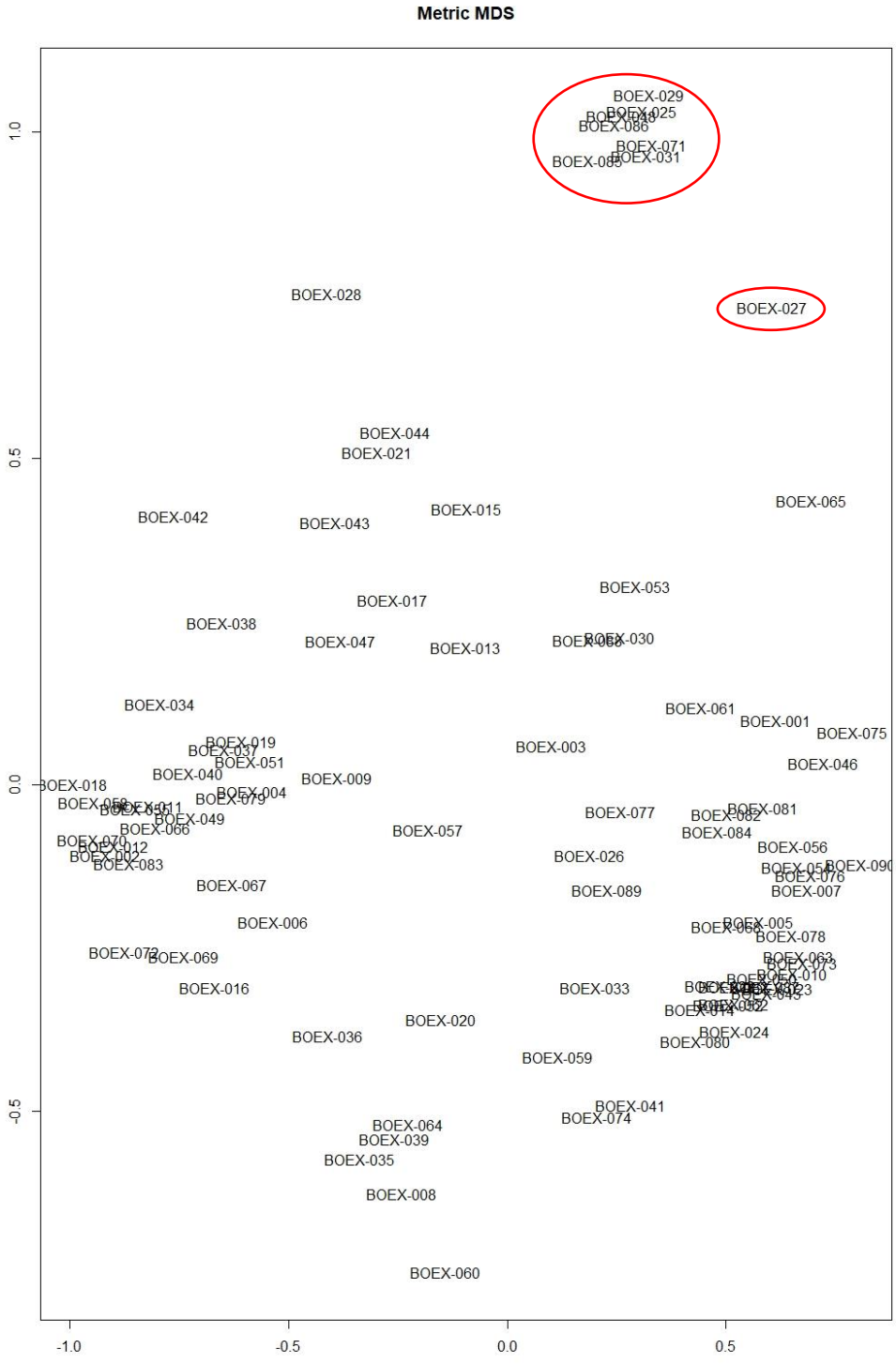

Figure 6. Output from MDS analysis of bioactivity profiles obtained from Canadian medicinal plant extracts from M1 dataset, with the extracts of interest circled in red.

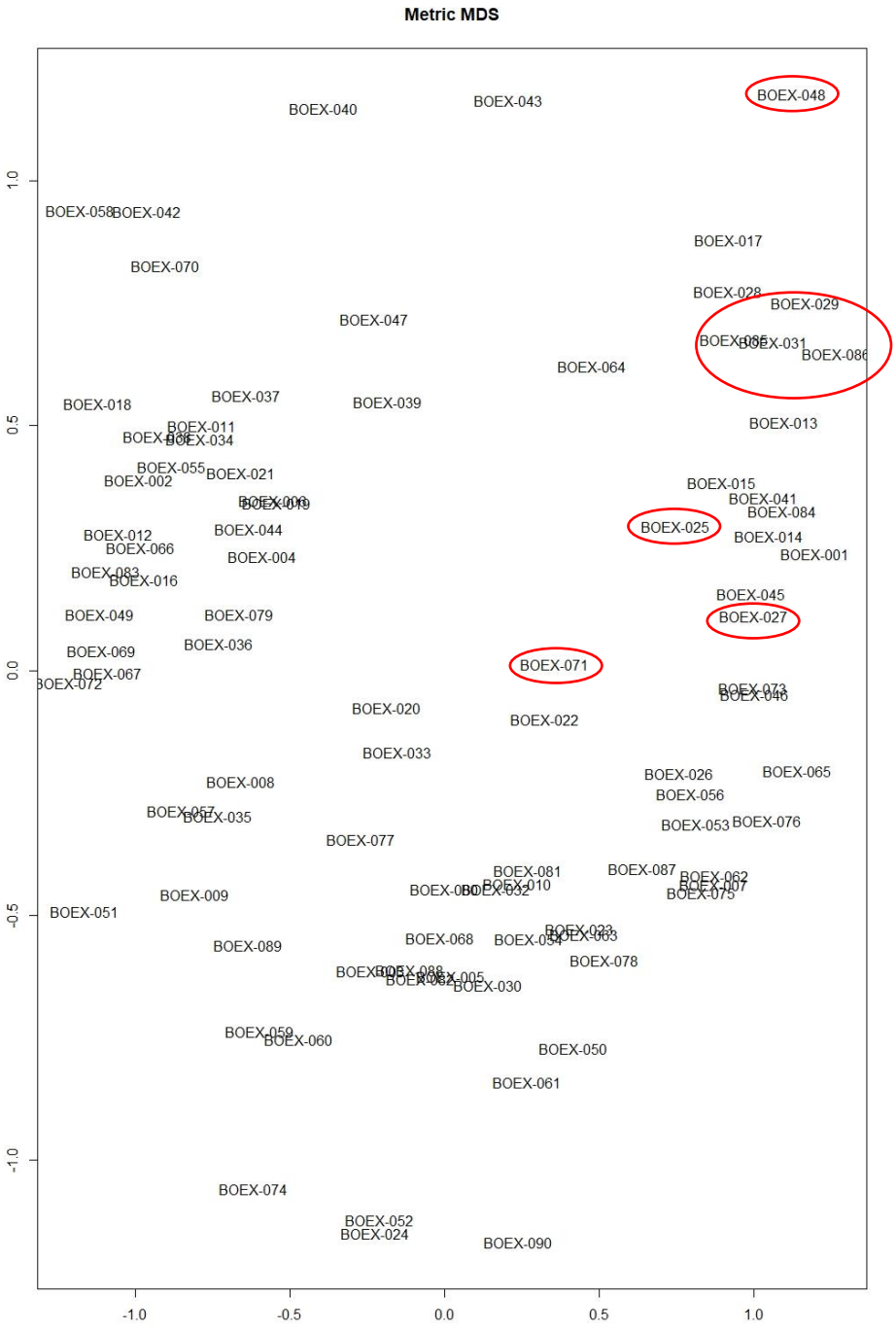

Figure 7. Output from MDS analysis of bioactivity profiles obtained from Canadian medicinal plant extracts from M2 dataset, with the extracts of interest circled in red.

Chemotaxonomy is a classification system based on the chemical make-up of an organism in comparison to others within the same taxonomic level (i.e. family, order, class). Although the consensus is that organisms that are related will produce similar primary and secondary metabolites, there have been differences observed within the different levels of taxonomy.[12, 13, 14] In other words, taxonomically-related organisms should have similar chemical structures (such as isomers, chemicals within the same class, and chemical analogues) within their extracts.[12, 13, 14] However, this is neither timely, nor cost effective. Consequently, a modified approach using the biological activity exhibited and the crude extract of the organism may be more ideal.

To achieve this, bioactivity profiling was utilized. This means that bioactivity profiles are created for each crude extract in the library, as well as a series of known antibiotics.[22, 23] These profiles are created by testing each extract and antibiotic against a panel of target microorganisms to quantify their antibiotic activity.[22, 23] This antibiotic activity is then transformed, so that the profiles are concentration-independent.[22, 23] This is important as crude extracts are chemical mixtures that contain different proportions of chemical compounds responsible for the exhibited antibiotic activity in their profiles.[22, 23] The bioactivity profiles can then be compared using cluster analysis to identify extracts that are unique from each other.[22, 23] This would aid in prioritizing extracts that should be investigated further from the rest of the extract library.

Hence, when analyzing the resulting dendrograms from the agglomerative hierarchical clustering analysis, a method that starts by slowly grouping the number of objects successively into larger sets until a single group is achieved with all objects within it,[35] one can be misled into thinking that there is a clustering pattern and therefore a linkage between the taxonomy of plants and their exhibited biological activity. This would mean that this method of extract prioritization

would be effective. However, when MDS plots are utilized, the clustering pattern, or lack thereof, is more evident. By eliminating all negative values (growth promotion values), there is a dispersal effect within the plots. This would mean that M2 is more efficient in distinguishing between plants, because it does not convert the growth promotion values to zero. Furthermore, though some clustering is exhibited within the same family using M2, there is still a significant lack of clustering that is consistent throughout the same family. Essentially, this is an ineffective way to prioritize extracts in most cases.

Although focusing on antibiotic activity of extracts from plants was not successful in reaching similar conclusions to those found within chemotaxonomy, this does not disprove the generalized outcome of chemotaxonomic findings. The difference between the two methods: the comparison of complex mixtures of chemical compounds within plant extracts against their purified chemical products, may be explained by chemical interactions within the complex mixtures used to obtain bioactivity profiles and bioactivity data. Furthermore, by limiting the biological activity of plants to antibiotic activity, this leaves many other biological activities that can and should be investigated. Also, certain families found in the NPRG library only had one plant within them, which left these clustering results inconclusive, more plants that are a part of these families should be included, so that the results may be more decisive. In conclusion, a larger data set may be more effective in determining the efficacy of relying on the family of Canadian medicinal plant in determining if novel bioactivity may be found, which may lead to the discovery of novel chemical compounds. This study may also be expanded to other plants as well, to determine if plants found in different habitats may have a link between their biological activity and their taxonomic relationships.

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Appendix A: Extract antibiotic raw data

Table 2. Antibiotic activity of extracts of Canadian medicinal plants before normalization[3].

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-001	*Symplocarpus foetidus*	-25.62338779	-14.16165665	-7.35694823	7.34364020	4.96481626	6.69671603	9.36806569	2.91324398
BOEX-002	*Nuphar lutea*	35.85554600	-4.80961924	56.13079019	41.84820801	-0.43002346	-0.25756600	5.15724185	15.20474073
BOEX-003	*Empetrum nigrum*	-2.35081374	94.58598726	23.70631265	18.27057183	0.40173053	-0.19815059	19.47551373	3.86198763
BOEX-004	*Geum macrophyllum*	7.91057610	2.93921176	34.95912807	8.74912157	3.51837373	0.70830650	3.71998571	3.89737999
BOEX-005	*Moneses uniflora*	28.71189774	-0.34742328	-16.56320542	2.55447032	4.75896168	11.09643329	88.37321295	-3.41221223
BOEX-006	*Sarracenia purpurea*	11.26397248	-11.89044756	41.34877384	17.91988756	-2.26739640	-2.12491951	13.23522281	-0.22137914
BOEX-007	*Acorus calamus*	-26.74118659	-9.81963928	-11.21253406	8.99508082	5.39483972	9.07920155	43.13432640	0.22828990
BOEX-008	*Rubus idaeus*	19.86242476	-5.27722111	45.17711172	19.32536894	-1.99374511	2.06052801	43.75573385	3.29416522
BOEX-009	*Acer spicatum*	35.85554600	80.23764853	43.81471390	26.00140548	1.60281470	-4.44301352	5.64159744	7.59304379
BOEX-010	*Actaea rubra*	-2.32158212	-13.42685371	1.17166213	10.47083626	-1.72009382	0.21352313	72.21946894	-5.94287429

[3]Mean percentage inhibition.

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 2 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-011	*Rumex* sp.	8.51246776	0.26720107	19.64577657	23.15530569	-3.32290852	-1.41661301	-3.61328022	4.01295463
BOEX-012	*Orthilia secunda*	28.06122449	1.89274448	38.61542511	32.52801120	4.22535211	6.51060717	5.82268317	0.09611498
BOEX-013	*Sambucus racemosa*	-14.37074830	-8.01261830	-4.42221637	8.71848739	0.00000000	-2.63350402	0.46730794	-6.02090773
BOEX-014	*Prunus pensylvanica*	-25.08503401	-18.10725552	4.15898921	6.61764706	1.18437900	1.82882224	15.42015159	-1.16823113
BOEX-015	*Prunus virginiana*	-17.09183673	-3.97476341	0.92129508	10.43417367	1.18437900	3.73079737	0.32890027	-1.12785237
BOEX-016	*Rubus pubescens*	33.58843537	-8.89589905	42.37957357	15.05602241	3.64916773	0.21945867	18.85518068	-0.65591175
BOEX-017	*Viburnum lantanoides*	-13.60544218	-14.00630915	2.05317189	7.59803922	0.83226633	-0.95098756	0.26178659	8.95614090
BOEX-018	*Corylus cornuta*	42.94217687	-13.69085174	48.90760727	21.04341737	0.44814341	-3.43818581	-0.68621524	17.47960871
BOEX-019	*Populus tremuloides*	3.65646259	-2.39747634	19.55777836	24.71988796	-0.44814341	-3.73079737	2.30671776	27.29545783
BOEX-020	*Alnus viridis*	-8.75850340	-8.13880126	54.35640958	37.60504202	5.56978233	17.04462326	46.43143784	22.94950270
BOEX-021	*Scutellaria lateriflora*	35.96938776	-12.93375394	-0.65806791	7.66806723	-0.03201024	10.82251082	-2.98637462	4.49947671
BOEX-022	*Ranunculus* sp.	-3.57142857	-12.17665615	4.50118452	5.28711485	-0.35211268	1.38990490	20.06997299	5.72918559
BOEX-023	*Sorbus decora*	-13.96263520	-0.52113492	-0.45146727	12.20886551	1.42901522	-1.88243065	40.34713810	-2.64619962

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 2 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-024	*Juniperus communis*	7.65262253	95.25718103	27.00272480	16.69009136	7.93588741	16.38763683	93.87178706	-7.34428323
BOEX-025	*Maianthemum canadense*	-31.00189036	-5.55205047	1.28312413	0.58118416	-0.80025608	50.98756401	-4.04593647	3.93569197
BOEX-026	*Sambucus racemosa var. pubens*	-17.29678639	3.65930599	2.81729428	4.90374137	-2.68886044	0.58522312	6.73298484	10.17959041
BOEX-027	*Polypodium virginianum*	-33.27032136	-3.34014997	-0.25104603	-0.98074827	2.14606022	9.33828077	5.07305504	5.32267233
BOEX-028	*Daphne mezereum*	-29.48960302	-16.29175187	6.83403068	5.66654559	4.42024343	8.16326531	-7.45927582	6.44862807
BOEX-029	*Arisaema triphyllum*	-25.51984877	-16.01908657	-3.51464435	-2.39738467	1.66559898	10.45145331	-7.74772406	1.59256517
BOEX-030	*Aralia nudiclaulis*	-31.76007866	92.41459178	10.18623025	6.70548460	1.30475303	15.91809775	19.31995231	-4.42555682
BOEX-031	*Pyrola elliptica*	-9.26275992	-10.15678255	-0.94839609	2.50635670	2.53042921	12.24489796	0.97946192	1.13063228
BOEX-032	*Anaphalis margaritacea*	-3.69733448	-3.31457161	3.18801090	8.50316233	1.95465207	-5.97864769	26.55181870	11.20984602
BOEX-033	*Abies balsamea*	6.89981096	-16.01908657	32.24546722	9.80748275	5.60538117	15.33704391	46.09526288	4.56861169
BOEX-034	*Acer pensylvanicum*	20.91836735	-5.04731861	44.95919979	19.81792717	1.05633803	6.58376006	-1.84794122	17.91528029
BOEX-035	*Alnus incana*	19.66568338	8.10654314	58.49322799	36.51389932	3.07548928	-10.75905292	49.35849083	25.83378519
BOEX-036	*Betula alleghaniensis*	20.98298677	-12.95160191	39.47001395	20.26879768	6.56630365	6.86456401	30.31366195	18.79981487

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 2 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-037	*Cornus canadensis*	20.79395085	-22.29038855	46.77824268	25.60842717	4.26008969	15.21335807	9.93898844	8.72655103
BOEX-038	*Crataegus* sp.	45.36862004	-9.06612134	24.22594142	10.31601889	4.61242793	7.66852195	-6.55259198	-15.67360907
BOEX-039	*Hypericum perforatum*	0.85984523	-16.90046760	16.18528610	11.20871398	0.15637217	-0.25756600	12.58501400	1.26920786
BOEX-040	*Picea glauca*	5.10396975	-20.04089980	19.21896792	9.88013077	5.95771941	0.28469751	-2.63107633	-3.81146176
BOEX-041	*Solanum dulcamara*	-31.28544423	-14.79209271	2.92887029	5.88448965	1.98590647	-4.41281139	8.08319735	-28.40094114
BOEX-042	*Spiraea alba*	23.53497164	-14.51942740	16.20641562	10.02542681	8.39205637	11.37909709	-7.96365074	9.67455040
BOEX-043	*Typha latifolia*	-11.90926276	-20.38173142	28.06136681	-2.90592081	3.58744395	13.20284698	-12.94288745	1.07600609
BOEX-044	*Vaccinium angustifolium*	31.56899811	-9.54328562	-0.55788006	10.93352706	4.35618193	14.90414348	2.09632974	-3.88039236
BOEX-045	*Daucus carota*	-13.61058601	-16.63258350	1.11576011	4.14093716	2.27418322	-8.71212121	16.83089732	-11.52392261
BOEX-046	*Achillea millefolium*	-16.63516068	-15.61008862	2.90097629	-0.18162005	2.62652146	12.19822109	22.77170546	-7.04841981
BOEX-047	*Apocynum cannabinum*	-2.86436394	-5.04430811	6.10624315	17.63492609	1.69762972	-26.70454545	-14.56755887	14.24674962
BOEX-048	*Arisaema atrorubens*	-20.72451559	-14.51942740	-3.34063527	2.40632520	0.99071207	11.05463787	-16.90140107	2.74129979
BOEX-049	*Cornus sericea*	73.38435374	4.00250156	44.27200903	41.80672269	1.98463508	-6.29114850	13.14652788	12.73187254

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 2 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-050	*Iris versicolor*	-16.17523168	10.25641026	-0.62979189	11.72224132	0.55727554	-6.96784074	30.85294482	20.58223249
BOEX-051	*Nymphaea odorata*	68.49199663	83.80237649	53.83351588	37.60742523	3.21981424	15.42879020	12.15133080	41.47214142
BOEX-052	*Pinus strobus*	1.85341196	91.93245779	35.67907996	16.05362668	6.78018576	24.80857580	94.77519337	16.53202907
BOEX-053	*Populus grandidentata*	-20.80876158	6.19136961	-0.62979189	13.09728429	3.21981424	8.57580398	9.47445108	18.61833054
BOEX-054	*Impatiens capensis*	-5.56023589	0.50031270	0.35596933	12.23788243	6.06811146	11.62642948	43.43701181	7.60613350
BOEX-055	*Betula papyrifera*	33.69839933	-5.94121326	65.16976999	37.98556205	5.44891641	-9.72434916	2.42974143	13.40108688
BOEX-056	*Coptis trifolia*	-16.24149660	-10.03154574	-0.55277705	10.81932773	2.11267606	9.58565244	25.80656734	2.09735868
BOEX-057	*Kalmia angustifalia*	33.02443134	5.56597874	1.25958379	15.77861808	3.31269350	-5.20673813	14.96194626	-0.08901171
BOEX-058	*Pteridium aquilinum*	19.88205560	-3.06441526	24.91785323	11.17222413	2.32198142	-9.80091884	-17.67315672	-2.46094650
BOEX-059	*Rumex crispus*	27.82694199	23.62478286	20.96501129	33.18933133	7.67319043	10.44568245	54.14371320	17.94716001
BOEX-060	*Scirpus microcarpus*	-3.03285594	13.75859912	15.38882804	16.77552424	2.04334365	-6.12557427	15.37424006	0.88606573
BOEX-061	*Tanacetum vulgare*	-37.56145526	84.82918356	4.40180587	0.22539444	8.63622243	15.59888579	38.89044178	17.20850647
BOEX-062	*Cypripedium acaule*	-20.21903960	1.37585991	0.27382256	10.07218976	4.48916409	-1.53139357	16.74759110	5.40240829

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 2 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-063	*Diervilla lonicera*	-16.16509028	-2.33800935	-4.60490463	9.55727337	-2.03283815	2.51126851	60.62080994	-12.65183076
BOEX-064	*Gaultheria hispidula*	-8.34049871	-12.95925184	9.04632153	10.92761771	-1.72009382	-1.22343851	8.09369357	-2.35661997
BOEX-065	*Mitchella repens*	-24.34709351	-4.62789243	1.83461117	3.64386387	3.09597523	23.35375191	19.00457314	-2.79984973
BOEX-066	*Quercus rubra*	32.68744735	-0.18761726	47.17962760	30.07906497	5.57275542	8.80551302	9.77045747	5.27924726
BOEX-067	*Gaultheria procumbens*	36.14153328	3.25203252	23.68565170	15.02234445	2.87925697	-1.22511485	11.46012087	0.29887127
BOEX-068	*Nemopanthus mucronatus*	3.53833193	2.06378987	1.83461117	15.15984875	5.63467492	7.42725881	26.03995284	-2.03121534
BOEX-069	*Rubus hispidus*	50.36166365	4.33656958	58.35816852	23.53556485	4.58204334	2.22052067	22.36139828	4.06117174
BOEX-070	*Spiraea tomentosa*	7.41410488	-4.40129450	15.06366838	15.30683403	3.77708978	-3.59877489	-4.45424856	0.60231699
BOEX-071	*Monotropa uniflora*	-6.41952984	4.46601942	-0.75860200	3.76569038	-1.91594561	32.54211332	2.04294264	7.65746090
BOEX-072	*Acer saccharum*	31.46473779	18.51132686	44.32403143	35.77405858	0.80346106	-19.31818182	9.01080423	6.38564643
BOEX-073	*Angelica atropurpurea*	-22.06148282	-3.49514563	-0.51476565	0.87168759	0.83436341	-2.22363405	9.28000340	-2.23407979
BOEX-074	*Berberis vulgaris*	36.98010850	76.31067961	41.72311027	21.30404463	3.95550062	11.37229987	83.84153139	-2.49486620
BOEX-075	*Chelone glabra*	-17.72151899	-4.91909385	-3.03440802	2.26638773	0.67985167	17.66200762	30.71037755	-1.82584256

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 2 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-076	*Sium suave*	-38.69801085	-2.65372168	-1.76104037	5.92747559	3.21384425	7.17916137	28.75382319	-2.80639612
BOEX-077	*Taxus canadensis*	6.78119349	-2.20064725	8.94066649	6.79916318	1.79233622	13.21473952	18.00165581	2.36290170
BOEX-078	*Tsuga canadensis*	-17.26943942	1.48867314	-2.41127066	7.49651325	0.12360939	2.47776366	40.89065273	12.07713985
BOEX-079	*Fragaria virginiana*	6.87876182	10.82164329	31.74386921	13.24666198	-4.53479281	1.67417901	1.66671849	2.09110899
BOEX-080	*Larix laricina*	2.62206148	-3.81877023	17.23110268	17.71269177	3.02843016	0.63532402	61.38142068	1.10226505
BOEX-081	*Tilia americana*	-6.32911392	-4.59546926	11.46030886	9.13528591	2.31767614	24.14231258	43.25341107	0.00759293
BOEX-082	*Verbascum thapsus*	5.24412297	6.60194175	9.83473313	6.41562064	3.55377009	18.17026684	37.15981511	20.69978422
BOEX-083	*Chamerion angustifolium*	64.01179941	6.07990735	80.89729120	44.25244177	-1.08729419	5.01981506	14.03400545	12.83950029
BOEX-084	*Linnaea borealis*	-17.45485813	-10.42084168	-0.40871935	7.55446240	-2.38467553	3.73470702	6.91831943	-4.49714483
BOEX-085	*Lycopodium* sp.	-39.87341772	-1.94174757	6.20428068	6.52022315	2.53399258	38.34180432	-23.33981076	-4.48238563
BOEX-086	*Clintonia borealis*	-24.31972789	-16.52996845	-6.29112924	6.86274510	1.69654289	24.48979592	-1.90573152	5.56247019
BOEX-087	*Chimaphila umbellata*	-21.15732369	-5.82524272	3.90138174	3.83542538	5.25339926	-14.34163701	31.84717493	1.53561451
BOEX-088	*Epifagus virginiana*	-8.04701627	83.04207120	6.44811704	4.77684798	2.07045735	-2.66836086	9.84586107	22.67367472

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 2 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-089	*Heracleum maixmum*	99.60668633	5.03763752	-0.87905426	-0.90157776	4.34917676	14.69359331	87.30739972	-5.02027964
BOEX-090	*Actaea pachypoda*	-26.05703048	99.88419224	-1.41083521	7.96393689	1.98819509	44.60306407	108.90023220	-2.23283371

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Appendix B: Extract normalized data using method 1

Table 3. Normalized antibiotic activity of extracts of Canadian medicinal plants using M1.

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-001	*Symplocarpus foetidus*	0.00000000	0.00000000	0.00000000	0.78390144	0.52997240	0.71484512	1.00000000	0.31097604
BOEX-002	*Nuphar lutea*	0.63878570	0.00000000	1.00000000	0.74554817	0.00000000	0.00000000	0.09187902	0.27088058
BOEX-003	*Empetrum nigrum*	0.00000000	1.00000000	0.25063240	0.19316362	0.00424725	0.00000000	0.20590274	0.04083044
BOEX-004	*Geum macrophyllum*	0.22628070	0.08407566	1.00000000	0.25026716	0.10064249	0.02026099	0.10640957	0.11148390
BOEX-005	*Moneses uniflora*	0.32489367	0.00000000	0.00000000	0.02890548	0.05385073	0.12556331	1.00000000	0.00000000
BOEX-006	*Sarracenia purpurea*	0.27241370	0.00000000	1.00000000	0.43338377	0.00000000	0.00000000	0.32008743	0.00000000
BOEX-007	*Acorus calamus*	0.00000000	0.00000000	0.00000000	0.20853649	0.12507068	0.21048669	1.00000000	0.00529253
BOEX-008	*Rubus idaeus*	0.43965681	0.00000000	1.00000000	0.42776902	0.00000000	0.04561000	0.96853766	0.07291668
BOEX-009	*Acer spicatum*	0.44686686	1.00000000	0.54606179	0.32405493	0.01997584	0.00000000	0.07031110	0.09463193
BOEX-010	*Actaea rubra*	0.00000000	0.00000000	0.01622363	0.14498634	0.00000000	0.00295659	1.00000000	0.00000000

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 3 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-011	*Rumex* sp.	0.36762494	0.01153952	0.84843521	1.00000000	0.00000000	0.00000000	0.00000000	0.17330605
BOEX-012	*Orthilia secunda*	0.72668433	0.04901524	1.00000000	0.84235797	0.10942135	0.16860120	0.15078646	0.00248903
BOEX-013	*Sambucus racemosa*	0.00000000	0.00000000	0.00000000	1.00000000	0.00000000	0.00000000	0.05359966	0.00000000
BOEX-014	*Prunus pensylvanica*	0.00000000	0.00000000	0.26971130	0.42915577	0.07680722	0.11859950	1.00000000	0.00000000
BOEX-015	*Prunus virginiana*	0.00000000	0.00000000	0.08829593	1.00000000	0.11350961	0.35755561	0.03152145	0.00000000
BOEX-016	*Rubus pubescens*	0.79256190	0.00000000	1.00000000	0.35526602	0.08610676	0.00517841	0.44491200	0.00000000
BOEX-017	*Viburnum lantanoides*	0.00000000	0.00000000	0.22924739	0.84836084	0.09292689	0.00000000	0.02922984	1.00000000
BOEX-018	*Corylus cornuta*	0.87802653	0.00000000	1.00000000	0.43026880	0.00916306	0.00000000	0.00000000	0.35740061
BOEX-019	*Populus tremuloides*	0.13395865	0.00000000	0.71652135	0.90564108	0.00000000	0.00000000	0.08450922	1.00000000
BOEX-020	*Alnus viridis*	0.00000000	0.00000000	1.00000000	0.69182351	0.10246781	0.31357154	0.85420355	0.42220417
BOEX-021	*Scutellaria lateriflora*	1.00000000	0.00000000	0.00000000	0.21318315	0.00000000	0.30088115	0.00000000	0.12509183
BOEX-022	*Ranunculus* sp.	0.00000000	0.00000000	0.22427457	0.26343408	0.00000000	0.06925295	1.00000000	0.28546055
BOEX-023	*Sorbus decora*	0.00000000	0.00000000	0.00000000	0.30259558	0.03541801	0.00000000	1.00000000	0.00000000

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 3 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-024	*Juniperus communis*	0.08033644	1.00000000	0.28347180	0.17521085	0.08331012	0.17203571	0.98545628	0.00000000
BOEX-025	*Maianthemum canadense*	0.00000000	0.00000000	0.02516543	0.01139855	0.00000000	1.00000000	0.00000000	0.07718925
BOEX-026	*Sambucus racemosa var. pubens*	0.00000000	0.35947478	0.27675910	0.48172286	0.00000000	0.05748985	0.66142001	1.00000000
BOEX-027	*Polypodium virginianum*	0.00000000	0.00000000	0.00000000	0.00000000	0.22981320	1.00000000	0.54325364	0.56998418
BOEX-028	*Daphne mezereum*	0.00000000	0.00000000	0.83716876	0.69415183	0.54147982	1.00000000	0.00000000	0.78995694
BOEX-029	*Arisaema triphyllum*	0.00000000	0.00000000	0.00000000	0.00000000	0.15936530	1.00000000	0.00000000	0.15237739
BOEX-030	*Aralia nudiclaulis*	0.00000000	1.00000000	0.11022318	0.07255872	0.01411847	0.17224658	0.20905738	0.00000000
BOEX-031	*Pyrola elliptica*	0.00000000	0.00000000	0.00000000	0.20468580	0.20665172	1.00000000	0.07998939	0.09233497
BOEX-032	*Anaphalis margaritacea*	0.00000000	0.00000000	0.12006752	0.32024783	0.07361650	0.00000000	1.00000000	0.42218750
BOEX-033	*Abies balsamea*	0.14968590	0.00000000	0.69953972	0.21276552	0.12160428	0.33272495	1.00000000	0.09911239
BOEX-034	*Acer pensylvanicum*	0.46527446	0.00000000	1.00000000	0.44079804	0.02349548	0.14643855	0.00000000	0.39847863
BOEX-035	*Alnus incana*	0.33620445	0.13858943	1.00000000	0.62424148	0.05257855	0.00000000	0.84383257	0.44165429
BOEX-036	*Betula alleghaniensis*	0.53161843	0.00000000	1.00000000	0.51352396	0.16636183	0.17391846	0.76801751	0.47630626

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 3 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-037	*Cornus canadensis*	0.44452185	0.00000000	1.00000000	0.54744312	0.09106990	0.32522295	0.21247033	0.18655149
BOEX-038	*Crataegus* sp.	1.00000000	0.00000000	0.53398013	0.22738225	0.10166560	0.16902700	0.00000000	0.00000000
BOEX-039	*Hypericum perforatum*	0.05312512	0.00000000	1.00000000	0.69252492	0.00966138	0.00000000	0.77755895	0.07841739
BOEX-040	*Picea glauca*	0.26556940	0.00000000	1.00000000	0.51408228	0.30999164	0.01481336	0.00000000	0.00000000
BOEX-041	*Solanum dulcamara*	0.00000000	0.00000000	0.36234056	0.72799035	0.24568328	0.00000000	1.00000000	0.00000000
BOEX-042	*Spiraea alba*	1.00000000	0.00000000	0.68860995	0.42597998	0.35657814	0.48349738	0.00000000	0.41107126
BOEX-043	*Typha latifolia*	0.00000000	0.00000000	1.00000000	0.00000000	0.12784281	0.47049907	0.00000000	0.03834475
BOEX-044	*Vaccinium angustifolium*	1.00000000	0.00000000	0.00000000	0.34633747	0.13798924	0.47211329	0.06640470	0.00000000
BOEX-045	*Daucus carota*	0.00000000	0.00000000	0.06629237	0.24603187	0.13511955	0.00000000	1.00000000	0.00000000
BOEX-046	*Achillea millefolium*	0.00000000	0.00000000	0.12739390	0.00000000	0.11534145	0.53567446	1.00000000	0.00000000
BOEX-047	*Apocynum cannabinum*	0.00000000	0.00000000	0.34625851	1.00000000	0.09626520	0.00000000	0.00000000	0.80787124
BOEX-048	*Arisaema atrorubens*	0.00000000	0.00000000	0.00000000	0.21767562	0.08961959	1.00000000	0.00000000	0.24797735
BOEX-049	*Cornus sericea*	1.00000000	0.05454162	0.60328949	0.56969532	0.02704439	0.00000000	0.17914620	0.17349574

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 3 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-050	*Iris versicolor*	0.00000000	0.33242889	0.00000000	0.37993914	0.01806231	0.00000000	1.00000000	0.66710755
BOEX-051	*Nymphaea odorata*	0.81730375	1.00000000	0.64238651	0.44876323	0.03842151	0.18410922	0.14499984	0.49488025
BOEX-052	*Pinus strobus*	0.01955588	0.97000549	0.37646011	0.16938638	0.07153967	0.26176233	1.00000000	0.17443414
BOEX-053	*Populus grandidentata*	0.00000000	0.33254161	0.00000000	0.70346180	0.17293786	0.46061079	0.50887758	1.00000000
BOEX-054	*Impatiens capensis*	0.00000000	0.01151812	0.00819507	0.28173859	0.13969910	0.26766182	1.00000000	0.17510720
BOEX-055	*Betula papyrifera*	0.51708636	0.00000000	1.00000000	0.58287089	0.08361110	0.00000000	0.03728326	0.20563348
BOEX-056	*Coptis trifolia*	0.00000000	0.00000000	0.00000000	0.41924707	0.08186583	0.37144237	1.00000000	0.08127228
BOEX-057	*Kalmia angustifalia*	1.00000000	0.16854124	0.03814097	0.47778622	0.10031039	0.00000000	0.45305689	0.00000000
BOEX-058	*Pteridium aquilinum*	0.79790403	0.00000000	1.00000000	0.44836223	0.09318545	0.00000000	0.00000000	0.00000000
BOEX-059	*Rumex crispus*	0.51394595	0.43633474	0.38721045	0.61298587	0.14171895	0.19292512	1.00000000	0.33147265
BOEX-060	*Scirpus microcarpus*	0.00000000	0.82015912	0.91733813	1.00000000	0.12180506	0.00000000	0.91646853	0.05281896
BOEX-061	*Tanacetum vulgare*	0.00000000	1.00000000	0.05189023	0.00265704	0.10180721	0.18388584	0.45845592	0.20286069
BOEX-062	*Cypripedium acaule*	0.00000000	0.08215271	0.01634997	0.60141125	0.26804835	0.00000000	1.00000000	0.32257823

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 3 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-063	*Diervilla lonicera*	0.00000000	0.00000000	0.00000000	0.15765664	0.00000000	0.04142585	1.00000000	0.00000000
BOEX-064	*Gaultheria hispidula*	0.00000000	0.00000000	0.82784023	1.00000000	0.00000000	0.00000000	0.74066405	0.00000000
BOEX-065	*Mitchella repens*	0.00000000	0.00000000	0.07855745	0.15602906	0.13256864	1.00000000	0.81376959	0.00000000
BOEX-066	*Quercus rubra*	0.69282970	0.00000000	1.00000000	0.63754350	0.11811783	0.18663804	0.20709060	0.11189676
BOEX-067	*Gaultheria procumbens*	1.00000000	0.08998048	0.65535824	0.41565321	0.07966615	0.00000000	0.31709006	0.00826947
BOEX-068	*Nemopanthus mucronatus*	0.13588089	0.07925475	0.07045371	0.58217651	0.21638576	0.28522551	1.00000000	0.00000000
BOEX-069	*Rubus hispidus*	0.86297540	0.07430956	1.00000000	0.40329512	0.07851589	0.03804987	0.38317512	0.06959046
BOEX-070	*Spiraea tomentosa*	0.48436567	0.00000000	0.98411392	1.00000000	0.24675839	0.00000000	0.00000000	0.03934955
BOEX-071	*Monotropa uniflora*	0.00000000	0.13723815	0.00000000	0.11571745	0.00000000	1.00000000	0.06277843	0.23530927
BOEX-072	*Acer saccharum*	0.70987987	0.41763635	1.00000000	0.80710300	0.01812699	0.00000000	0.20329388	0.14406737
BOEX-073	*Angelica atropurpurea*	0.00000000	0.00000000	0.00000000	0.09393182	0.08990982	0.00000000	1.00000000	0.00000000
BOEX-074	*Berberis vulgaris*	0.44107148	0.91017755	0.49764251	0.25409894	0.04717830	0.13564041	1.00000000	0.00000000
BOEX-075	*Chelone glabra*	0.00000000	0.00000000	0.00000000	0.07379876	0.02213752	0.57511529	1.00000000	0.00000000

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 3 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-076	*Sium suave*	0.00000000	0.00000000	0.00000000	0.20614565	0.11177102	0.24967676	1.00000000	0.00000000
BOEX-077	*Taxus canadensis*	0.37669832	0.00000000	0.49665801	0.37769654	0.09956508	0.73408467	1.00000000	0.13126024
BOEX-078	*Tsuga canadensis*	0.00000000	0.03640620	0.00000000	0.18333073	0.00302293	0.06059487	1.00000000	0.29535209
BOEX-079	*Fragaria virginiana*	0.21669576	0.34090499	1.00000000	0.41729828	0.00000000	0.05274023	0.05250521	0.06587442
BOEX-080	*Larix laricina*	0.04271751	0.00000000	0.28072180	0.28856764	0.04933790	0.01035043	1.00000000	0.01795763
BOEX-081	*Tilia americana*	0.00000000	0.00000000	0.26495734	0.21120383	0.05358366	0.55815974	1.00000000	0.00017555
BOEX-082	*Verbascum thapsus*	0.14112349	0.17766347	0.26466044	0.17264942	0.09563476	0.48897624	1.00000000	0.55704756
BOEX-083	*Chamerion angustifolium*	0.79127247	0.07515588	1.00000000	0.54702007	0.00000000	0.06205171	0.17347930	0.15871360
BOEX-084	*Linnaea borealis*	0.00000000	0.00000000	0.00000000	1.00000000	0.00000000	0.49437098	0.91579242	0.00000000
BOEX-085	*Lycopodium* sp.	0.00000000	0.00000000	0.16181504	0.17005520	0.06608955	1.00000000	0.00000000	0.00000000
BOEX-086	*Clintonia borealis*	0.00000000	0.00000000	0.00000000	0.28022876	0.06927550	1.00000000	0.00000000	0.22713420
BOEX-087	*Chimaphila umbellata*	0.00000000	0.00000000	0.12250323	0.12043220	0.16495652	0.00000000	1.00000000	0.04821823
BOEX-088	*Epifagus virginiana*	0.00000000	1.00000000	0.07764880	0.05752323	0.02493263	0.00000000	0.11856473	0.27303841

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 3 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-089	*Heracleum maixmum*	1.00000000	0.05057529	0.00000000	0.00000000	0.04366350	0.14751613	0.87652148	0.00000000
BOEX-090	*Actaea pachypoda*	0.00000000	0.91720826	0.00000000	0.07313058	0.01825703	0.40957731	1.00000000	0.00000000

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Appendix C: Extract normalized data using method 2

Table 4. Normalized antibiotic activity of extracts of Canadian medicinal plants using M2.

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-001	*Symplocarpus foetidus*	-1.00000000	-0.55268479	-0.28711848	0.28659911	0.19376112	0.26135170	0.36560605	0.11369472
BOEX-002	*Nuphar lutea*	0.63878570	-0.08568593	1.00000000	0.74554817	-0.00766110	-0.00458868	0.09187902	0.27088058
BOEX-003	*Empetrum nigrum*	-0.02485372	1.00000000	0.25063240	0.19316362	0.00424725	-0.00209493	0.20590274	0.04083044
BOEX-004	*Geum macrophyllum*	0.22628070	0.08407566	1.00000000	0.25026716	0.10064249	0.02026099	0.10640957	0.11148390
BOEX-005	*Moneses uniflora*	0.32489367	-0.00393132	-0.18742337	0.02890548	0.05385073	0.12556331	1.00000000	-0.03861139
BOEX-006	*Sarracenia purpurea*	0.27241370	-0.28756470	1.00000000	0.43338377	-0.05483588	-0.05139015	0.32008743	-0.00535395
BOEX-007	*Acorus calamus*	-0.61995141	-0.22765255	-0.25994457	0.20853649	0.12507068	0.21048669	1.00000000	0.00529253
BOEX-008	*Rubus idaeus*	0.43965681	-0.11681183	1.00000000	0.42776902	-0.04413175	0.04561000	0.96853766	0.07291668
BOEX-009	*Acer spicatum*	0.44686686	1.00000000	0.54606179	0.32405493	0.01997584	-0.05537318	0.07031110	0.09463193
BOEX-010	*Actaea rubra*	-0.03214621	-0.18591737	0.01622363	0.14498634	-0.02381759	0.00295659	1.00000000	-0.08228909

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 4 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-011	*Rumex* sp.	0.36762494	0.01153952	0.84843521	1.00000000	-0.14350528	-0.06117877	-0.15604546	0.17330605
BOEX-012	*Orthilia secunda*	0.72668433	0.04901524	1.00000000	0.84235797	0.10942135	0.16860120	0.15078646	0.00248903
BOEX-013	*Sambucus racemosa*	-1.00000000	-0.55756444	-0.30772346	0.60668291	0.00000000	-0.18325448	0.03251800	-0.41896967
BOEX-014	*Prunus pensylvanica*	-1.00000000	-0.72183500	0.16579564	0.26380857	0.04721457	0.07290491	0.61471520	-0.04657084
BOEX-015	*Prunus virginiana*	-1.00000000	-0.23255332	0.05390264	0.61047703	0.06929501	0.21827949	0.01924312	-0.06598778
BOEX-016	*Rubus pubescens*	0.79256190	-0.20991007	1.00000000	0.35526602	0.08610676	0.00517841	0.44491200	-0.01547707
BOEX-017	*Viburnum lantanoides*	-0.97137954	-1.00000000	0.14658907	0.54247262	0.05942082	-0.06789709	0.01869062	0.63943619
BOEX-018	*Corylus cornuta*	0.87802653	-0.27993297	1.00000000	0.43026880	0.00916306	-0.07029961	-0.01403085	0.35740061
BOEX-019	*Populus tremuloides*	0.13395865	-0.08783426	0.71652135	0.90564108	-0.01641824	-0.13668199	0.08450922	1.00000000
BOEX-020	*Alnus viridis*	-0.16113101	-0.14973030	1.00000000	0.69182351	0.10246781	0.31357154	0.85420355	0.42220417
BOEX-021	*Scutellaria lateriflora*	1.00000000	-0.35957671	-0.01829522	0.21318315	-0.00088993	0.30088115	-0.08302545	0.12509183
BOEX-022	*Ranunculus* sp.	-0.17794885	-0.60671014	0.22427457	0.26343408	-0.01754425	0.06925295	1.00000000	0.28546055
BOEX-023	*Sorbus decora*	-0.34606259	-0.01291628	-0.01118957	0.30259558	0.03541801	-0.04665587	1.00000000	-0.06558581

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 4 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-024	*Juniperus communis*	0.08033644	1.00000000	0.28347180	0.17521085	0.08331012	0.17203571	0.98545628	-0.07709952
BOEX-025	*Maianthemum canadense*	-0.60802847	-0.10889029	0.02516543	0.01139855	-0.01569512	1.00000000	-0.07935144	0.07718925
BOEX-026	*Sambucus racemosa var. pubens*	-1.00000000	0.21155988	0.16287964	0.28350592	-0.15545434	0.03383421	0.38926218	0.58852495
BOEX-027	*Polypodium virginianum*	-1.00000000	-0.10039428	-0.00754564	-0.02947817	0.06450374	0.28067901	0.15247989	0.15998259
BOEX-028	*Daphne mezereum*	-1.00000000	-0.55245748	0.23174373	0.19215401	0.14989159	0.27681842	-0.25294596	0.21867463
BOEX-029	*Arisaema triphyllum*	-1.00000000	-0.62771087	-0.13772199	-0.09394196	0.06526680	0.40954213	-0.30359600	0.06240496
BOEX-030	*Aralia nudiclaulis*	-0.34366952	1.00000000	0.11022318	0.07255872	0.01411847	0.17224658	0.20905738	-0.04788807
BOEX-031	*Pyrola elliptica*	-0.75645873	-0.82947057	-0.07745235	0.20468580	0.20665172	1.00000000	0.07998939	0.09233497
BOEX-032	*Anaphalis margaritacea*	-0.13924976	-0.12483407	0.12006752	0.32024783	0.07361650	-0.22516905	1.00000000	0.42218750
BOEX-033	*Abies balsamea*	0.14968590	-0.34752132	0.69953972	0.21276552	0.12160428	0.33272495	1.00000000	0.09911239
BOEX-034	*Acer pensylvanicum*	0.46527446	-0.11226442	1.00000000	0.44079804	0.02349548	0.14643855	-0.04110263	0.39847863
BOEX-035	*Alnus incana*	0.33620445	0.13858943	1.00000000	0.62424148	0.05257855	-0.18393673	0.84383257	0.44165429
BOEX-036	*Betula alleghaniensis*	0.53161843	-0.32813776	1.00000000	0.51352396	0.16636183	0.17391846	0.76801751	0.47630626

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 4 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-037	*Cornus canadensis*	0.44452185	-0.47651188	1.00000000	0.54744312	0.09106990	0.32522295	0.21247033	0.18655149
BOEX-038	*Crataegus* sp.	1.00000000	-0.19983242	0.53398013	0.22738225	0.10166560	0.16902700	-0.14443005	-0.34547247
BOEX-039	*Hypericum perforatum*	0.05087701	-1.00000000	0.95768274	0.66321916	0.00925253	-0.01524017	0.74465478	0.07509898
BOEX-040	*Picea glauca*	0.25467767	-1.00000000	0.95898728	0.49299836	0.29727804	0.01420582	-0.13128534	-0.19018416
BOEX-041	*Solanum dulcamara*	-1.00000000	-0.47281070	0.09361767	0.18809033	0.06347701	-0.14104998	0.25836927	-0.90780048
BOEX-042	*Spiraea alba*	1.00000000	-0.61692989	0.68860995	0.42597998	0.35657814	0.48349738	-0.33837520	0.41107126
BOEX-043	*Typha latifolia*	-0.42440067	-0.72632711	1.00000000	-0.10355593	0.12784281	0.47049907	-0.46123510	0.03834475
BOEX-044	*Vaccinium angustifolium*	1.00000000	-0.30229929	-0.01767177	0.34633747	0.13798924	0.47211329	0.06640470	-0.12291782
BOEX-045	*Daucus carota*	-0.80866669	-0.98821728	0.06629237	0.24603187	0.13511955	-0.51762666	1.00000000	-0.68468855
BOEX-046	*Achillea millefolium*	-0.73051888	-0.68550371	0.12739390	-0.00797569	0.11534145	0.53567446	1.00000000	-0.30952534
BOEX-047	*Apocynum cannabinum*	-0.10726129	-0.18889324	0.22865932	0.66037170	0.06357082	-1.00000000	-0.54550859	0.53349531
BOEX-048	*Arisaema atrorubens*	-1.00000000	-0.70059188	-0.16119244	0.11611008	0.04780387	0.53340875	-0.81552695	0.13227329
BOEX-049	*Cornus sericea*	1.00000000	0.05454162	0.60328949	0.56969532	0.02704439	-0.08572874	0.17914620	0.17349574

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Table 4 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-050	*Iris versicolor*	-0.52426865	0.33242889	-0.02041270	0.37993914	0.01806231	-0.22584038	1.00000000	0.66710755
BOEX-051	*Nymphaea odorata*	0.81730375	1.00000000	0.64238651	0.44876323	0.03842151	0.18410922	0.14499984	0.49488025
BOEX-052	*Pinus strobus*	0.01955588	0.97000549	0.37646011	0.16938638	0.07153967	0.26176233	1.00000000	0.17443414
BOEX-053	*Populus grandidentata*	-1.00000000	0.29753667	-0.03026571	0.62941200	0.15473358	0.41212467	0.45531067	0.89473516
BOEX-054	*Impatiens capensis*	-0.12800687	0.01151812	0.00819507	0.28173859	0.13969910	0.26766182	1.00000000	0.17510720
BOEX-055	*Betula papyrifera*	0.51708636	-0.09116517	1.00000000	0.58287089	0.08361110	-0.14921564	0.03728326	0.20563348
BOEX-056	*Coptis trifolia*	-0.62935517	-0.38872065	-0.02142001	0.41924707	0.08186583	0.37144237	1.00000000	0.08127228
BOEX-057	*Kalmia angustifalia*	1.00000000	0.16854124	0.03814097	0.47778622	0.10031039	-0.15766322	0.45305689	-0.00269533
BOEX-058	*Pteridium aquilinum*	0.79790403	-0.12298071	1.00000000	0.44836223	0.09318545	-0.39332918	-0.70925679	-0.09876238
BOEX-059	*Rumex crispus*	0.51394595	0.43633474	0.38721045	0.61298587	0.14171895	0.19292512	1.00000000	0.33147265
BOEX-060	*Scirpus microcarpus*	-0.18079053	0.82015912	0.91733813	1.00000000	0.12180506	-0.36514950	0.91646853	0.05281896
BOEX-061	*Tanacetum vulgare*	-0.44278931	1.00000000	0.05189023	0.00265704	0.10180721	0.18388584	0.45845592	0.20286069
BOEX-062	*Cypripedium acaule*	-1.00000000	0.06804774	0.01354281	0.49815372	0.22202657	-0.07574017	0.82830794	0.26719411

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 4 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-063	*Diervilla lonicera*	-0.26665909	-0.03856777	-0.07596244	0.15765664	-0.03353367	0.04142585	1.00000000	-0.20870442
BOEX-064	*Gaultheria hispidula*	-0.64359415	-1.00000000	0.69805893	0.84322906	-0.13273095	-0.09440657	0.62454945	-0.18184846
BOEX-065	*Mitchella repens*	-1.00000000	-0.19007987	0.07535237	0.14966320	0.12715995	0.95920081	0.78056845	-0.11499729
BOEX-066	*Quercus rubra*	0.69282970	-0.00397666	1.00000000	0.63754350	0.11811783	0.18663804	0.20709060	0.11189676
BOEX-067	*Gaultheria procumbens*	1.00000000	0.08998048	0.65535824	0.41565321	0.07966615	-0.03389770	0.31709006	0.00826947
BOEX-068	*Nemopanthus mucronatus*	0.13588089	0.07925475	0.07045371	0.58217651	0.21638576	0.28522551	1.00000000	-0.07800380
BOEX-069	*Rubus hispidus*	0.86297540	0.07430956	1.00000000	0.40329512	0.07851589	0.03804987	0.38317512	0.06959046
BOEX-070	*Spiraea tomentosa*	0.48436567	-0.28753787	0.98411392	1.00000000	0.24675839	-0.23510903	-0.29099738	0.03934955
BOEX-071	*Monotropa uniflora*	-0.19726838	0.13723815	-0.02331139	0.11571745	-0.05887588	1.00000000	0.06277843	0.23530927
BOEX-072	*Acer saccharum*	0.70987987	0.41763635	1.00000000	0.80710300	0.01812699	-0.43583991	0.20329388	0.14406737
BOEX-073	*Angelica atropurpurea*	-1.00000000	-0.15842750	-0.02333323	0.03951174	0.03781992	-0.10079259	0.42064278	-0.10126608
BOEX-074	*Berberis vulgaris*	0.44107148	0.91017755	0.49764251	0.25409894	0.04717830	0.13564041	1.00000000	-0.02975693
BOEX-075	*Chelone glabra*	-0.57705311	-0.16017693	-0.09880725	0.07379876	0.02213752	0.57511529	1.00000000	-0.05945360

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 4 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-076	*Sium suave*	-1.00000000	-0.06857514	-0.04550726	0.15317262	0.08304934	0.18551758	0.74303104	-0.07252042
BOEX-077	*Taxus canadensis*	0.37669832	-0.12224694	0.49665801	0.37769654	0.09956508	0.73408467	1.00000000	0.13126024
BOEX-078	*Tsuga canadensis*	-0.42233220	0.03640620	-0.05896875	0.18333073	0.00302293	0.06059487	1.00000000	0.29535209
BOEX-079	*Fragaria virginiana*	0.21669576	0.34090499	1.00000000	0.41729828	-0.14285570	0.05274023	0.05250521	0.06587442
BOEX-080	*Larix laricina*	0.04271751	-0.06221378	0.28072180	0.28856764	0.04933790	0.01035043	1.00000000	0.01795763
BOEX-081	*Tilia americana*	-0.14632635	-0.10624524	0.26495734	0.21120383	0.05358366	0.55815974	1.00000000	0.00017555
BOEX-082	*Verbascum thapsus*	0.14112349	0.17766347	0.26466044	0.17264942	0.09563476	0.48897624	1.00000000	0.55704756
BOEX-083	*Chamerion angustifolium*	0.79127247	0.07515588	1.00000000	0.54702007	-0.01344043	0.06205171	0.17347930	0.15871360
BOEX-084	*Linnaea borealis*	-1.00000000	-0.59701669	-0.02341579	0.43279999	-0.13661959	0.21396376	0.39635495	-0.25764431
BOEX-085	*Lycopodium* sp.	-1.00000000	-0.04869780	0.15559942	0.16352306	0.06355093	0.96158811	-0.58534763	-0.11241539
BOEX-086	*Clintonia borealis*	-0.99305556	-0.67497371	-0.25688778	0.28022876	0.06927550	1.00000000	-0.07781737	0.22713420
BOEX-087	*Chimaphila umbellata*	-0.66433911	-0.18291238	0.12250323	0.12043220	0.16495652	-0.45032682	1.00000000	0.04821823
BOEX-088	*Epifagus virginiana*	-0.09690288	1.00000000	0.07764880	0.05752323	0.02493263	-0.03213264	0.11856473	0.27303841

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Table 4 (continued)

Plant code	Plant	SA	EF	PA	EC	CA	SC	MT	MS
BOEX-089	*Heracleum maixmum*	1.00000000	0.05057529	-0.00882525	-0.00905138	0.04366350	0.14751613	0.87652148	-0.05040103
BOEX-090	*Actaea pachypoda*	-0.23927433	0.91720826	-0.01295530	0.07313058	0.01825703	0.40957731	1.00000000	-0.02050348

SA: *Staphylococcus aureus*; EF: *Enterococcus faecium*; PA: *Pseudomonas aeruginosa*; EC: *Escherichia coli*; CA: *Candida albicans*; SC: *Saccharomyces cerevisiae*; MT: *Mycobacterium tuberculosis*; MS: *Mycobacterium smegmatis*

Appendix D: Bioactivity profiles (M1)

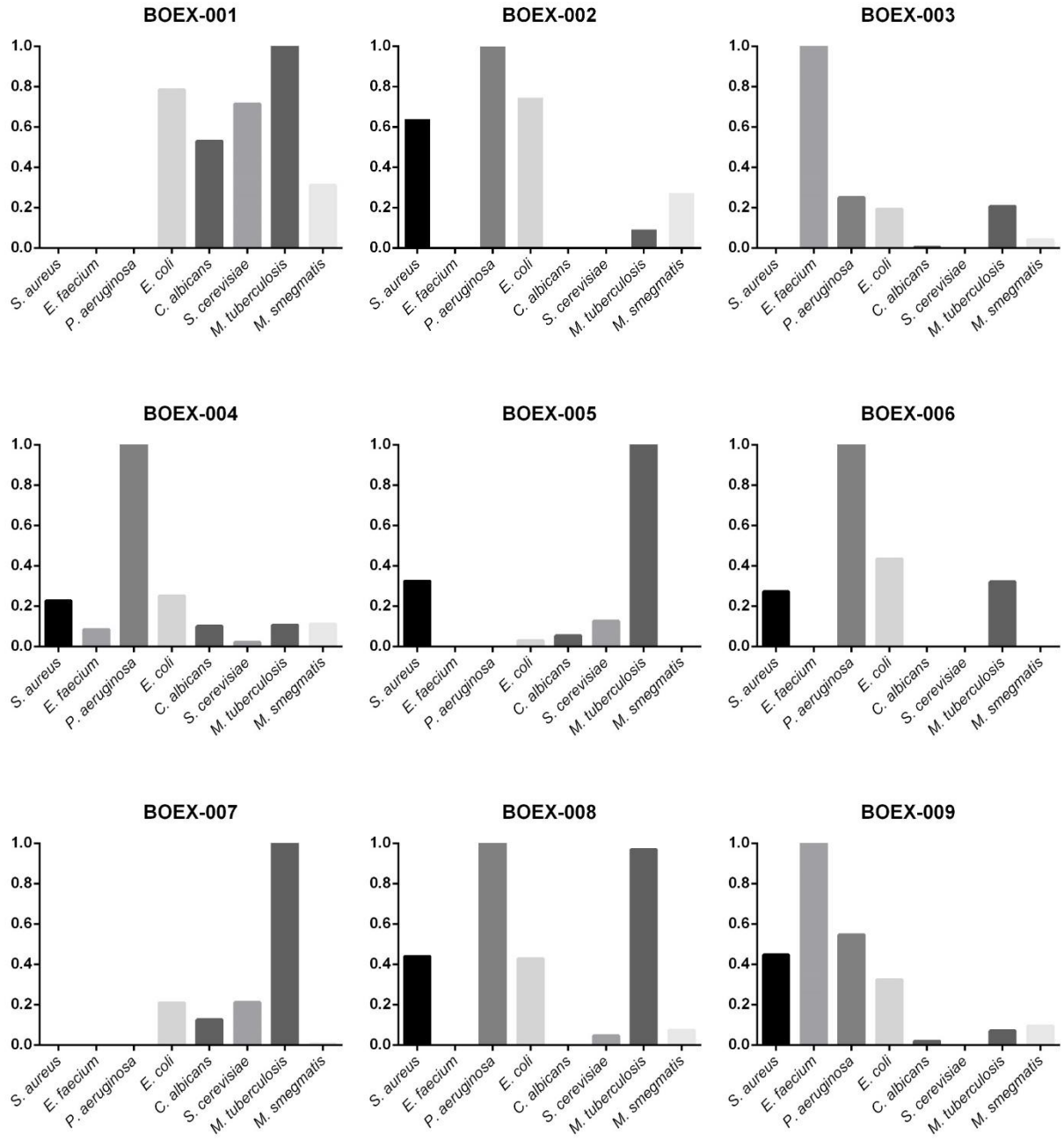

Figure 8. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition values only.

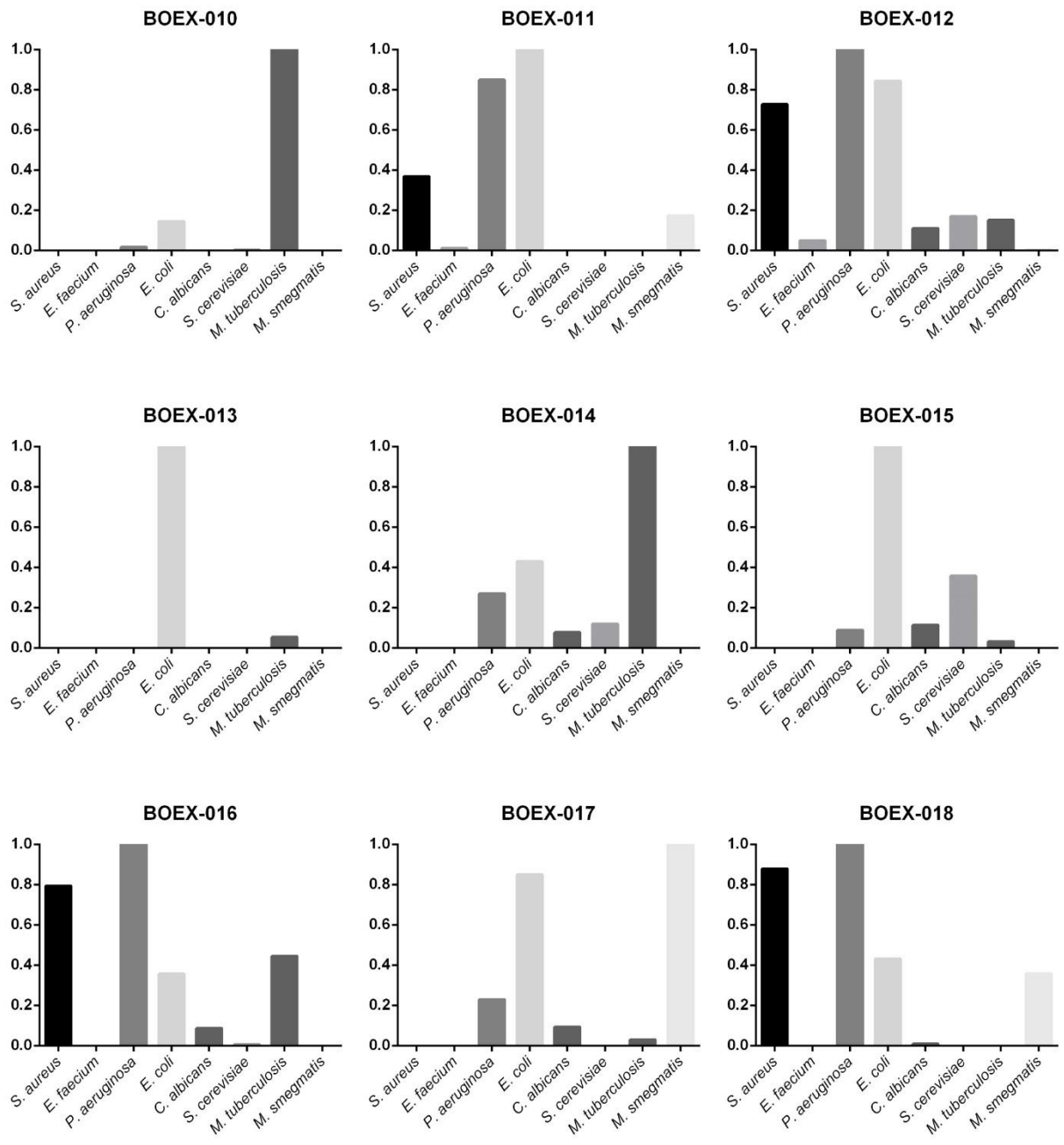

Figure 8. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition values only, continued.

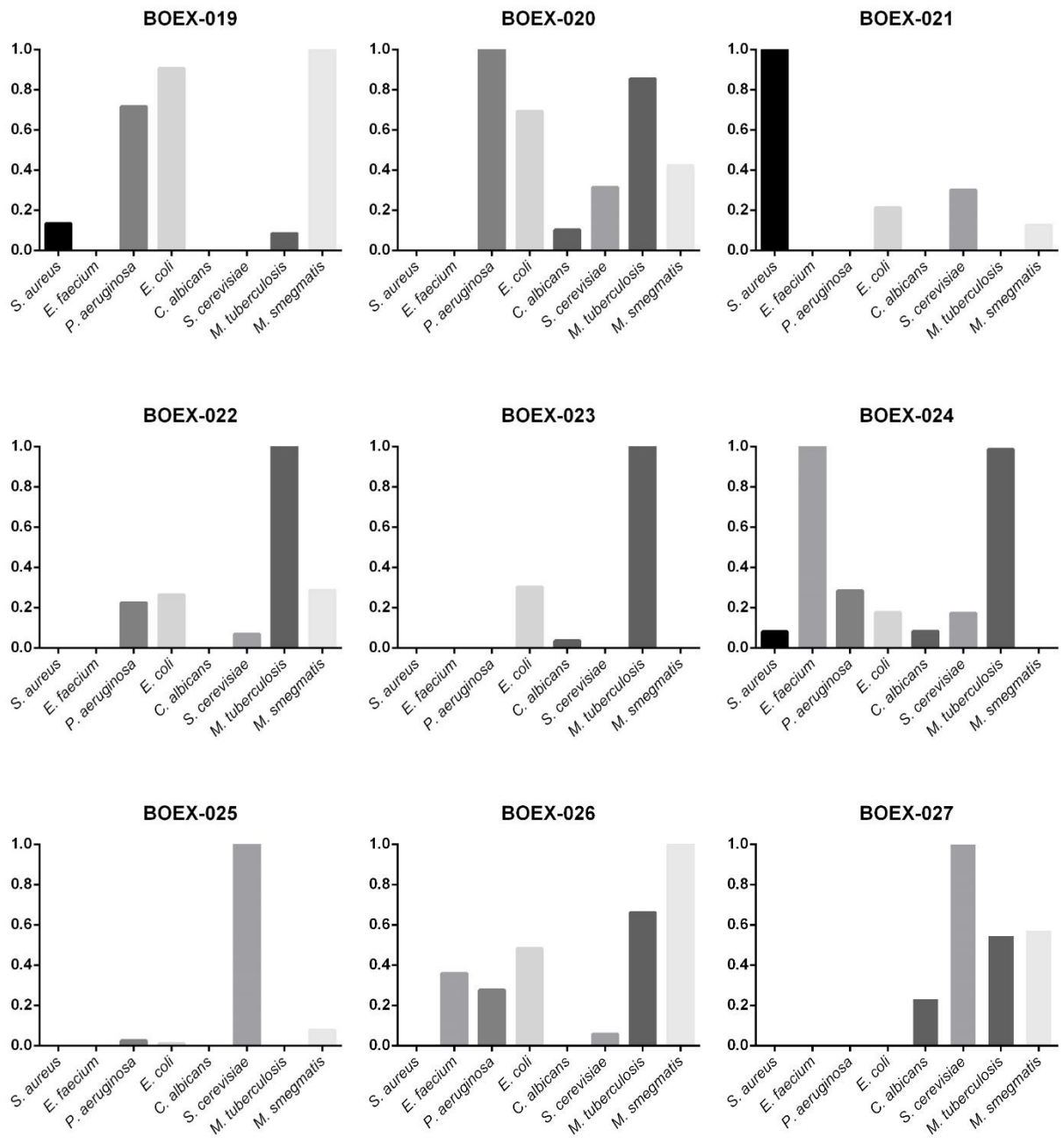

Figure 8. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition values only, continued.

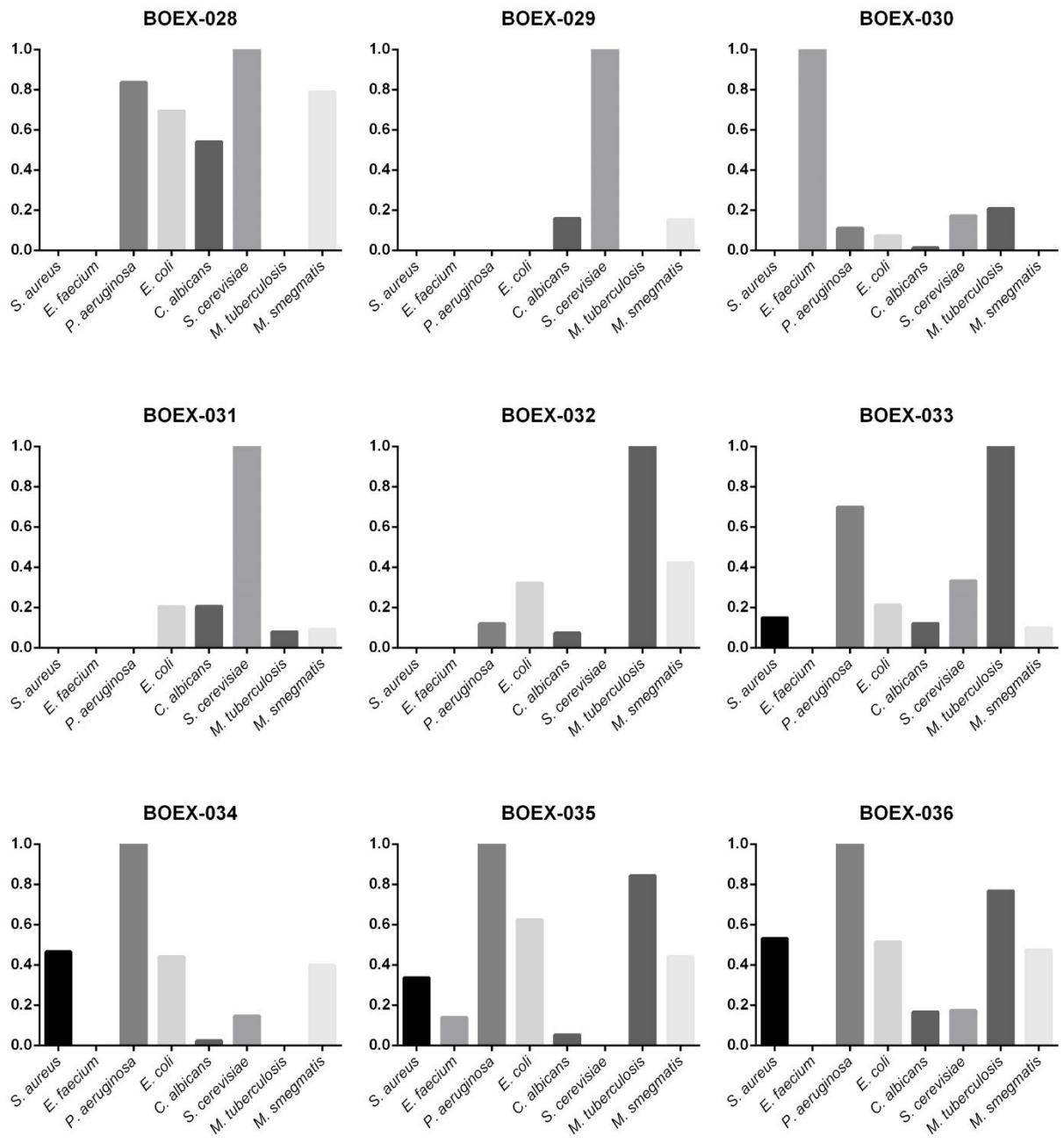

Figure 8. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition values only, continued.

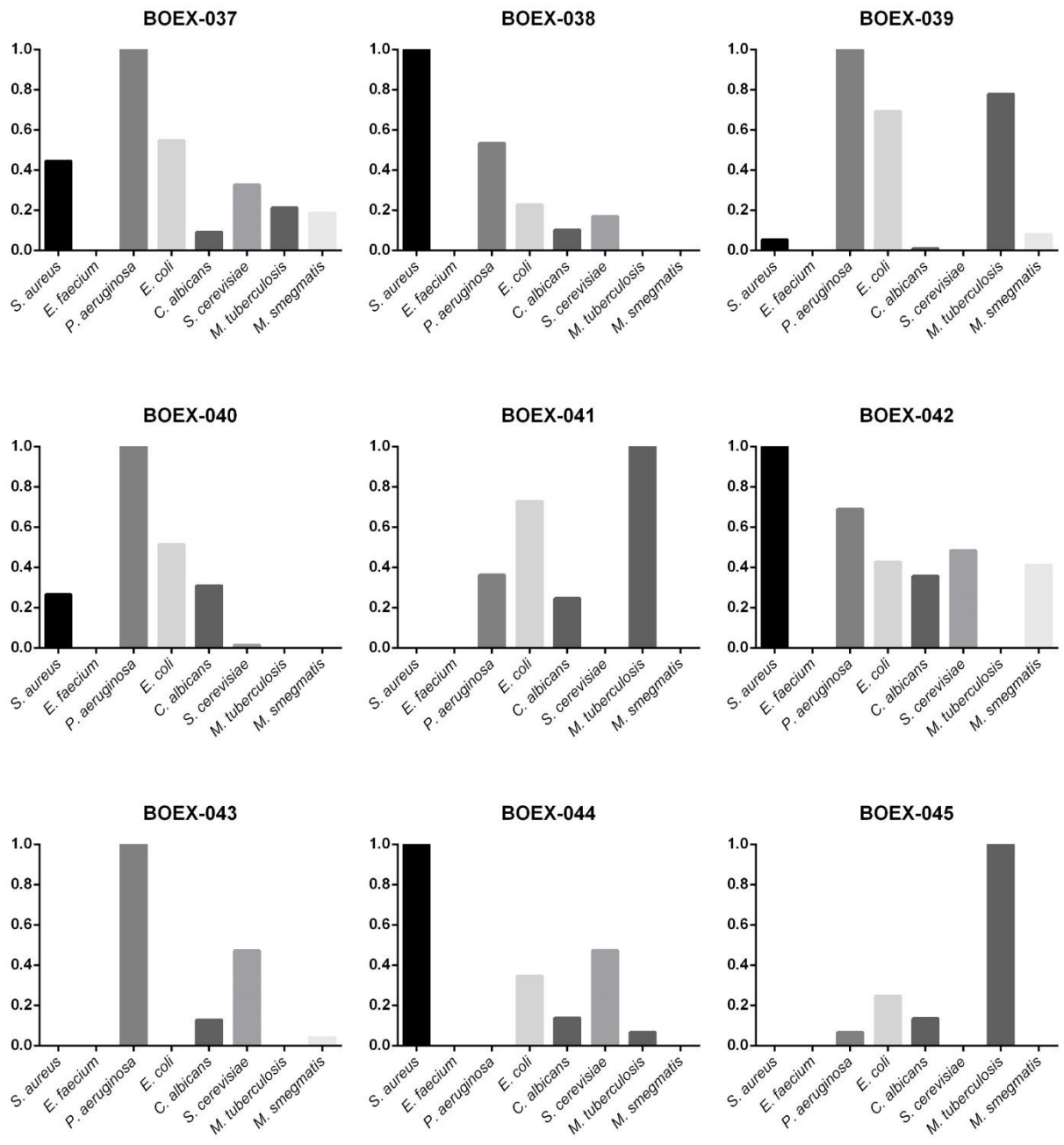

Figure 8. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition values only, continued.

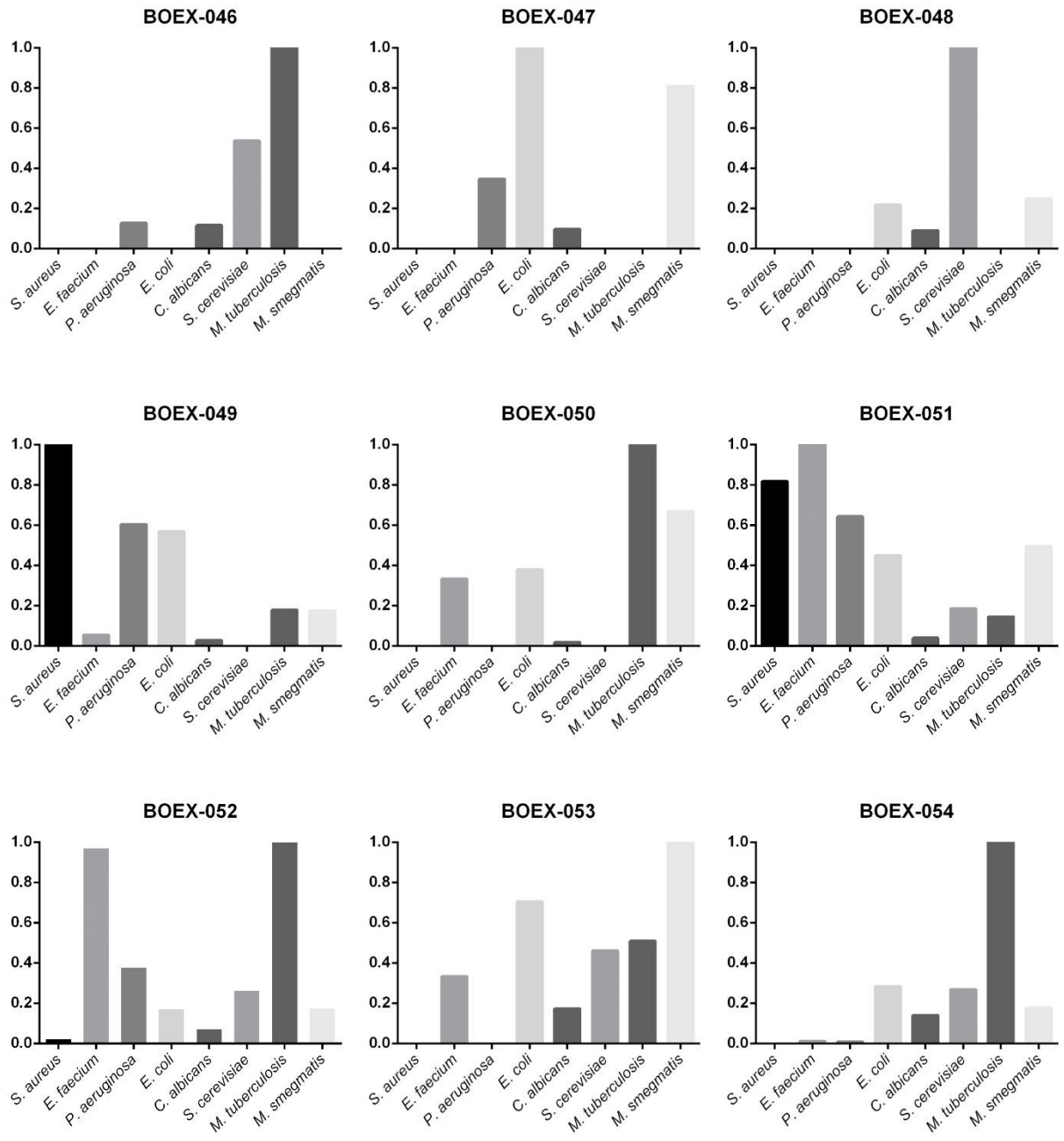

Figure 8. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition values only, continued.

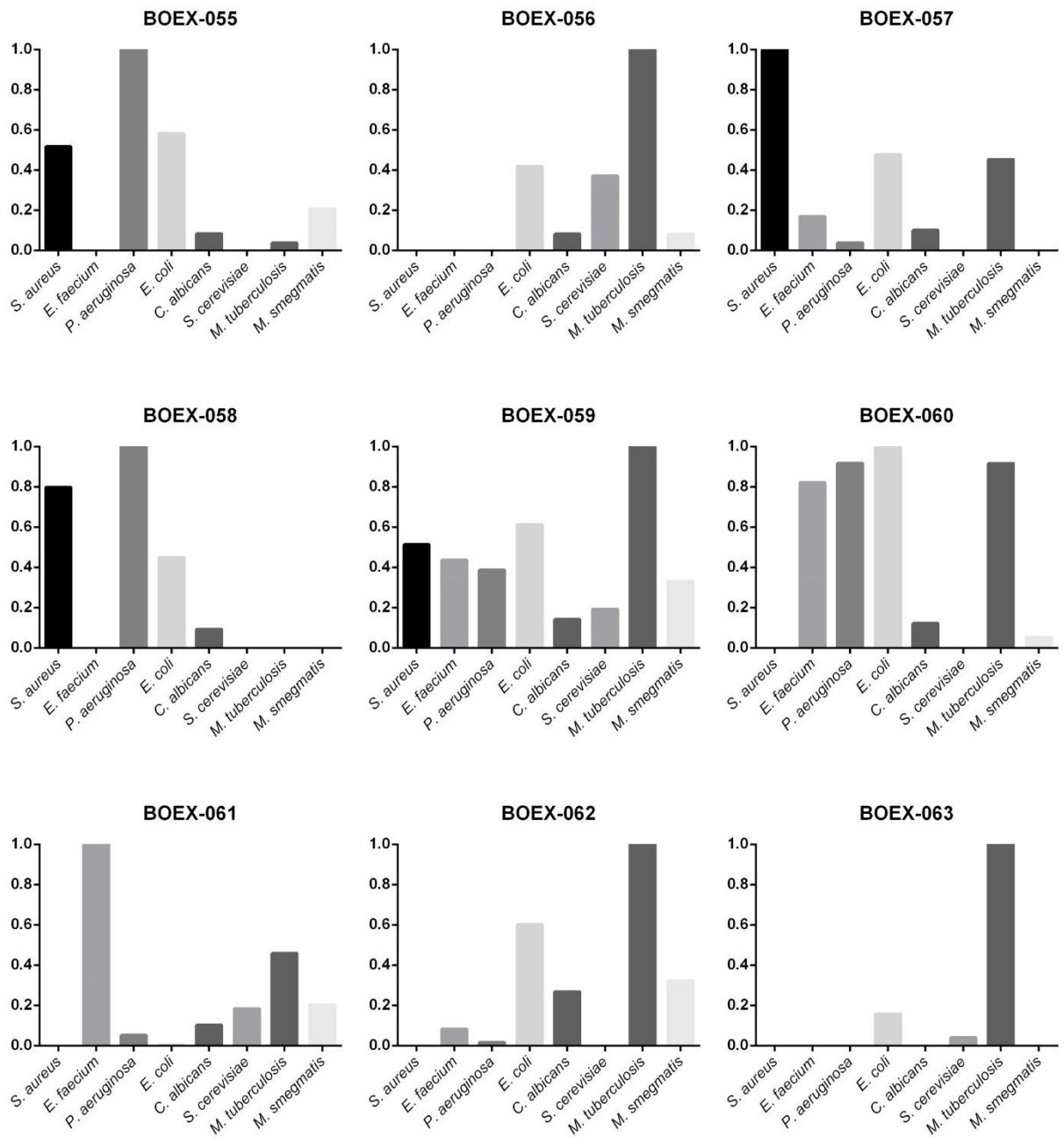

Figure 8. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition values only, continued.

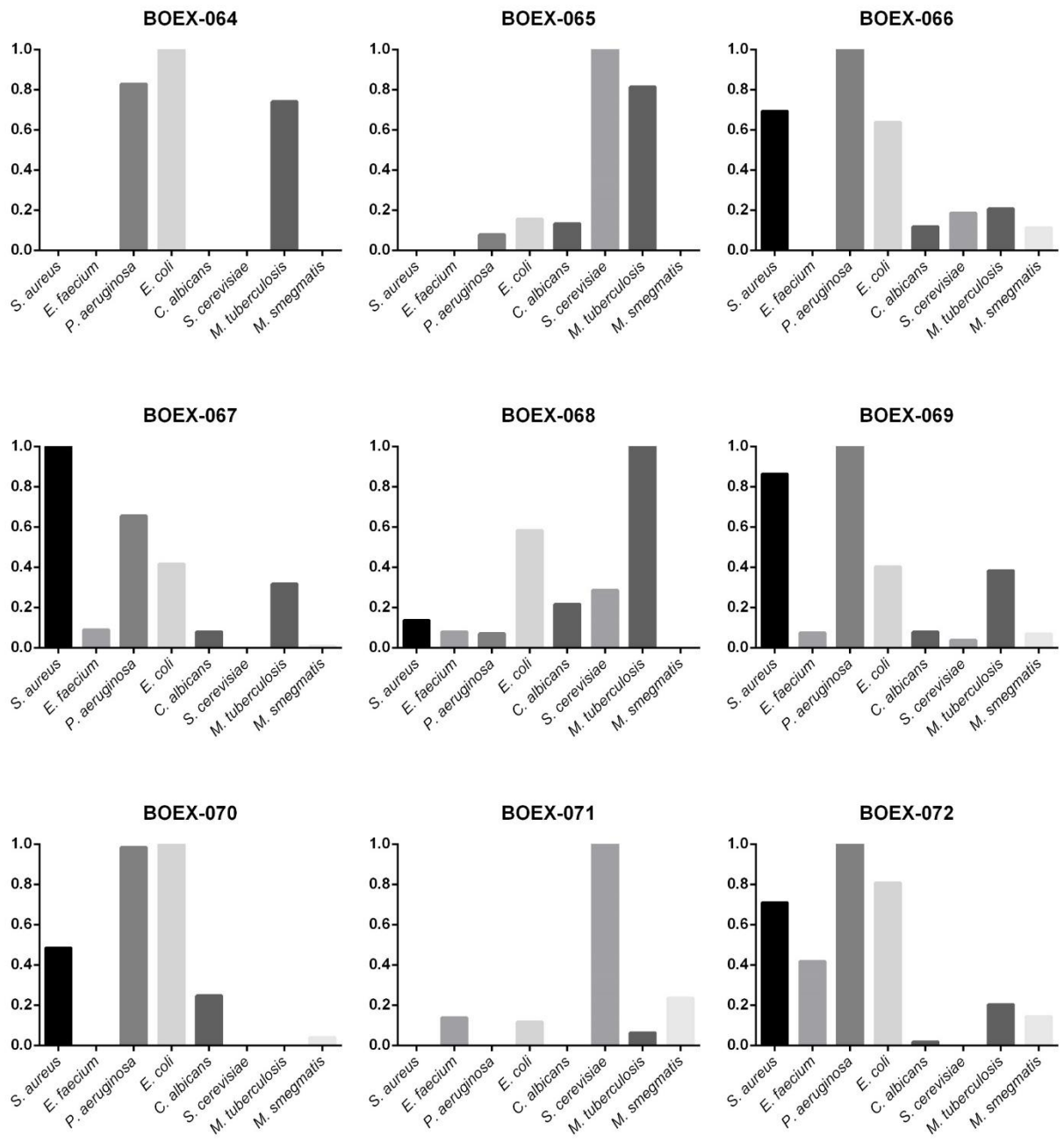

Figure 8. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition values only, continued.

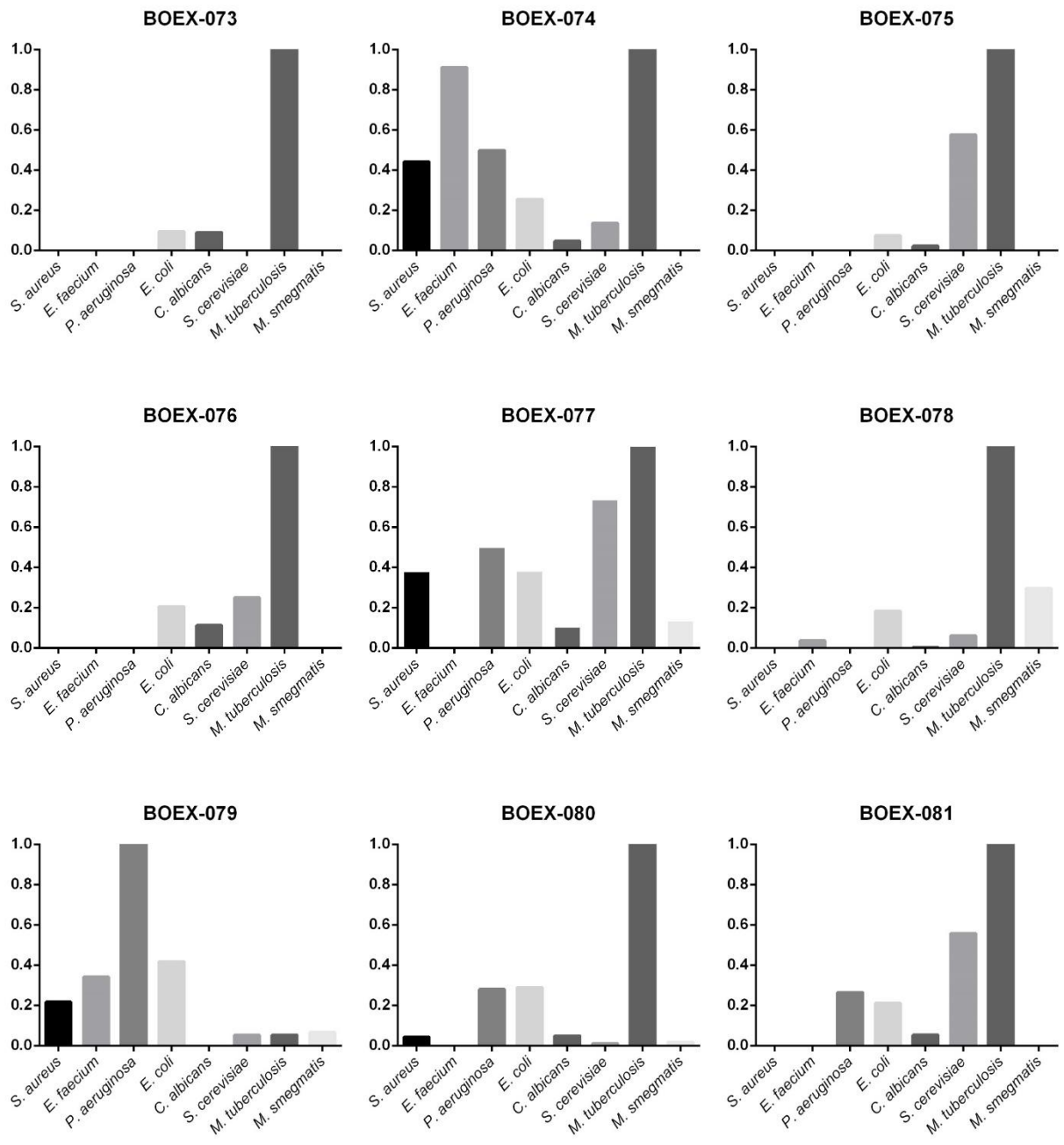

Figure 8. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition values only, continued.

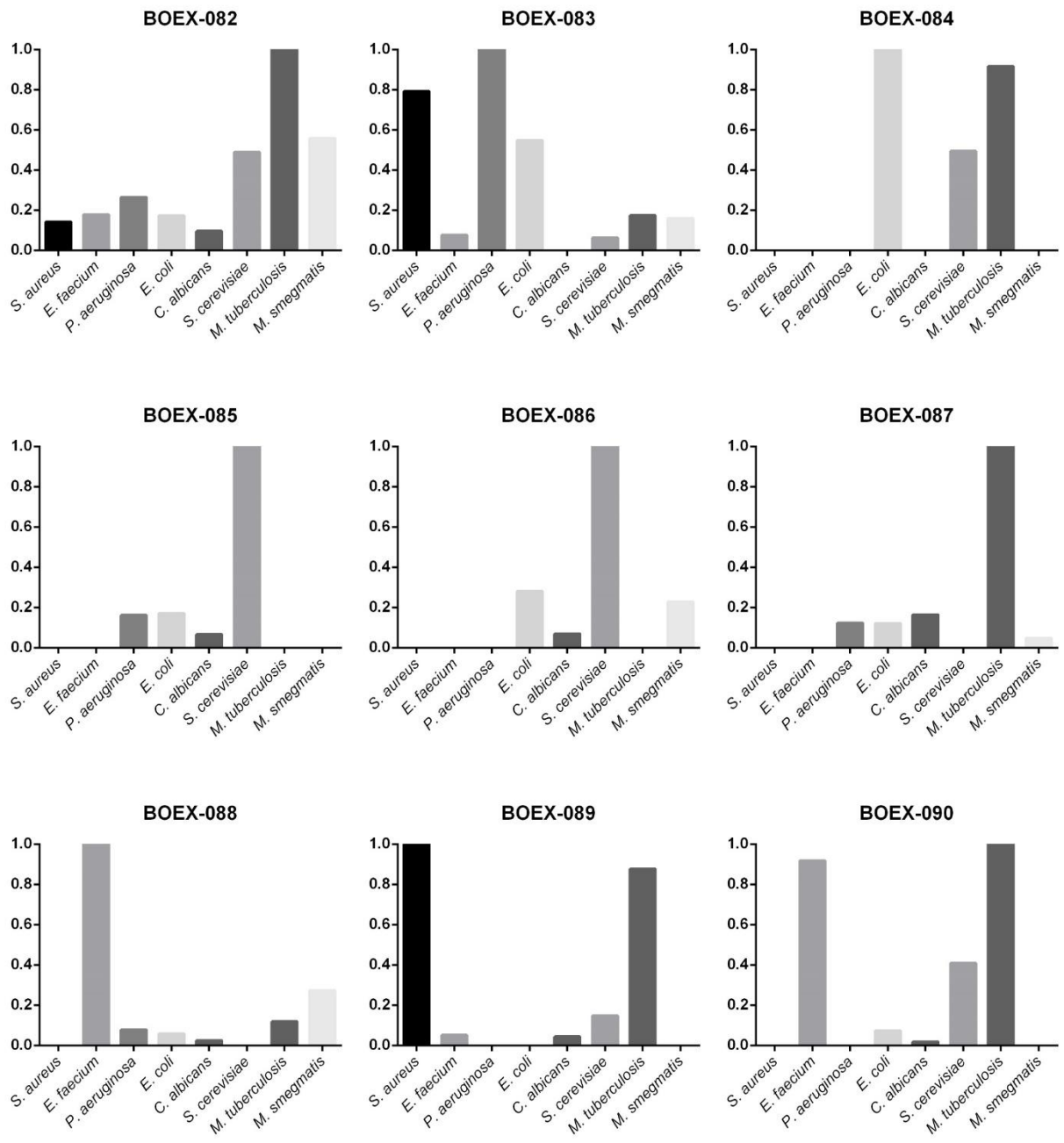

Figure 8. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition values only, continued.

Appendix E: Bioactivity profiles (M2)

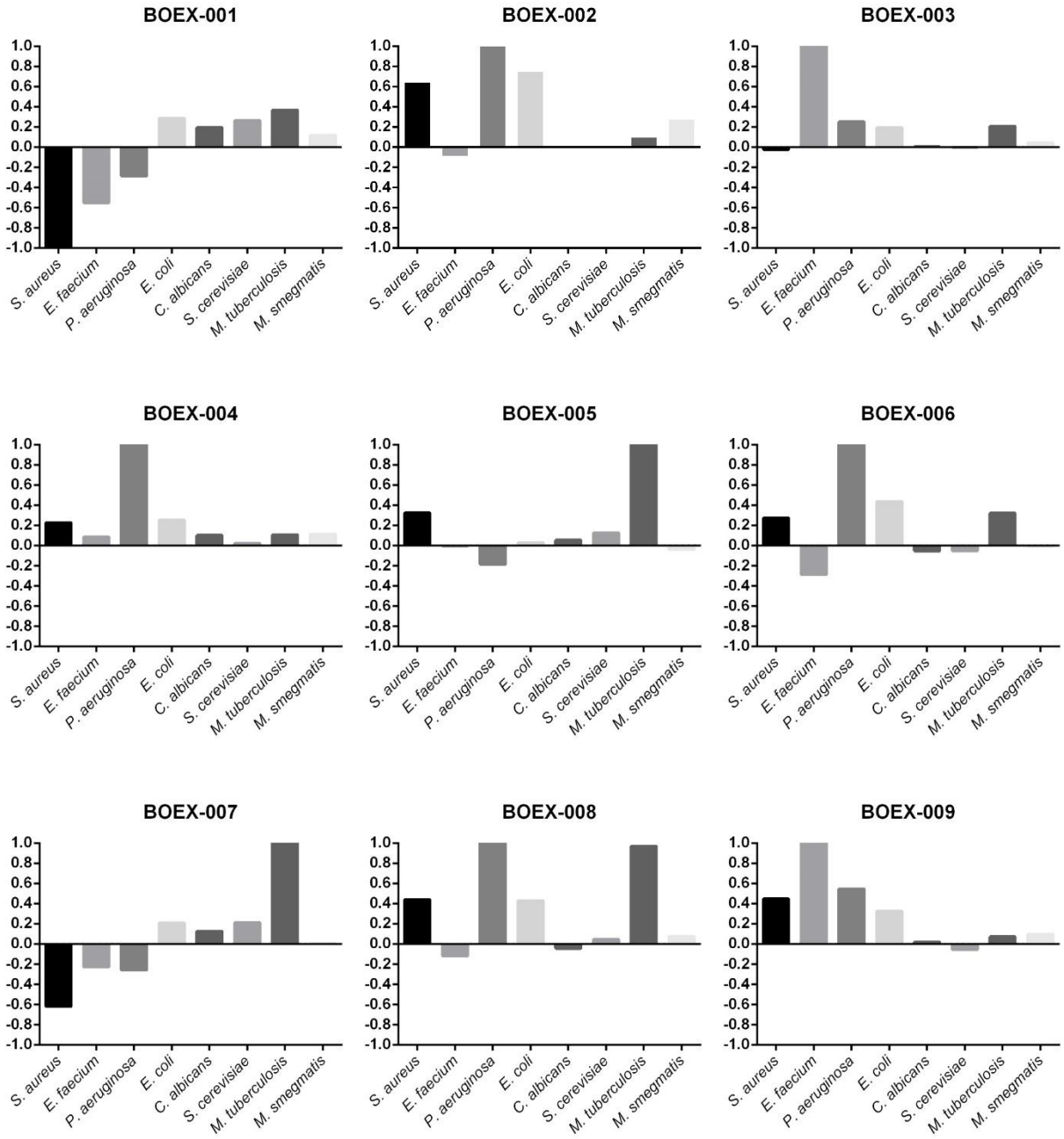

Figure 9. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition and growth promotion values.

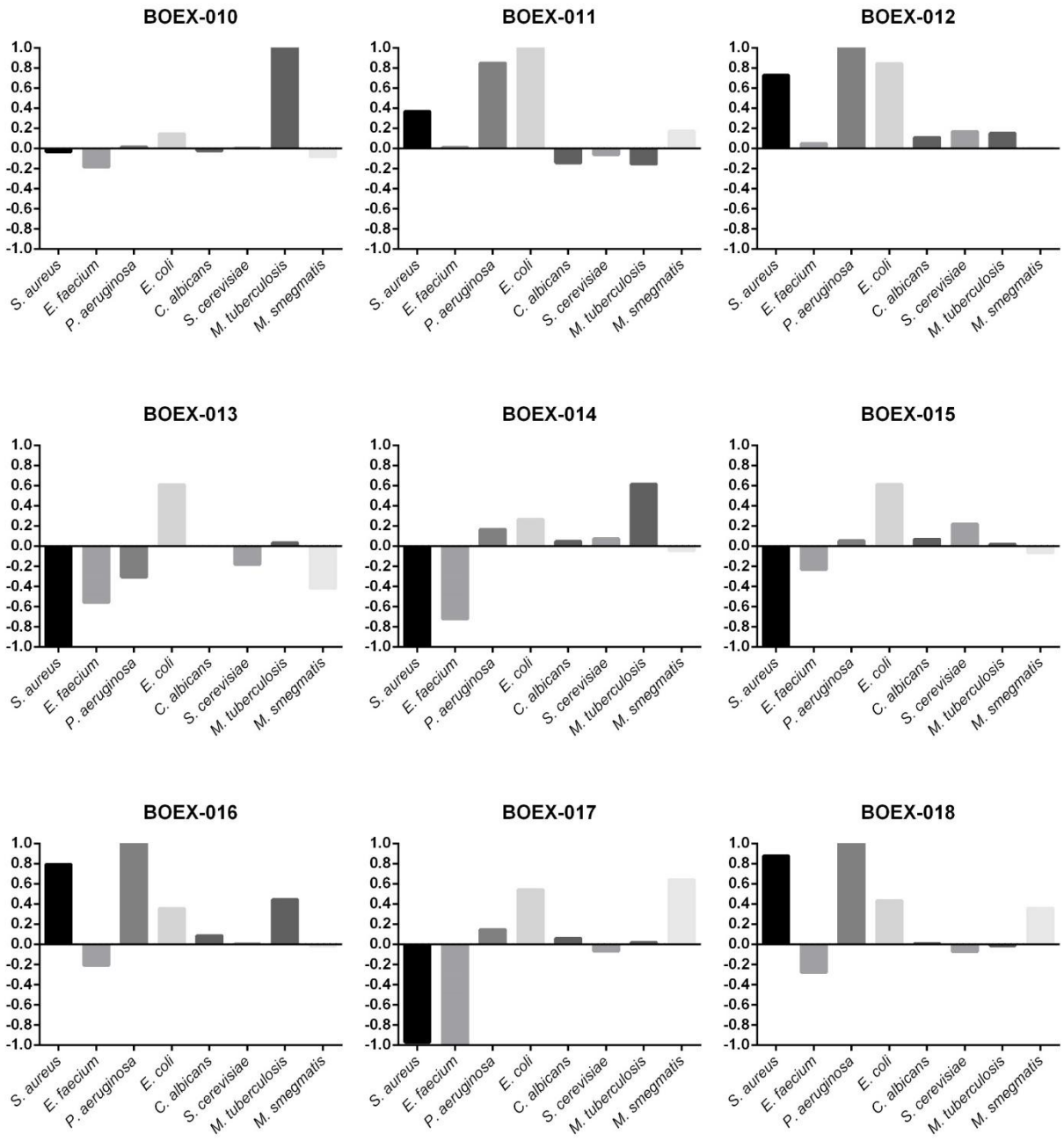

Figure 9. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition and growth promotion values, continued.

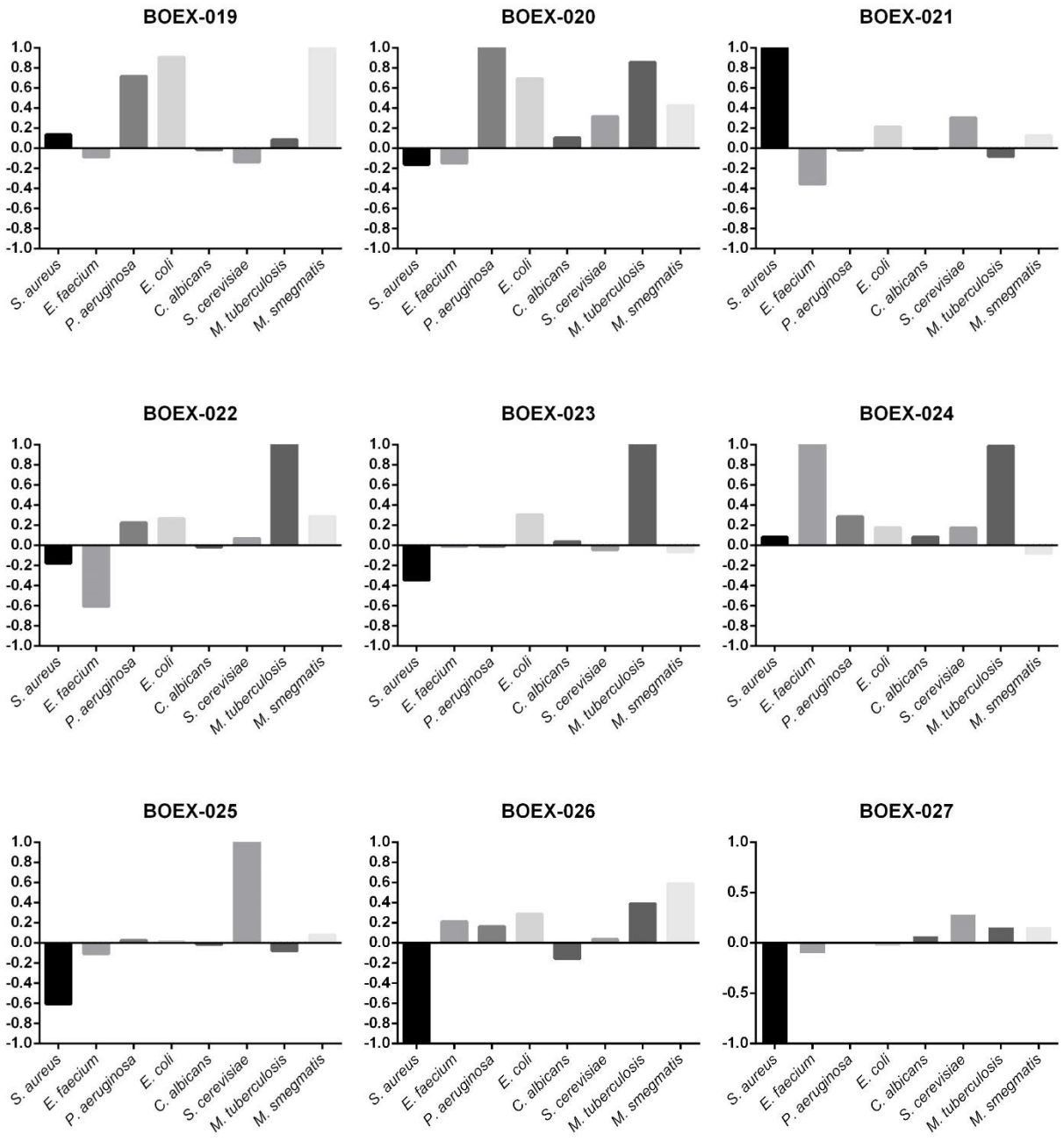

Figure 9. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition and growth promotion values, continued.

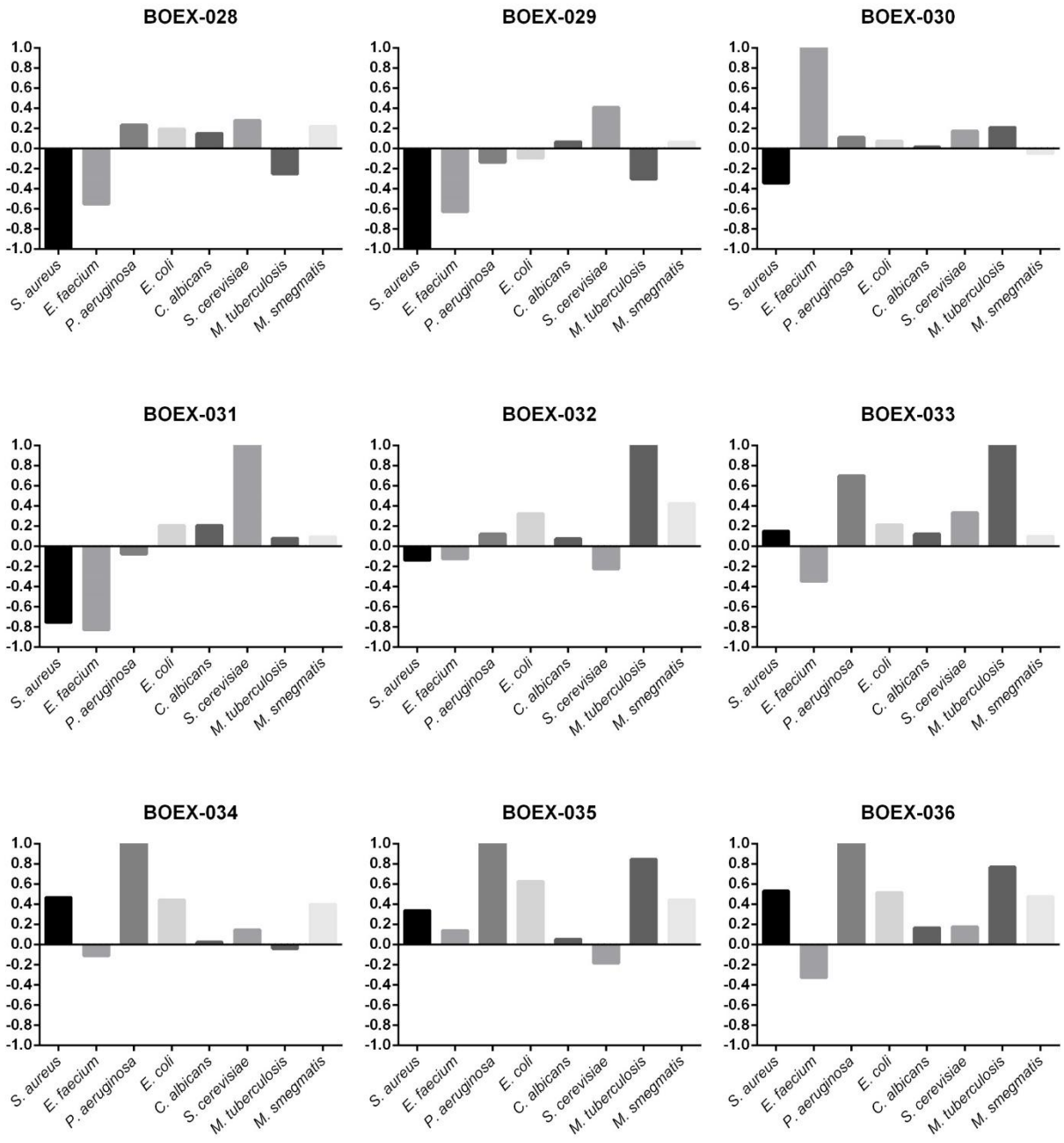

Figure 9. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition and growth promotion values, continued.

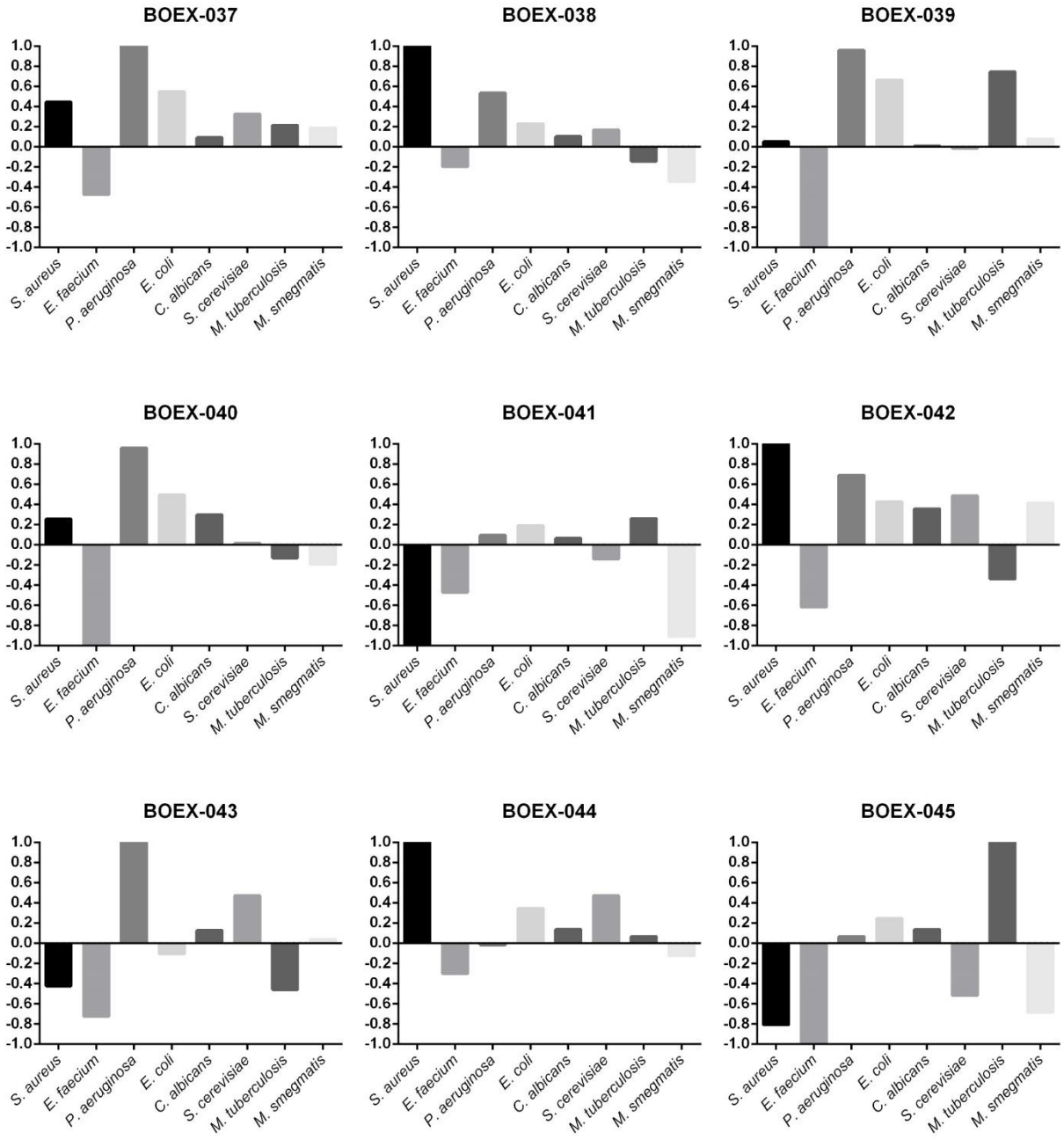

Figure 9. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition and growth promotion values, continued.

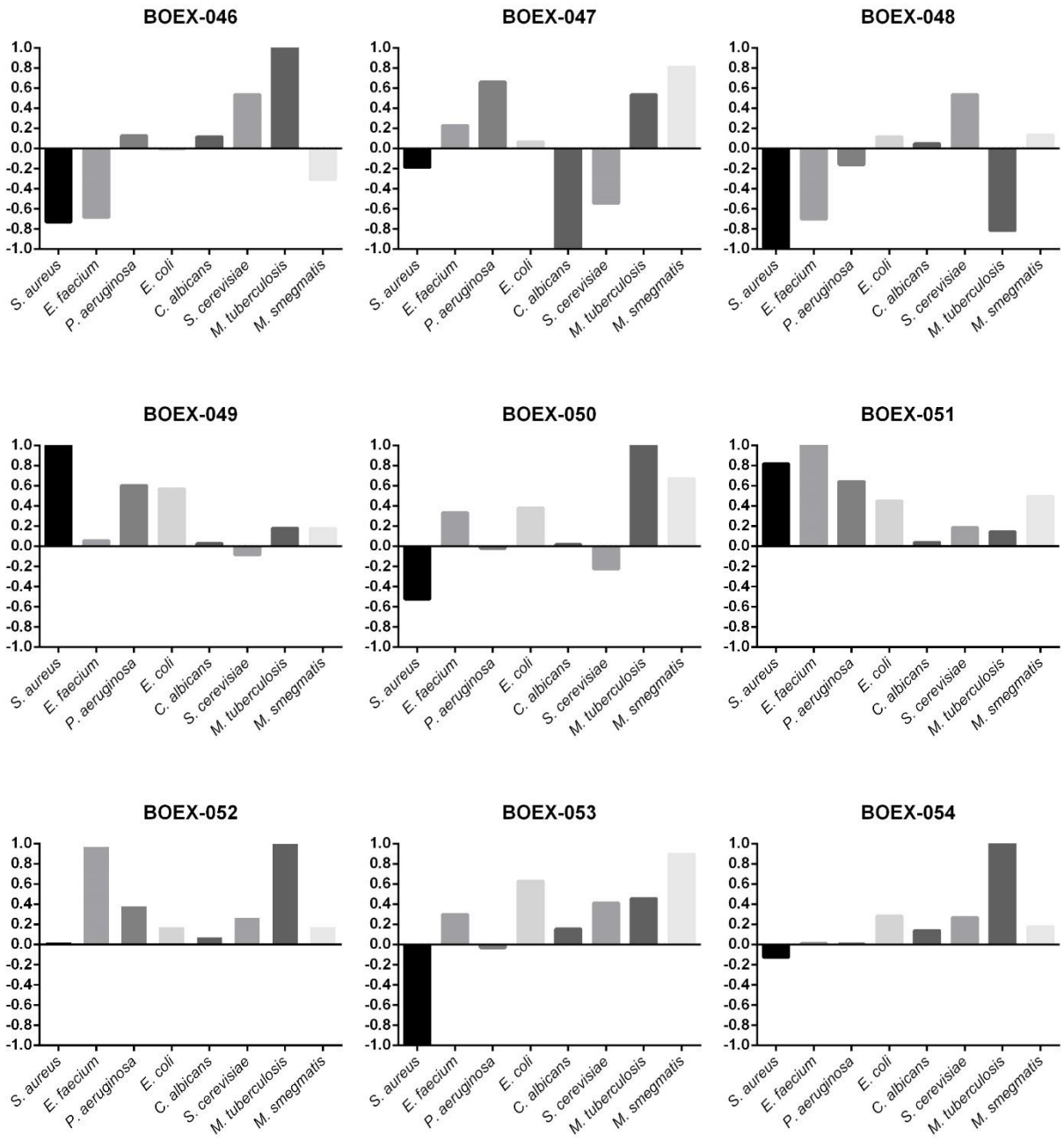

Figure 9. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition and growth promotion values, continued.

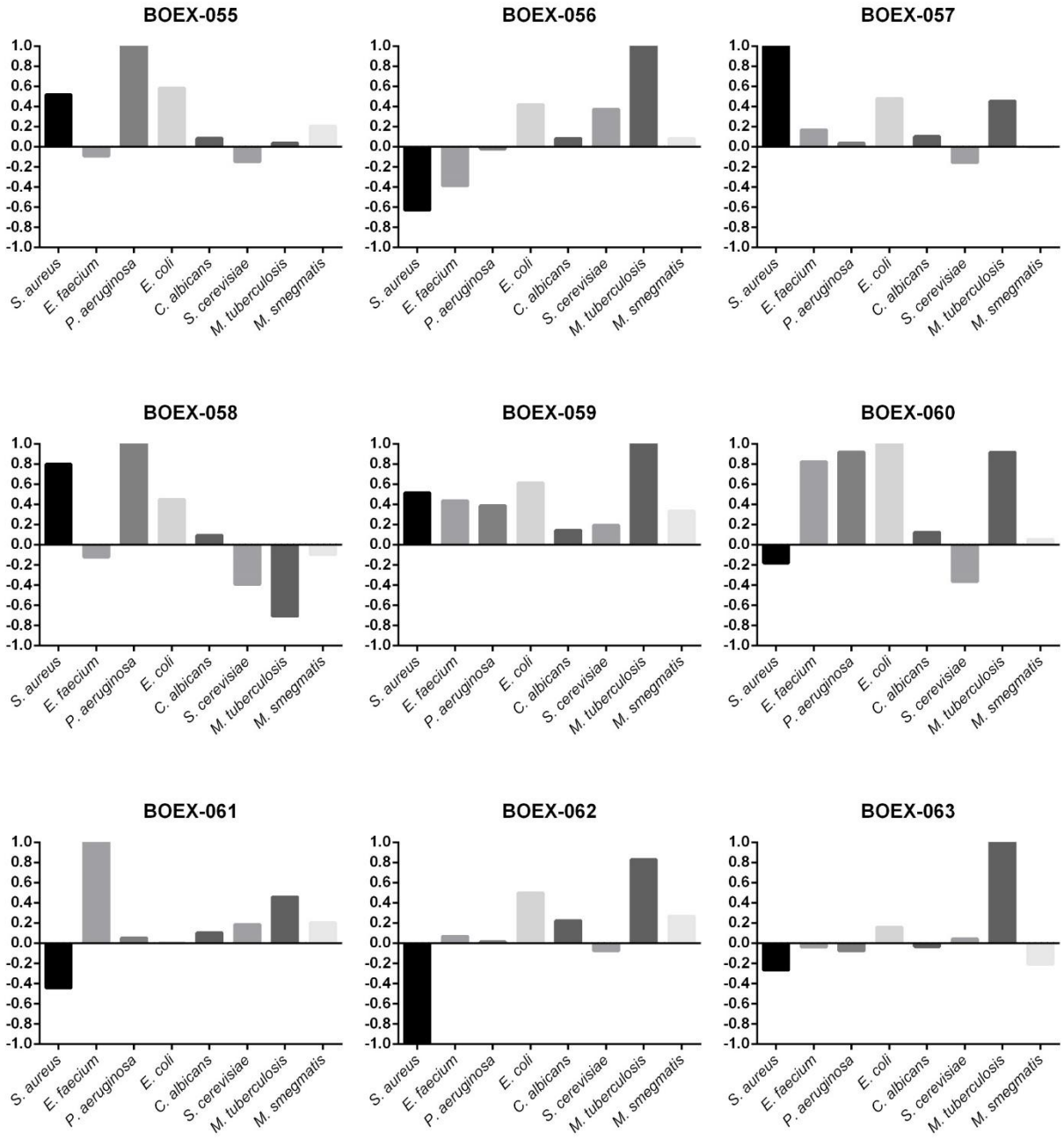

Figure 9. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition and growth promotion values, continued.

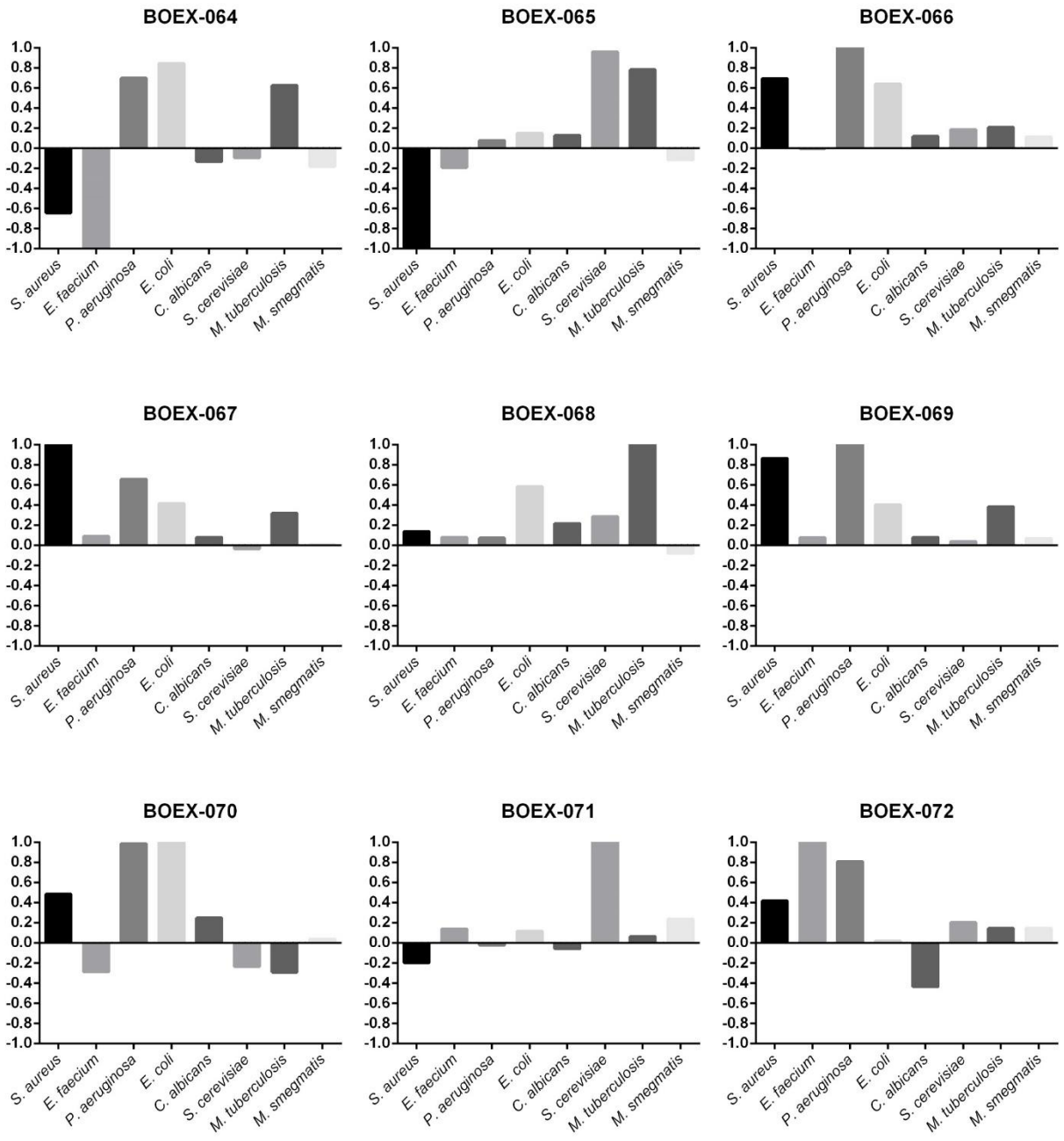

Figure 9. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition and growth promotion values, continued.

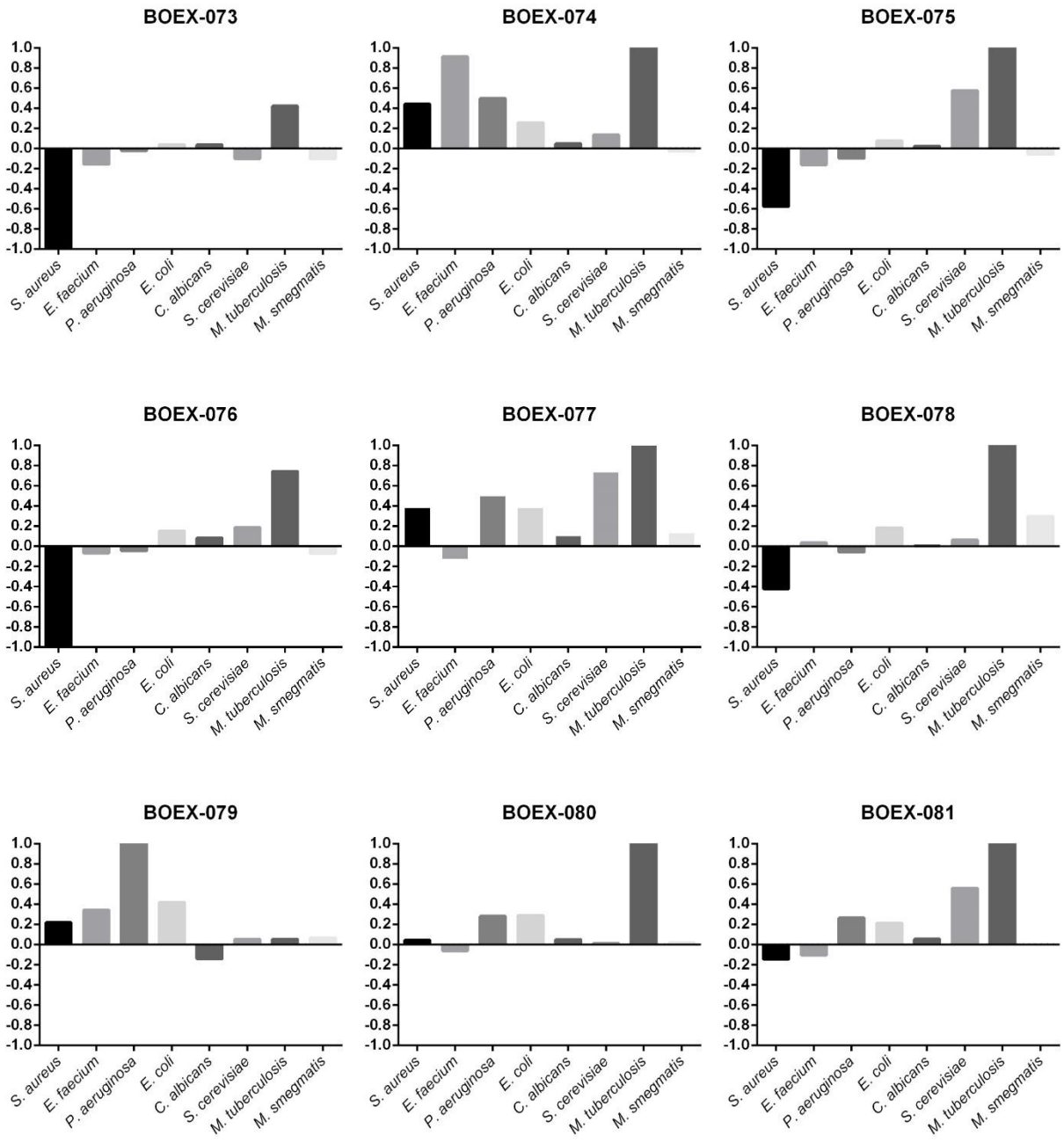

Figure 9. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition and growth promotion values, continued.

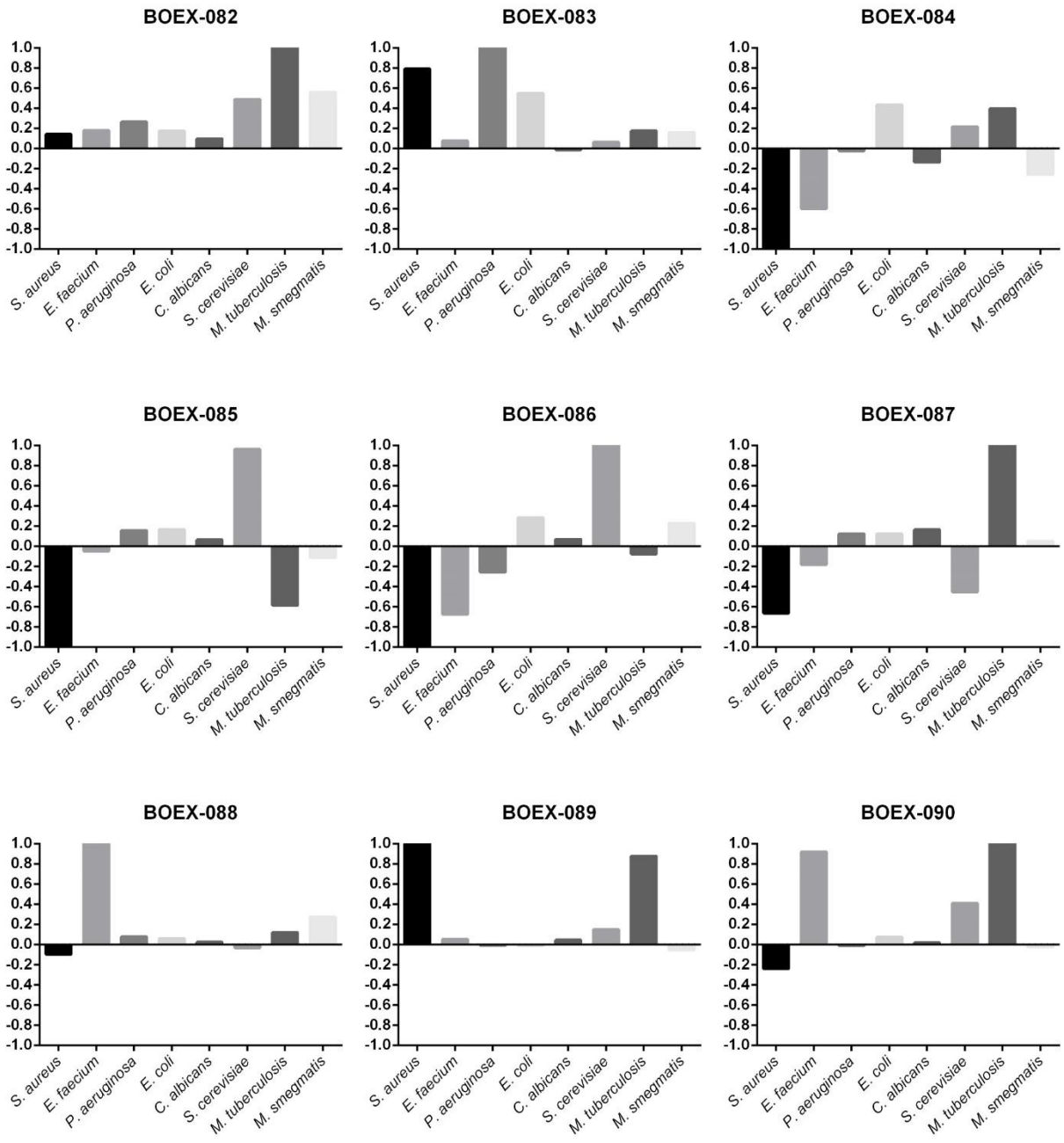

Figure 9. Bioactivity profiles of antibiotic activity Canadian medicinal plants with growth inhibition and growth promotion values, continued.

Appendix F: R Script

```
library(dendextend)

library(NbClust)

#_____________________________________________________________


BOEX_M1 <- read.csv("C:/Users/jkthe/Desktop/BOEX - M1.csv")

BO <- BOEX_M1[,-c(1)]

row.names(BO) <- (BOEX_M1[,1])

d <- dist(BO, method = "euclidean")

fit <- hclust(d, method="ward.D2")

hcd <- as.dendrogram(fit)


NbClust(data=BO, diss = NULL, distance = "euclidean", min.nc = 2, max.nc =

15, method = "ward.D2")


plot(hcd, horiz=TRUE, type = "rectangle")

groups <- cutree(fit, k=7)

hcd %>% rect.dendrogram(k = 7, horiz = TRUE, border = "red")


BOEX_M2 <- read.csv("C:/Users/jkthe/Desktop/BOEX - M2.csv")

BO2 <- BOEX_Class_M2[,-c(1)]

row.names(BO2) <- (BOEX_M2[,1])

d2 <- dist(BO2, method = "euclidean")

fit2 <- hclust(d2, method="ward.D2")

hcd2 <- as.dendrogram(fit2)
```

```
NbClust(data=BO2, diss = NULL, distance = "euclidean", min.nc = 2, max.nc =
15, method = "ward.D2")


plot(hcd2, horiz=TRUE, type = "rectangle")
groups <- cutree(fit2, k=3)
hcd2 %>% rect.dendrogram(k = 3, horiz = TRUE, border = "red")


#_


library(dendextend)
#_____________________________________________________________
#CLASS M1
BOEX_Class_M1 <- read.csv("C:/Users/jkthe/Desktop/BOEX - Class M1.csv")
BO <- BOEX_Class_M1[,-c(1)]
row.names(BO) <- (BOEX_Class_M1[,1])
d <- dist(BO, method = "euclidean")
fit <- hclust(d, method="ward.D2")
hcd <- as.dendrogram(fit)


plot(hcd, horiz=TRUE, type = "rectangle")
groups <- cutree(fit, k=7)
hcd %>% rect.dendrogram(k = 7, horiz = TRUE, border = "red")
legend("topleft", legend = c("Ma = Magnoliopsida", "Ly = Lycopodiopsida",
                             "Pi = Pinopsida", "Po = Polypodiopsida"))
#_____________________________________________________________
#CLASS M2
BOEX_Class_M2 <- read.csv("C:/Users/jkthe/Desktop/BOEX - Class M2.csv")
BO2 <- BOEX_Class_M2[,-c(1)]
```

```
row.names(BO2) <- (BOEX_Class_M2[,1])
d2 <- dist(BO2, method = "euclidean")
fit2 <- hclust(d2, method="ward.D2")
hcd2 <- as.dendrogram(fit2)

plot(hcd2, horiz=TRUE, type = "rectangle")
groups <- cutree(fit, k=3)
hcd %>% rect.dendrogram(k = 3, horiz = TRUE, border = "red")
legend("topleft", legend = c("Ma = Magnoliopsida", "Ly = Lycopodiopsida",
                             "Pi = Pinopsida", "Po = Polypodiopsida"))
#_____________________________________________________________
#ORDER M1
BOEX_Order_M1 <- read.csv("C:/Users/jkthe/Desktop/BOEX - Order M1.csv")
BO3 <- BOEX_Order_M1[,-c(1)]
row.names(BO3) <- (BOEX_Order_M1[,1])
d3 <- dist(BO3, method = "euclidean")
fit3 <- hclust(d3, method="ward.D2")
hcd3 <- as.dendrogram(fit3)

plot(hcd3, horiz=TRUE, type = "rectangle")
groups <- cutree(fit, k=7)
hcd %>% rect.dendrogram(k = 7, horiz = TRUE, border = "red")
legend("topleft", legend = c("Ac = Acorales", "Al = Alismatales", "Ap =
Apiales",
                             "Aq = Aquifoliales", "Asp = Asparagales", "Ast =
Asterales",
                             "Ca = Caryophyllales", "Co = Cornales", "Di =
Dipsacales",
```

```
                              "Er = Ericales", "Fa = Fagales", "Ge =
Gentianales",
                              "La = Lamiales", "Li = Liliales", "Ly =
Lycopodiales",
                              "Malp = Malpighiales", "Malv = Malvales", "My =
Myrtales",
                              "Ny = Nymphaeales", "Pi = Pinales", "Po =
Poales",
                              "Pol = Polypodiales", "Ra = Ranunculales", "Ro =
Rosales",
                              "Sa = Sapindales", "So = Solanales"))
#_____________________________________________________________
#ORDER M2
BOEX_Order_M2 <- read.csv("C:/Users/jkthe/Desktop/BOEX - Order M2.csv")
BO4<- BOEX_Order_M2[,-c(1)]
row.names(BO4) <- (BOEX_Order_M2[,1])
d4 <- dist(BO4, method = "euclidean")
fit4<- hclust(d4, method="ward.D2")
hcd4 <- as.dendrogram(fit4)

plot(hcd4, horiz=TRUE, type = "rectangle")
groups <- cutree(fit, k=3)
hcd %>% rect.dendrogram(k = 3, horiz = TRUE, border = "red")
legend("topleft", legend = c("Ac = Acorales", "Al = Alismatales", "Ap =
Apiales",
                              "Aq = Aquifoliales", "Asp = Asparagales", "Ast =
Asterales",
```

```
                              "Ca = Caryophyllales", "Co = Cornales", "Di =
Dipsacales",
                              "Er = Ericales", "Fa = Fagales", "Ge =
Gentianales",
                              "La = Lamiales", "Li = Liliales", "Ly =
Lycopodiales",
                              "Malp = Malpighiales", "Malv = Malvales", "My =
Myrtales",
                              "Ny = Nymphaeales", "Pi = Pinales", "Po =
Poales",
                              "Pol = Polypodiales", "Ra = Ranunculales", "Ro =
Rosales",
                              "Sa = Sapindales", "So = Solanales"))
#_____________________________________________________________
#FAMILY M1
BOEX_Family_M1 <- read.csv("C:/Users/jkthe/Desktop/BOEX - Family M1.csv")
BO5<- BOEX_Family_M1[,-c(1)]
row.names(BO5) <- (BOEX_Family_M1[,1])
d5 <- dist(BO5, method = "euclidean")
fit5<- hclust(d5, method="ward.D2")
hcd5 <- as.dendrogram(fit5)

plot(hcd5, horiz=TRUE, type = "rectangle")
groups <- cutree(fit, k=7)
hcd %>% rect.dendrogram(k = 7, horiz = TRUE, border = "red")
legend("topleft", legend = c("Ac = Acoraceae", "Ad = Adoxaceae", "Api =
Apiaceae",
```

```
                            "Apo = Aponycaceae", "Aq = Aquifoliaceae", "Arac
= Araceae",
                            "Aral = Araliaceae", "Asp = Asparagaceae", "Ast
= Asteraceae",
                            "Ba = Balsaminaceae", "Ber = Berberidaceae",
"Bet = Betulaceae",
                            "Ca = Caprifoliaceae", "Co = Cornaceae", "Cu =
Cupressaceae",
                            "Cy = Cyperaceae", "De = Dennstaedtiaceae", "Er
= Ericaceae",
                            "Fa = Fagaceae", "Hy = Hypericaceae", "Ir =
Iridaceae",
                            "La = Lamiaceae", "Li = Liliaceae", "Ly =
Lycopodiaceae",
                            "Ma = Malvaceae", "Ny = Nymphaeaceae", "On =
Onagraceae",
                            "Orc = Orchidaceae", "Oro = Orobanchaceae", "Pi
= Pinaceae",
                            "Pl = Plantaginaceae", "Po = Polygonaceae",
"Polp = Polypodiaceae",
                            "Ra = Ranunculaceae", "Ro = Rosaceae", "Ru =
Rubiaceae",
                            "Sal = Salicaceae", "Sap = Sapindaceae","Sar =
Sarraceniaceae",
                            "Sc = Scrophulariaceae", "So = Solanaceae", "Ta
= Taxaceae",
                            "Th = Thymelaeaceae", "Ty = Typhaceae"))
#_____________________________________________________________
```

```
#FAMILY 2
BOEX_Family_M2 <- read.csv("C:/Users/jkthe/Desktop/BOEX - Family M2.csv")
BO6<- BOEX_Family_M2[,-c(1)]
row.names(BO6) <- (BOEX_Family_M2[,1])
d6 <- dist(BO6, method = "euclidean")
fit6<- hclust(d6, method="ward.D2")
hcd6 <- as.dendrogram(fit6)

plot(hcd6, horiz=TRUE, type = "rectangle")
groups <- cutree(fit, k=3)
hcd %>% rect.dendrogram(k = 3, horiz = TRUE, border = "red")
legend("topleft", legend = c("Ac = Acoraceae", "Ad = Adoxaceae", "Api =
Apiaceae",
                             "Apo = Aponycaceae", "Aq = Aquifoliaceae", "Arac
= Araceae",
                             "Aral = Araliaceae", "Asp = Asparagaceae", "Ast
= Asteraceae",
                             "Ba = Balsaminaceae", "Ber = Berberidaceae",
"Bet = Betulaceae",
                             "Ca = Caprifoliaceae", "Co = Cornaceae", "Cu =
Cupressaceae",
                             "Cy = Cyperaceae", "De = Dennstaedtiaceae", "Er
= Ericaceae",
                             "Fa = Fagaceae", "Hy = Hypericaceae", "Ir =
Iridaceae",
                             "La = Lamiaceae", "Li = Liliaceae", "Ly =
Lycopodiaceae",
```

```
                              "Ma = Malvaceae", "Ny = Nymphaeaceae", "On =
Onagraceae",
                              "Orc = Orchidaceae", "Oro = Orobanchaceae", "Pi
= Pinaceae",
                              "Pl = Plantaginaceae", "Po = Polygonaceae",
"Polp = Polypodiaceae",
                              "Ra = Ranunculaceae", "Ro = Rosaceae", "Ru =
Rubiaceae",
                              "Sal = Salicaceae", "Sap = Sapindaceae","Sar =
Sarraceniaceae",
                              "Sc = Scrophulariaceae", "So = Solanaceae", "Ta
= Taxaceae",
                              "Th = Thymelaeaceae", "Ty = Typhaceae"))

#_

library(dendextend)
library(pvclust)
#_____________________________________________________________
BOEX_M1 <- read.csv("C:/Users/jkthe/Desktop/BOEX - M1.csv")
BO <- BOEX_M1[,-c(1)]
BOE <- t(BO)
result<- pvclust(BOE, method.hclust="ward.D2", method.dist = "euclidean",
nboot=10000)
plot(result)
pvrect(result, alpha=0.95)

BOEX_M2 <- read.csv("C:/Users/jkthe/Desktop/BOEX - M2.csv")
```

```
BO2 <- BOEX_M2[,-c(1)]
BOE2 <- t(BO2)
result2<- pvclust(BOE2, method.hclust="ward.D2", method.dist = "euclidean",
nboot=10000)
plot(result2)
pvrect(result2, alpha=0.95, pv="au")

#_

BOEX_M1 <- read.csv("C:/Users/jkthe/Desktop/BOEX - M1.csv")
BO <- BOEX_M1[,-c(1)]
row.names(BO) <- (BOEX_M1[,1])
d <- dist(BO, method = "euclidean")

mds<- cmdscale(d)
plot(mds, type='n', axes=TRUE, xlab='', ylab='', main='Metric MDS')
text(mds[,1], mds[,2], row.names(BO))

#_____________________________
BOEX_M2 <- read.csv("C:/Users/jkthe/Desktop/BOEX - M2.csv")
BO2 <- BOEX_M2[,-c(1)]
row.names(BO2) <- (BOEX_M2[,1])
d2 <- dist(BO2, method = "euclidean")

mds2<- cmdscale(d2)
plot(mds2, type='n', axes=TRUE, xlab='', ylab='', main='Metric MDS')
text(mds2[,1], mds2[,2], row.names(BO2))
```

```
#_

library(dendextend)

BOEX_Class_M12 <- read.csv("C:/Users/jkthe/Desktop/BOEX - Class M12.csv")
BO <- BOEX_Class_M12[,-c(1)]
d <- dist(BO, method = "euclidean")

my.labels<-rep(NA,90)
my.labels[BOEX_Class_M12[,1]=="Lycopodiopsida"]<-0
my.labels[BOEX_Class_M12[,1]=="Magnoliopsida"]<-1
my.labels[BOEX_Class_M12[,1]=="Pinopsida"]<-2
my.labels[BOEX_Class_M12[,1]=="Polypodiopsida"]<-3

mds<- cmdscale(d)
par(mar=c(5.1, 4.1, 4.1, 8.1), xpd=TRUE)
plot(mds, type='n',xlab='', ylab='', main = 'Metric MDS')
pchs<-c(0:3)
points(mds, pch=my.labels)
legend('topright', inset=c(-0.125,0),legend = levels(BOEX_Class_M12$Class),
pch=pchs, cex = 0.7)

#_____________________________
BOEX_Class_M22 <- read.csv("C:/Users/jkthe/Desktop/BOEX - Class M22.csv")
BO2 <- BOEX_Class_M22[,-c(1)]
d2 <- dist(BO2, method = "euclidean")

mds2<- cmdscale(d2)
```

```
par(mar=c(5.1, 4.1, 4.1, 8.1), xpd=TRUE)
plot(mds2, type='n', xlab='', ylab='', main = 'Metric MDS')
pchs2<-c(0:3)
points(mds2, pch=my.labels)
legend('topright', inset=c(-0.125,0),legend = levels(BOEX_Class_M22$Class),
pch=pchs2, cex = 0.7)

#____________________
BOEX_Order_M12 <- read.csv("C:/Users/jkthe/Desktop/BOEX - Order M12.csv")
BO3 <- BOEX_Order_M12[,-c(1)]
d3 <- dist(BO3, method = "euclidean")

my.labels3<-rep(NA,90)
my.labels3[BOEX_Order_M12[,1]=="Acorales"]<-0
my.labels3[BOEX_Order_M12[,1]=="Alismatales"]<-1
my.labels3[BOEX_Order_M12[,1]=="Apiales"]<-2
my.labels3[BOEX_Order_M12[,1]=="Aquifoliales"]<-3
my.labels3[BOEX_Order_M12[,1]=="Asparagales"]<-4
my.labels3[BOEX_Order_M12[,1]=="Asterales"]<-5
my.labels3[BOEX_Order_M12[,1]=="Caryophyllales"]<-6
my.labels3[BOEX_Order_M12[,1]=="Cornales"]<-7
my.labels3[BOEX_Order_M12[,1]=="Dipsacales"]<-8
my.labels3[BOEX_Order_M12[,1]=="Ericales"]<-9
my.labels3[BOEX_Order_M12[,1]=="Fagales"]<-10
my.labels3[BOEX_Order_M12[,1]=="Gentianales"]<-11
my.labels3[BOEX_Order_M12[,1]=="Lamiales"]<-12
my.labels3[BOEX_Order_M12[,1]=="Liliales"]<-13
my.labels3[BOEX_Order_M12[,1]=="Lycopodiales"]<-14
```

```
my.labels3[BOEX_Order_M12[,1]=="Malpighiales"]<-15
my.labels3[BOEX_Order_M12[,1]=="Malvales"]<-16
my.labels3[BOEX_Order_M12[,1]=="Myrtales"]<-17
my.labels3[BOEX_Order_M12[,1]=="Nymphaeales"]<-18
my.labels3[BOEX_Order_M12[,1]=="Pinales"]<-19
my.labels3[BOEX_Order_M12[,1]=="Poales"]<-20
my.labels3[BOEX_Order_M12[,1]=="Polypodiales"]<-21
my.labels3[BOEX_Order_M12[,1]=="Ranunculales"]<-22
my.labels3[BOEX_Order_M12[,1]=="Rosales"]<-23
my.labels3[BOEX_Order_M12[,1]=="Sapindales"]<-24
my.labels3[BOEX_Order_M12[,1]=="Solanales"]<-25

mds3<- cmdscale(d3)
par(mar=c(5.1, 4.1, 4.1, 8.1), xpd=TRUE)
plot(mds3, type='n', xlab='', ylab='', main = 'Metric MDS')
pchs3<-c(0:25)
points(mds3, pch=my.labels3)
legend('topright', inset=c(-0.125,0),legend = levels(BOEX_Order_M12$Order),
pch=pchs3, cex = 0.7)

#_______________________________
BOEX_Order_M22 <- read.csv("C:/Users/jkthe/Desktop/BOEX - Order M22.csv")
BO4 <- BOEX_Order_M22[,-c(1)]
d4 <- dist(BO4, method = "euclidean")

mds4<- cmdscale(d4)
par(mar=c(5.1, 4.1, 4.1, 8.1), xpd=TRUE)
plot(mds4, type='n', xlab='', ylab='', main = 'Metric MDS')
```

```
pchs4<-c(0:25)
points(mds4, pch=my.labels3)
legend('topright', inset=c(-0.125,0),legend = levels(BOEX_Order_M22$Order),
pch=pchs4, cex = 0.7)

#_____________________________
BOEX_Family_M12 <- read.csv("C:/Users/jkthe/Desktop/BOEX - Family M12.csv")
BO5 <- BOEX_Family_M12[,-c(1)]
d5 <- dist(BO5, method = "euclidean")

my.labels5<-rep(NA,90)
my.labels5[BOEX_Family_M12[,1]=="Acoraceae"]<-0
my.labels5[BOEX_Family_M12[,1]=="Adoxaceae"]<-1
my.labels5[BOEX_Family_M12[,1]=="Apiaceae"]<-2
my.labels5[BOEX_Family_M12[,1]=="Apocynaceae"]<-3
my.labels5[BOEX_Family_M12[,1]=="Aquifoliaceae"]<-4
my.labels5[BOEX_Family_M12[,1]=="Araceae"]<-5
my.labels5[BOEX_Family_M12[,1]=="Araliaceae"]<-6
my.labels5[BOEX_Family_M12[,1]=="Asparagaceae"]<-7
my.labels5[BOEX_Family_M12[,1]=="Asteraceae"]<-8
my.labels5[BOEX_Family_M12[,1]=="Balsaminaceae"]<-9
my.labels5[BOEX_Family_M12[,1]=="Berberidaceae"]<-10
my.labels5[BOEX_Family_M12[,1]=="Betulaceae"]<-11
my.labels5[BOEX_Family_M12[,1]=="Caprifoliaceae"]<-12
my.labels5[BOEX_Family_M12[,1]=="Cornaceae"]<-13
my.labels5[BOEX_Family_M12[,1]=="Cupressaceae"]<-14
my.labels5[BOEX_Family_M12[,1]=="Cyperaceae"]<-15
my.labels5[BOEX_Family_M12[,1]=="Dennstaedtiaceae"]<-16
```

```
my.labels5[BOEX_Family_M12[,1]=="Ericaceae"]<-17
my.labels5[BOEX_Family_M12[,1]=="Fagaceae"]<-18
my.labels5[BOEX_Family_M12[,1]=="Hypericaceae"]<-19
my.labels5[BOEX_Family_M12[,1]=="Iridaceae"]<-20
my.labels5[BOEX_Family_M12[,1]=="Lamiaceae"]<-21
my.labels5[BOEX_Family_M12[,1]=="Liliaceae"]<-22
my.labels5[BOEX_Family_M12[,1]=="Lycopodiaceae"]<-23
my.labels5[BOEX_Family_M12[,1]=="Malvaceae"]<-24
my.labels5[BOEX_Family_M12[,1]=="Nymphaeaceae"]<-25
my.labels5[BOEX_Family_M12[,1]=="Onagraceae"]<-33
my.labels5[BOEX_Family_M12[,1]=="Orchidaceae"]<-34
my.labels5[BOEX_Family_M12[,1]=="Orobanchaceae"]<-35
my.labels5[BOEX_Family_M12[,1]=="Pinaceae"]<-36
my.labels5[BOEX_Family_M12[,1]=="Plantaginaceae"]<-37
my.labels5[BOEX_Family_M12[,1]=="Polygonaceae"]<-38
my.labels5[BOEX_Family_M12[,1]=="Polypodiaceae"]<-39
my.labels5[BOEX_Family_M12[,1]=="Ranunculaceae"]<-40
my.labels5[BOEX_Family_M12[,1]=="Rosaceae"]<-41
my.labels5[BOEX_Family_M12[,1]=="Rubiaceae"]<-42
my.labels5[BOEX_Family_M12[,1]=="Salicaceae"]<-43
my.labels5[BOEX_Family_M12[,1]=="Sapindaceae"]<-44
my.labels5[BOEX_Family_M12[,1]=="Sarraceniceae"]<-45
my.labels5[BOEX_Family_M12[,1]=="Scrophulariaceae"]<-46
my.labels5[BOEX_Family_M12[,1]=="Solanaceae"]<-47
my.labels5[BOEX_Family_M12[,1]=="Taxaceae"]<-48
my.labels5[BOEX_Family_M12[,1]=="Thymelaeaceae"]<-49
my.labels5[BOEX_Family_M12[,1]=="Typhaceae"]<-50
```

```
mds5<- cmdscale(d5)
par(mar=c(5.1, 4.1, 4.1, 8.1), xpd=TRUE)
plot(mds5, type='n', xlab='', ylab='', main = 'Metric MDS')
pchs5<-c(0:25, 33:50)
points(mds5, pch=my.labels5)
legend('topright', inset=c(-0.125,0),legend = levels(BOEX_Family_M12$Family),
pch=pchs5, cex = 0.7)

#_______________________________
BOEX_Family_M22 <- read.csv("C:/Users/jkthe/Desktop/BOEX - Family M22.csv")
BO6 <- BOEX_Family_M22[,-c(1)]
d6 <- dist(BO6, method = "euclidean")

mds6<- cmdscale(d6)
par(mar=c(5.1, 4.1, 4.1, 8.1), xpd=TRUE)
plot(mds6, type='n', xlab='', ylab='', main = 'Metric MDS')
pchs6<-c(0:25, 33:50)
points(mds6, pch=my.labels5)
legend('topright', inset=c(-0.125,0),legend = levels(BOEX_Family_M22$Family),
pch=pchs6, cex = 0.7)
```

Appendix G: R output for NbClust

```
> NbClust(data=BO, diss = NULL, distance = "euclidean", min.nc = 2, max.nc = 15, method = "ward.D2")
*** : The Hubert index is a graphical method of determining the number of clusters.
                In the plot of Hubert index, we seek a significant knee that corresponds to a
                significant increase of the value of the measure i.e the significant peak in Hubert
                index second differences plot.

*** : The D index is a graphical method of determining the number of clusters.
                In the plot of D index, we seek a significant knee (the significant peak in Dindex
                second differences plot) that corresponds to a significant increase of the value of
                the measure.

*******************************************************************
* Among all indices:
* 1 proposed 2 as the best number of clusters
* 2 proposed 3 as the best number of clusters
* 4 proposed 4 as the best number of clusters
* 2 proposed 5 as the best number of clusters
* 5 proposed 7 as the best number of clusters
```

```
* 2 proposed 8 as the best number of clusters

* 2 proposed 9 as the best number of clusters

* 1 proposed 10 as the best number of clusters

* 1 proposed 11 as the best number of clusters

* 3 proposed 15 as the best number of clusters


                   ***** Conclusion *****


* According to the majority rule, the best number of clusters is  7



*******************************************************************

$All.index

       KL      CH Hartigan     CCC     Scott     Marriot  TrCovW  TraceW Friedman   Rubin Cindex     DB

2  1.7881 30.1542  16.9627  8.3023  372.6185 2182538.651 76.7719 56.5944  15.4798  2.6358 0.4844 1.7079

3  0.6414 26.1639  19.3888  7.6816  510.1356 1065508.439 54.6725 47.4483  20.9064  3.1439 0.4415 1.5812

4  0.9794 27.4733  19.8479  9.6047  652.4206  389797.113 35.2444 38.8011  28.9538  3.8446 0.4258 1.1280

5  1.7200 29.9698  13.3412 12.6114  768.6037  167501.154 21.4315 31.5254  35.7776  4.7319 0.4044 1.3915

6  0.9712 30.0495  13.9290 14.8146  853.3917   94023.465 15.6592 27.2486  41.3663  5.4745 0.3886 1.1462
```

7	2.6031	31.1399	7.0281	17.1873	933.1657	52744.940	10.3487	23.3729	48.3328	6.3823	0.3550	1.0716
8	1.0076	29.5946	6.7733	17.0253	988.4391	37277.208	8.4438	21.5483	53.9683	6.9228	0.3782	1.0154
9	0.9868	28.5287	6.7117	17.0054	1064.4253	20280.452	7.4233	19.9042	72.9292	7.4946	0.3716	1.0051
10	0.9346	27.8576	7.0233	17.1264	1119.4377	13587.208	6.4237	18.3811	78.2178	8.1156	0.3582	1.0648
11	0.9450	27.6256	7.4236	17.4505	1165.2500	9882.086	5.7477	16.8976	82.6277	8.8281	0.3242	1.2066
12	1.1276	27.7927	6.8780	17.9722	1218.6984	6493.980	4.9328	15.4462	86.6951	9.6577	0.4110	1.1445
13	1.1036	27.9336	6.4794	18.4258	1287.0270	3567.106	4.0099	14.1945	96.0035	10.5093	0.3824	1.0947
14	1.0436	28.0835	6.3948	18.8400	1349.0340	2077.165	3.4256	13.0928	104.6078	11.3936	0.3884	1.0010
15	1.0573	28.3505	6.2621	19.2883	1393.3457	1457.376	3.0058	12.0766	110.6873	12.3523	0.3811	0.9537

	Silhouette	Duda	Pseudot2	Beale	Ratkowsky	Ball	Ptbiserial	Frey	McClain	Dunn	Hubert	SDindex	Dindex
2	0.2604	0.6762	21.5452	2.4755	0.2807	28.2972	0.4949	0.3019	0.7474	0.2051	0.0287	4.6585	0.7523
3	0.2788	0.3177	34.3583	10.6818	0.2936	15.8161	0.5545	-0.1120	1.1901	0.2051	0.0314	3.9492	0.6739
4	0.3325	0.7433	14.1578	1.7816	0.2977	9.7003	0.5923	0.0913	1.2513	0.2051	0.0329	2.8801	0.5916
5	0.3502	0.6115	8.8947	3.1340	0.3034	6.3051	0.6992	0.0177	1.7542	0.2398	0.0390	3.2321	0.5378
6	0.3486	0.6148	15.6638	3.1841	0.2917	4.5414	0.7274	0.0828	1.8117	0.2447	0.0406	3.1774	0.5005
7	0.3685	0.6415	3.9111	2.5839	0.2784	3.3390	0.7543	0.0796	1.9180	0.2447	0.0424	3.0408	0.4669
8	0.3578	0.6411	4.4792	2.6304	0.2661	2.6935	0.7598	0.2873	1.9369	0.2656	0.0432	2.9269	0.4505
9	0.3632	0.7182	8.2413	1.9799	0.2534	2.2116	0.7583	0.9697	1.9850	0.2656	0.0437	2.7966	0.4302
10	0.3324	0.7692	8.0996	1.5289	0.2439	1.8381	0.7122	0.6804	2.3663	0.1785	0.0452	3.5682	0.4127

11	0.2964	0.4844	4.2577	4.5006	0.2398	1.5361	0.6172	0.0291	3.4852	0.1785	0.0481	4.1744	0.3926
12	0.3107	0.6848	5.0623	2.2296	0.2355	1.2872	0.6211	0.1377	3.4860	0.2297	0.0486	4.2357	0.3769
13	0.3247	1.1032	-0.1872	-0.3297	0.2325	1.0919	0.6177	0.0130	3.6551	0.2297	0.0495	3.7347	0.3620
14	0.3429	0.2704	10.7928	11.4084	0.2315	0.9352	0.6198	0.1002	3.6465	0.2359	0.0498	3.7491	0.3470
15	0.3533	0.6832	6.4905	2.2869	0.2253	0.8051	0.6199	0.2361	3.6704	0.2359	0.0502	3.6212	0.3335

	SDbw
2	0.8161
3	0.7138
4	0.4524
5	0.4780
6	0.4287
7	0.3956
8	0.3753
9	0.3281
10	0.3018
11	0.2907
12	0.2622
13	0.2536
14	0.2014

15 0.1791

$All.CriticalValues

	CritValue_Duda	CritValue_PseudoT2	Fvalue_Beale
2	0.6992	19.3613	0.0127
3	0.5629	12.4235	0.0000
4	0.6891	18.4965	0.0797
5	0.5412	11.8671	0.0031
6	0.6285	14.7761	0.0020
7	0.4148	9.8744	0.0178
8	0.4408	10.1499	0.0148
9	0.6042	13.7594	0.0518
10	0.6388	15.2691	0.1485
11	0.3012	9.2802	0.0010
12	0.4997	11.0113	0.0325
13	0.1620	10.3432	1.0000
14	0.3012	9.2802	0.0000
15	0.5412	11.8671	0.0263

$Best.nc

	KL	CH	Hartigan	CCC	Scott	Marriot	TrCovW	TraceW	Friedman	Rubin	Cindex
Number_clusters	7.0000	7.0000	7.0000	15.0000	4.0000	4.0	3.0000	5.0000	9.0000	7.0000	11.0000
Value_Index	2.6031	31.1399	6.9008	19.2883	142.2851	453415.4	22.0994	2.9989	18.9608	-0.3674	0.3242

	DB	Silhouette	Duda	PseudoT2	Beale	Ratkowsky	Ball	PtBiserial	Frey	McClain	Dunn
Number_clusters	15.0000	7.0000	4.0000	4.0000	10.0000	5.0000	3.0000	8.0000	1	2.0000	8.0000
Value_Index	0.9537	0.3685	0.7433	14.1578	1.5289	0.3034	12.4811	0.7598	NA	0.7474	0.2656

	Hubert	SDindex	Dindex	SDbw
Number_clusters	0	9.0000	0	15.0000
Value_Index	0	2.7966	0	0.1791

$Best.partition

BOEX-001	BOEX-002	BOEX-003	BOEX-004	BOEX-005	BOEX-006	BOEX-007	BOEX-008	BOEX-009	BOEX-010	BOEX-011	BOEX-012
1	2	3	2	1	2	1	4	3	1	2	2
BOEX-013	BOEX-014	BOEX-015	BOEX-016	BOEX-017	BOEX-018	BOEX-019	BOEX-020	BOEX-021	BOEX-022	BOEX-023	BOEX-024
5	1	5	2	5	2	5	4	6	1	1	3
BOEX-025	BOEX-026	BOEX-027	BOEX-028	BOEX-029	BOEX-030	BOEX-031	BOEX-032	BOEX-033	BOEX-034	BOEX-035	BOEX-036
7	5	7	5	7	3	7	1	1	2	4	4
BOEX-037	BOEX-038	BOEX-039	BOEX-040	BOEX-041	BOEX-042	BOEX-043	BOEX-044	BOEX-045	BOEX-046	BOEX-047	BOEX-048

```
       2        2        4        2        1        2        2        6        1        1        5        7
BOEX-049 BOEX-050 BOEX-051 BOEX-052 BOEX-053 BOEX-054 BOEX-055 BOEX-056 BOEX-057 BOEX-058 BOEX-059 BOEX-060
       2        5        3        3        5        1        2        1        6        2        1        4
BOEX-061 BOEX-062 BOEX-063 BOEX-064 BOEX-065 BOEX-066 BOEX-067 BOEX-068 BOEX-069 BOEX-070 BOEX-071 BOEX-072
       3        1        1        4        1        2        2        1        2        2        7        2
BOEX-073 BOEX-074 BOEX-075 BOEX-076 BOEX-077 BOEX-078 BOEX-079 BOEX-080 BOEX-081 BOEX-082 BOEX-083 BOEX-084
       1        3        1        1        1        1        2        1        1        1        2        1
BOEX-085 BOEX-086 BOEX-087 BOEX-088 BOEX-089 BOEX-090
       7        7        1        3        6        3

> NbClust(data=BO2, diss = NULL, distance = "euclidean", min.nc = 2, max.nc = 15, method = "ward.D2")
*** : The Hubert index is a graphical method of determining the number of clusters.
                In the plot of Hubert index, we seek a significant knee that corresponds to a
                significant increase of the value of the measure i.e the significant peak in Hubert
                index second differences plot.

*** : The D index is a graphical method of determining the number of clusters.
                In the plot of D index, we seek a significant knee (the significant peak in Dindex
                second differences plot) that corresponds to a significant increase of the value of
                the measure.
```

```
*****************************************************************
* Among all indices:
* 4 proposed 2 as the best number of clusters
* 9 proposed 3 as the best number of clusters
* 3 proposed 4 as the best number of clusters
* 1 proposed 5 as the best number of clusters
* 1 proposed 6 as the best number of clusters
* 2 proposed 7 as the best number of clusters
* 1 proposed 11 as the best number of clusters
* 1 proposed 13 as the best number of clusters
* 1 proposed 15 as the best number of clusters

                   ***** Conclusion *****

* According to the majority rule, the best number of clusters is  3


*****************************************************************
```

$All.index

	KL	CH	Hartigan	CCC	Scott	Marriot	TrCovW	TraceW	Friedman	Rubin	Cindex	DB
2	1.3180	37.3872	26.6209	10.2264	293.6364	26745534.3	217.8084	90.2263	10.9730	1.9166	0.4704	1.3980
3	3.3010	37.2311	11.7829	7.9419	419.7712	14817373.2	105.8251	69.2711	15.5670	2.4963	0.4302	1.4316
4	0.9268	31.7409	10.8531	7.3155	494.8039	11444016.5	77.9677	61.0083	18.0172	2.8344	0.4130	1.2320
5	1.3054	29.1799	8.6328	7.7951	554.9884	9161753.6	55.8782	54.1719	19.8679	3.1921	0.4048	1.3140
6	1.0798	27.1185	7.7599	8.2066	601.3698	7880037.0	45.4574	49.1773	21.8767	3.5163	0.3710	1.3338
7	1.2365	25.6705	6.5157	8.0425	670.8037	4958710.7	37.5049	45.0185	27.3122	3.8412	0.3476	1.3782
8	1.2041	24.3643	5.5849	7.8212	722.1808	3659592.7	33.5015	41.7417	29.1721	4.1427	0.3668	1.3547
9	0.9388	23.1827	5.5850	7.5606	764.3870	2897825.6	29.3406	39.0800	31.2834	4.4249	0.3628	1.2916
10	1.0402	22.3686	5.3047	7.4614	796.5110	2503646.2	24.2825	36.5592	33.0942	4.7300	0.3924	1.2449
11	1.2300	21.7222	4.5356	7.6811	825.6238	2192171.6	21.6526	34.2858	34.4772	5.0436	0.3767	1.2267
12	0.9197	21.0240	4.6927	7.5787	857.7518	1825653.3	18.9579	32.4242	36.8588	5.3332	0.3638	1.2629
13	1.0498	20.5555	4.4790	7.5980	896.5199	1392730.1	17.0073	30.5842	39.0347	5.6540	0.3832	1.2424
14	1.0684	20.1574	4.2319	7.6206	931.3109	1097369.0	15.8053	28.9029	41.5239	5.9829	0.3688	1.2890
15	0.9347	19.7981	4.4172	7.6284	976.1327	765582.6	14.0723	27.3784	44.7908	6.3161	0.3638	1.2423

	Silhouette	Duda	Pseudot2	Beale	Ratkowsky	Ball	Ptbiserial	Frey	McClain	Dunn	Hubert	SDindex	Dindex
2	0.2743	0.6833	27.3483	2.4090	0.2354	45.1131	0.5151	0.4660	0.5700	0.1956	0.0177	3.1108	0.9649
3	0.2576	0.5767	18.3537	3.7309	0.2808	23.0904	0.5804	0.6414	1.3271	0.2131	0.0195	2.9238	0.8297

4	0.2441	0.7159	10.7149	2.0225	0.2618	15.2521	0.5695	0.3545	1.6015	0.2131	0.0197	2.5346	0.7661
5	0.2347	0.8056	7.7227	1.2368	0.2585	10.8344	0.5695	0.1022	1.9418	0.2219	0.0218	2.5956	0.7212
6	0.2415	0.7713	8.3046	1.5135	0.2444	8.1962	0.5934	0.5395	2.1655	0.2219	0.0232	2.5512	0.6922
7	0.2185	0.7373	6.4128	1.7838	0.2412	6.4312	0.5635	0.2881	2.7196	0.1658	0.0247	2.7145	0.6632
8	0.2198	0.7678	6.3517	1.5259	0.2398	5.2177	0.5556	0.0846	3.0259	0.1821	0.0255	2.6320	0.6413
9	0.2247	0.6823	8.8483	2.3383	0.2329	4.3422	0.5636	0.5266	3.1594	0.1899	0.0262	2.5840	0.6253
10	0.2121	0.6898	5.8449	2.2065	0.2245	3.6559	0.5411	0.3471	3.5911	0.2102	0.0268	2.6061	0.6039
11	0.2011	0.6672	4.4901	2.3731	0.2185	3.1169	0.5267	0.2340	3.9538	0.2102	0.0277	2.5827	0.5833
12	0.2051	0.6128	4.4229	2.9220	0.2117	2.7020	0.5202	0.1573	4.1825	0.2102	0.0281	2.5695	0.5641
13	0.2074	0.7031	5.9129	2.0834	0.2076	2.3526	0.5181	0.6409	4.3130	0.2253	0.0285	2.6568	0.5485
14	0.2004	0.3938	3.0789	5.4243	0.2033	2.0645	0.4829	0.0442	5.1345	0.2253	0.0288	3.2125	0.5328
15	0.2094	0.5847	5.6821	3.3368	0.2029	1.8252	0.4840	0.1073	5.1552	0.2253	0.0289	3.0977	0.5201

	SDbw
2	0.6682
3	0.5431
4	0.4293
5	0.3829
6	0.3872
7	0.3616

```
8  0.3351

9  0.3319

10 0.3020

11 0.2819

12 0.2773

13 0.2663

14 0.2539

15 0.2330


$All.CriticalValues

   CritValue_Duda CritValue_PseudoT2 Fvalue_Beale

2          0.7262            22.2427       0.0148

3          0.6285            14.7761       0.0004

4          0.6388            15.2691       0.0451

5          0.6603            16.4630       0.2778

6          0.6435            15.5122       0.1535

7          0.5813            12.9672       0.0848

8          0.6042            13.7594       0.1515

9          0.5894            13.2343       0.0213
```

```
10          0.5288            11.5843       0.0326
11          0.4631            10.4344       0.0250
12          0.4148             9.8744       0.0085
13          0.5412            11.8671       0.0432
14          0.1620            10.3432       0.0020
15          0.4408            10.1499       0.0030


$Best.nc
                    KL      CH Hartigan     CCC    Scott Marriot   TrCovW  TraceW Friedman   Rubin Cindex
Number_clusters 3.000  2.0000    3.000  2.0000   3.0000       3   3.0000  3.0000   7.0000  3.0000 7.0000
Value_Index     3.301 37.3872   14.838 10.2264 126.1348 8554804 111.9833 12.6925   5.4355 -0.2417 0.3476
                     DB Silhouette   Duda PseudoT2  Beale Ratkowsky    Ball PtBiserial Frey McClain    Dunn
Number_clusters 11.0000     2.0000 4.0000   4.0000 5.0000    3.0000  3.0000     6.0000    1    2.00 13.0000
Value_Index      1.2267     0.2743 0.7159  10.7149 1.2368    0.2808 22.0228     0.5934   NA    0.57  0.2253
                Hubert SDindex Dindex   SDbw
Number_clusters      0  4.0000      0 15.000
Value_Index          0  2.5346      0  0.233


$Best.partition
```

```
BOEX-001 BOEX-002 BOEX-003 BOEX-004 BOEX-005 BOEX-006 BOEX-007 BOEX-008 BOEX-009 BOEX-010 BOEX-011 BOEX-012
       1        2        3        2        3        2        1        2        3        3        2        2
BOEX-013 BOEX-014 BOEX-015 BOEX-016 BOEX-017 BOEX-018 BOEX-019 BOEX-020 BOEX-021 BOEX-022 BOEX-023 BOEX-024
       1        1        1        2        1        2        2        2        2        3        3        3
BOEX-025 BOEX-026 BOEX-027 BOEX-028 BOEX-029 BOEX-030 BOEX-031 BOEX-032 BOEX-033 BOEX-034 BOEX-035 BOEX-036
       1        1        1        1        1        3        1        3        3        2        2        2
BOEX-037 BOEX-038 BOEX-039 BOEX-040 BOEX-041 BOEX-042 BOEX-043 BOEX-044 BOEX-045 BOEX-046 BOEX-047 BOEX-048
       2        2        2        2        1        2        2        2        1        1        2        1
BOEX-049 BOEX-050 BOEX-051 BOEX-052 BOEX-053 BOEX-054 BOEX-055 BOEX-056 BOEX-057 BOEX-058 BOEX-059 BOEX-060
       2        1        3        3        1        3        2        1        2        2        3        3
BOEX-061 BOEX-062 BOEX-063 BOEX-064 BOEX-065 BOEX-066 BOEX-067 BOEX-068 BOEX-069 BOEX-070 BOEX-071 BOEX-072
       3        1        3        2        1        2        2        3        2        2        1        2
BOEX-073 BOEX-074 BOEX-075 BOEX-076 BOEX-077 BOEX-078 BOEX-079 BOEX-080 BOEX-081 BOEX-082 BOEX-083 BOEX-084
       1        3        1        1        3        3        2        3        3        3        2        1
BOEX-085 BOEX-086 BOEX-087 BOEX-088 BOEX-089 BOEX-090
       1        1        1        3        3        3
```

>

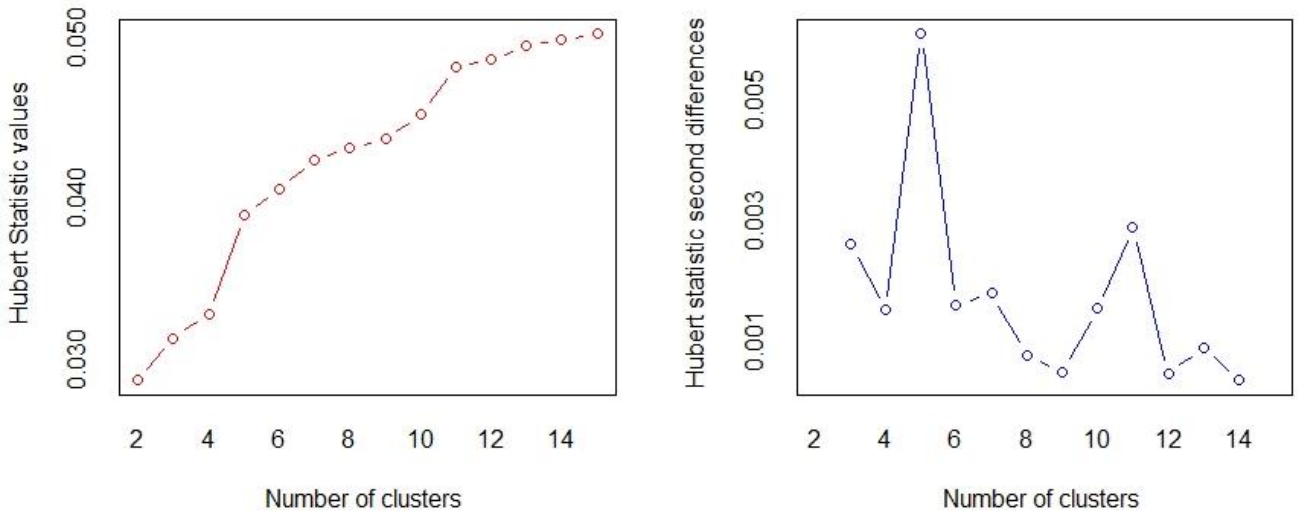

Figure 10. Hubert plots from NbClust analysis in determining the optimal number of clusters of the M1 dataset.

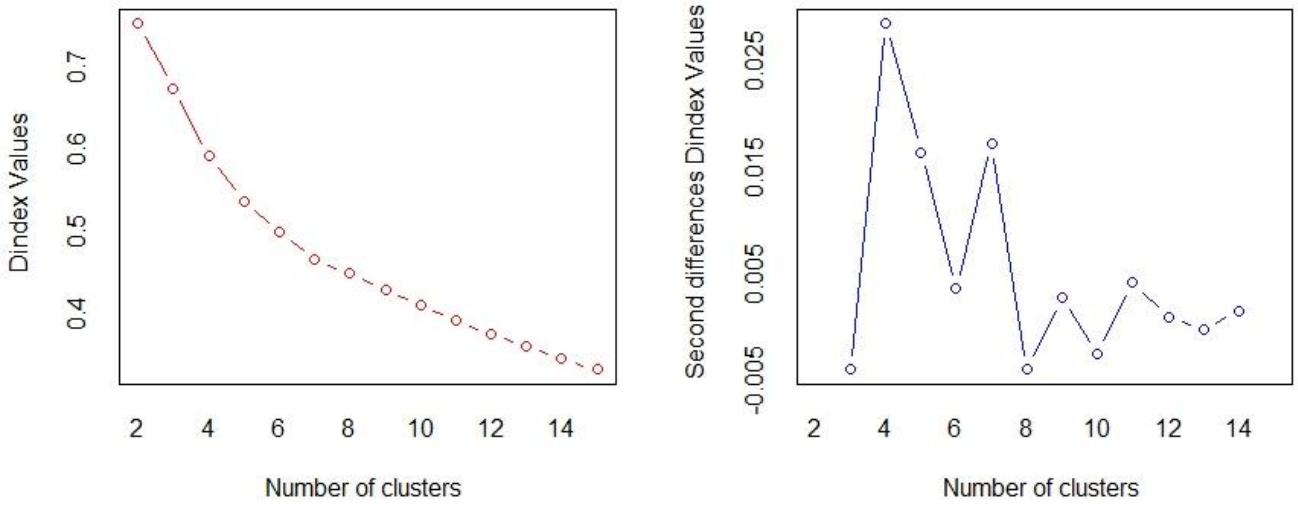

Figure 11. Dindex plots from NbClust analysis in determining the optimal number of clusters of the M1 dataset.

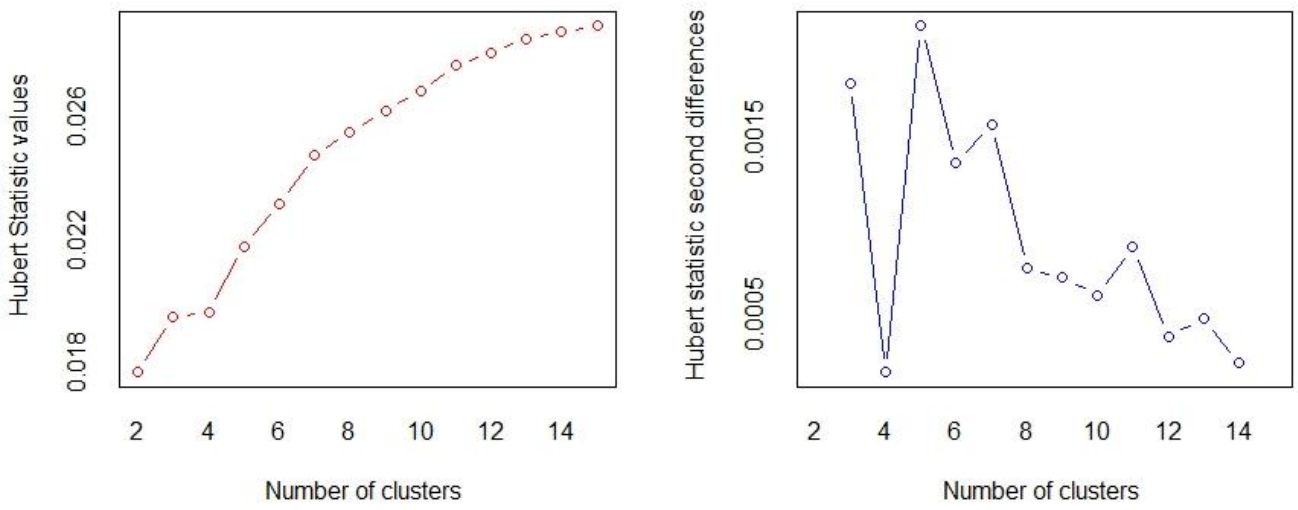

Figure 12. Hubert plots from NbClust analysis in determining the optimal number of clusters of the M2 dataset.

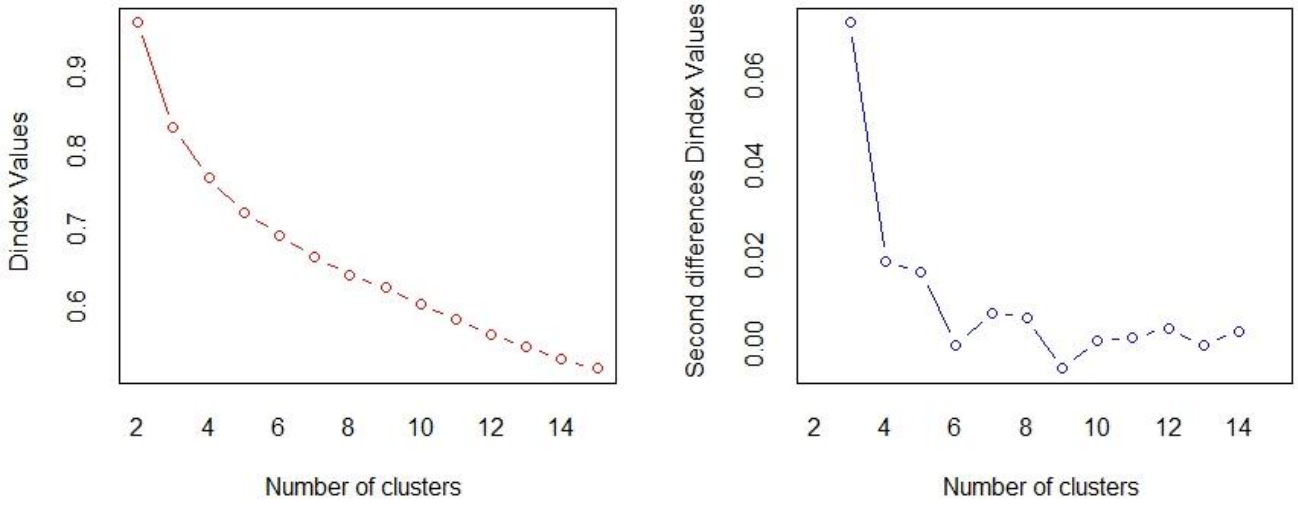

Figure 13. Dindex plots from NbClust analysis in determining the optimal number of clusters of the M2 dataset.

Appendix H: Dendrograms

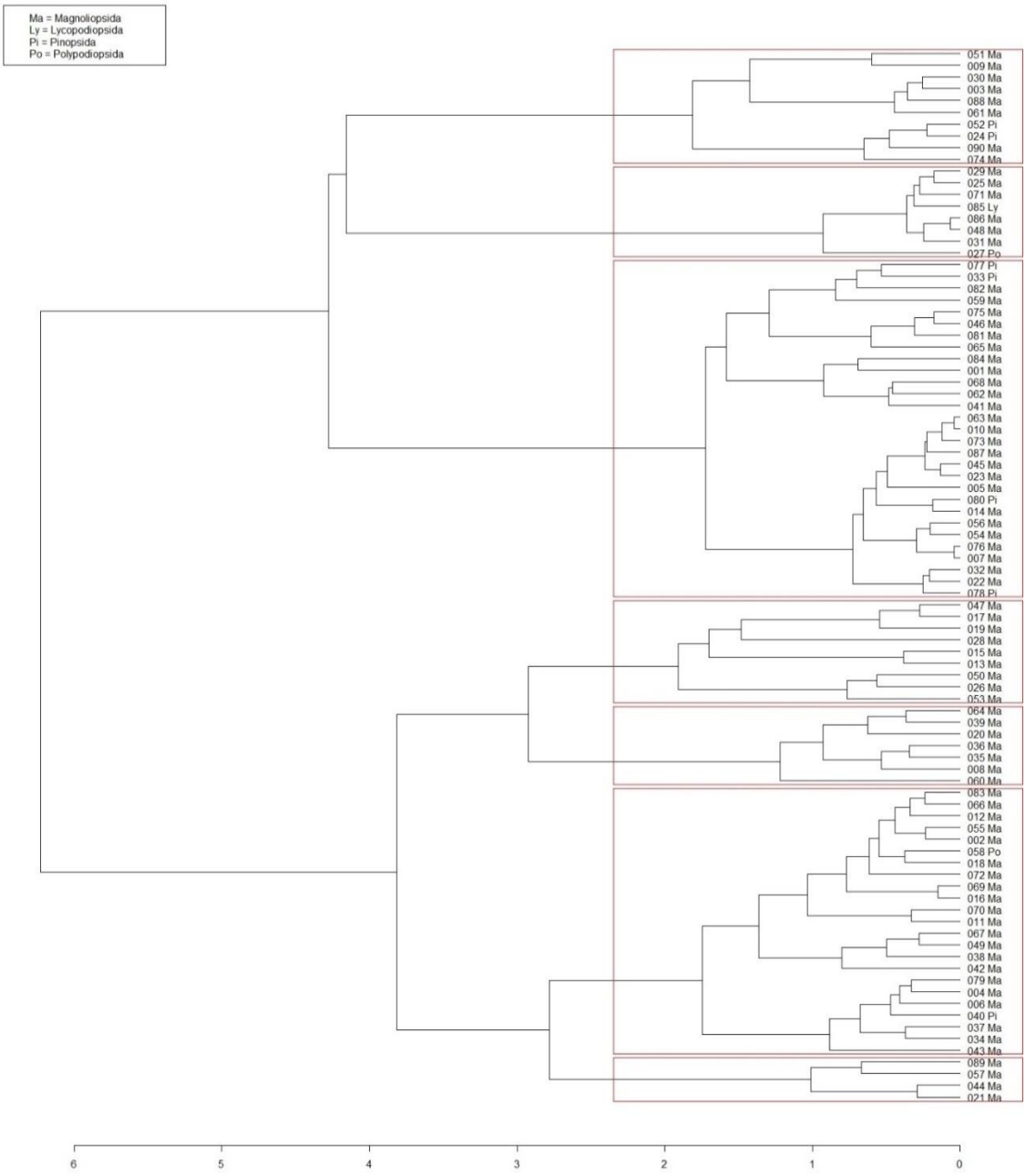

Figure 14. Hierarchical cluster analysis (Euclidean distance, Ward's method) of bioactivity profiles of Canadian medicinal plant extracts using the M1 dataset, and labeled with the extracts' class, where k was found to be seven.

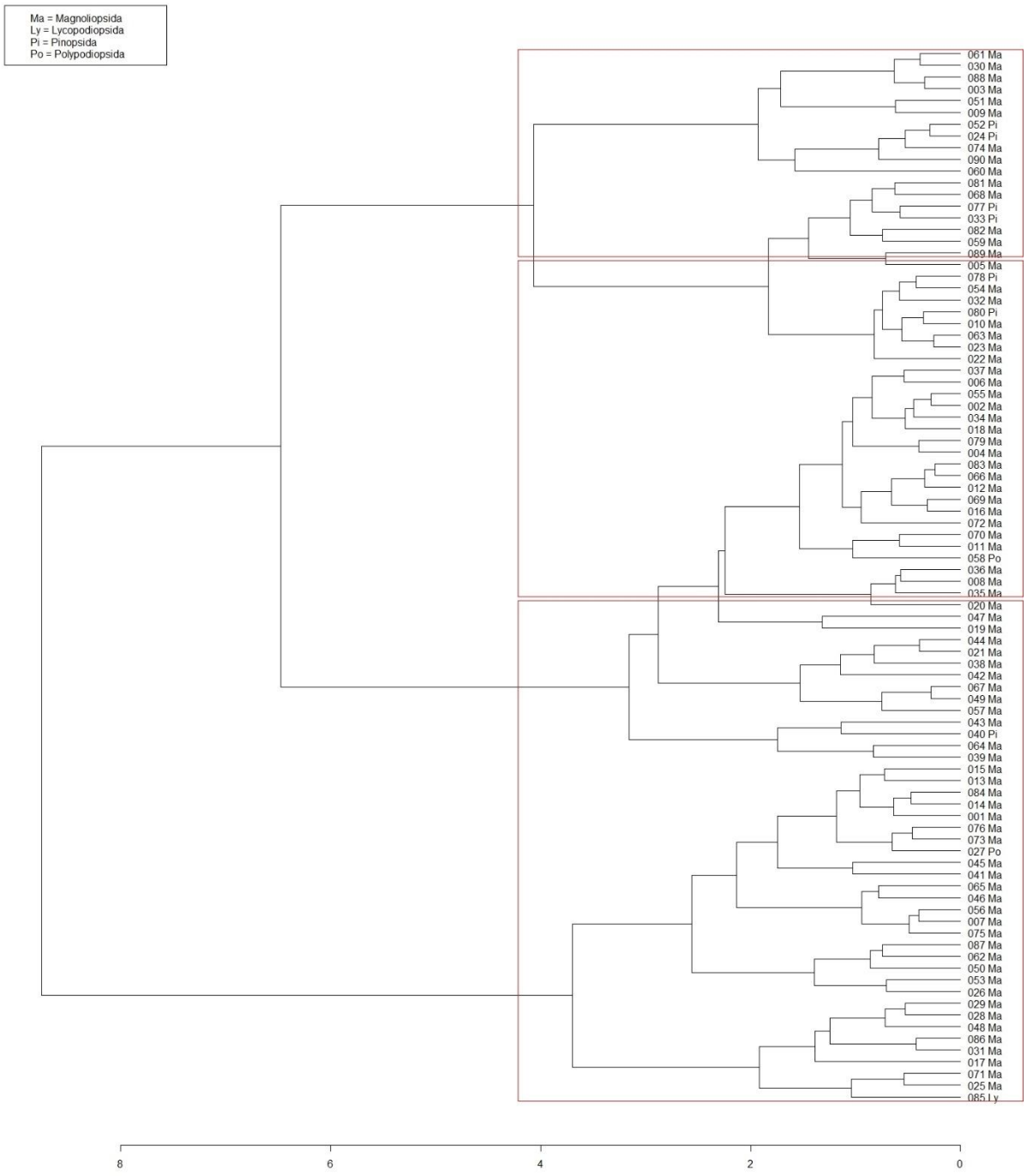

Figure 15. Hierarchical cluster analysis (Euclidean distance, Ward's method) of bioactivity profiles of Canadian medicinal plants extracts using the M2 data, and labeled with the extracts' class, where k was found to be three.

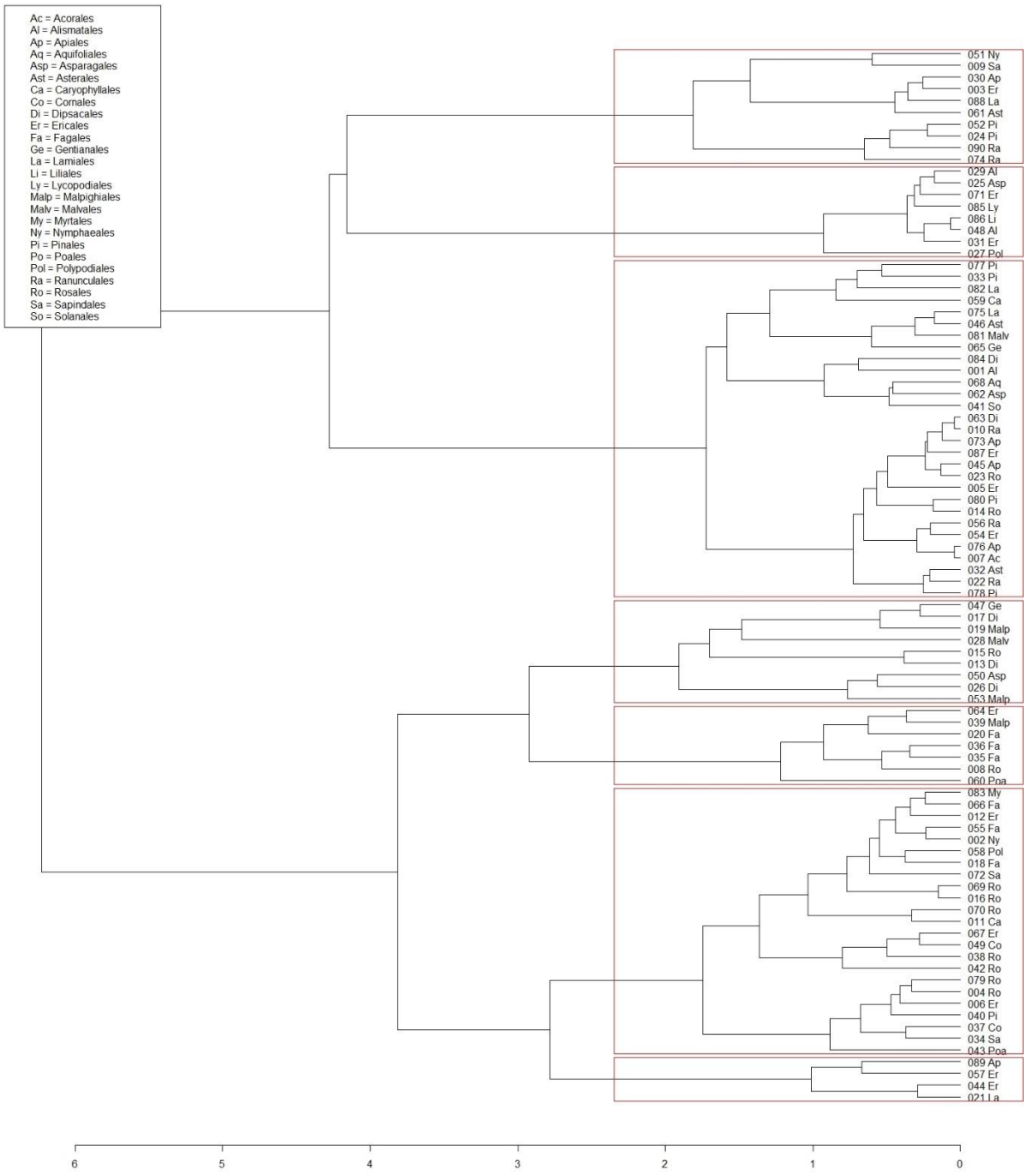

Figure 16. Hierarchical cluster analysis (Euclidean distance, Ward's method) of bioactivity profiles of Canadian medicinal plant extracts using the M1 dataset, and labeled with the extracts' order, where k was found to be seven.

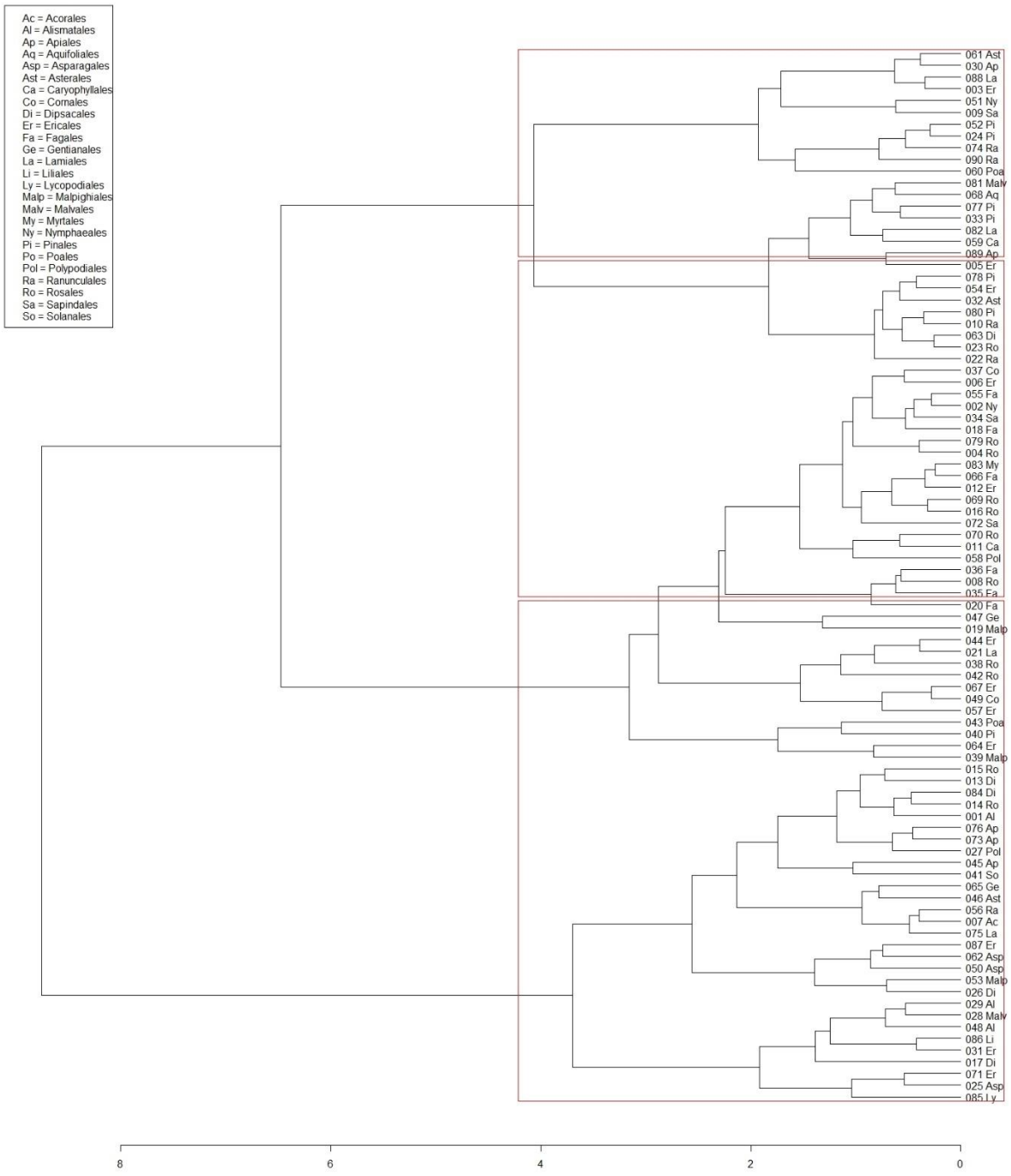

Figure 17. Hierarchical cluster analysis (Euclidean distance, Ward's method) of bioactivity profiles of Canadian medicinal plants extracts using the M2 data, and labeled with the extracts' order, where k was found to be three.

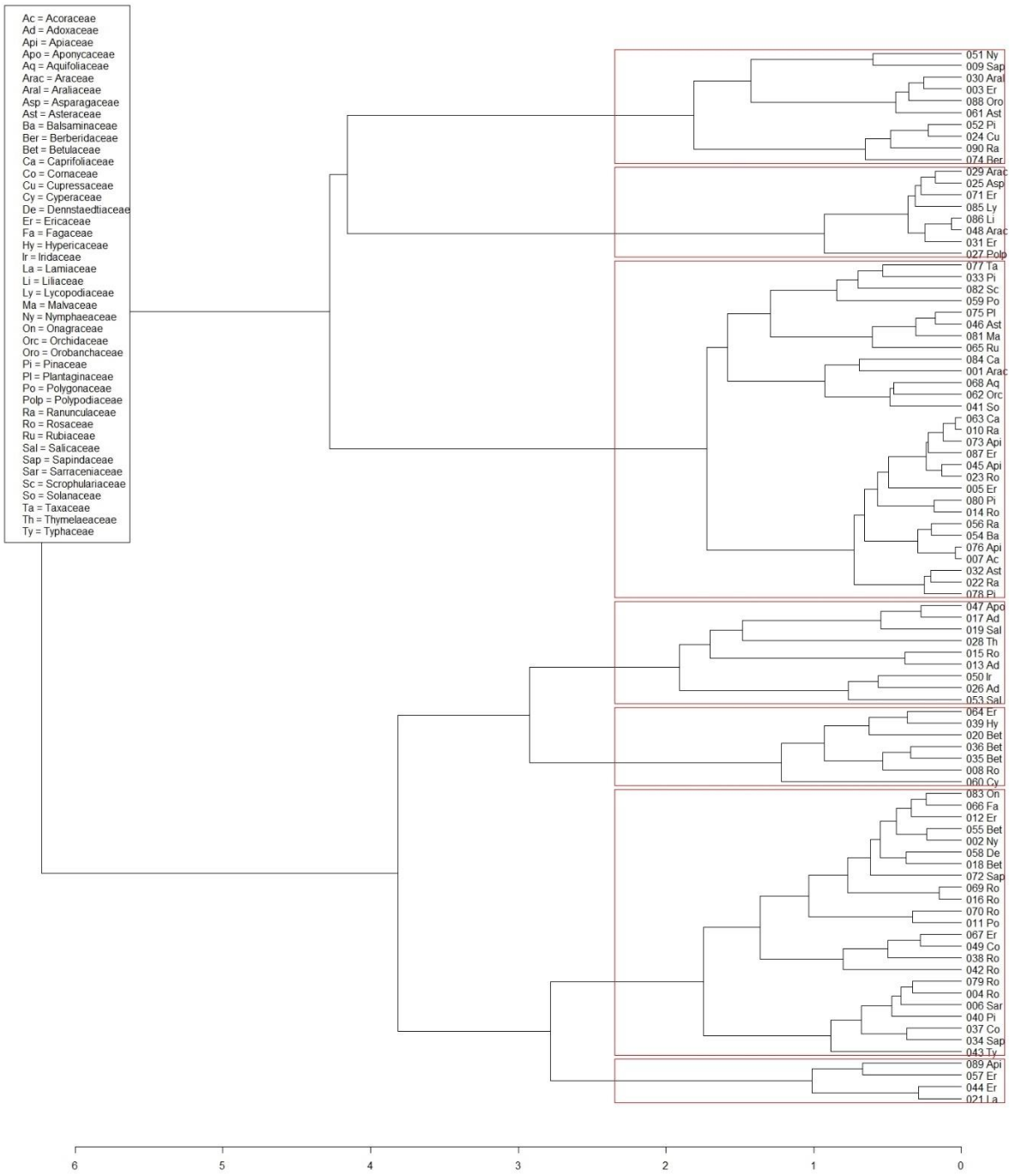

Figure 18. Hierarchical cluster analysis (Euclidean distance, Ward's method) of bioactivity profiles of Canadian medicinal plants extracts using the M1 data, and labeled with the extracts' family, where k was found to be seven.

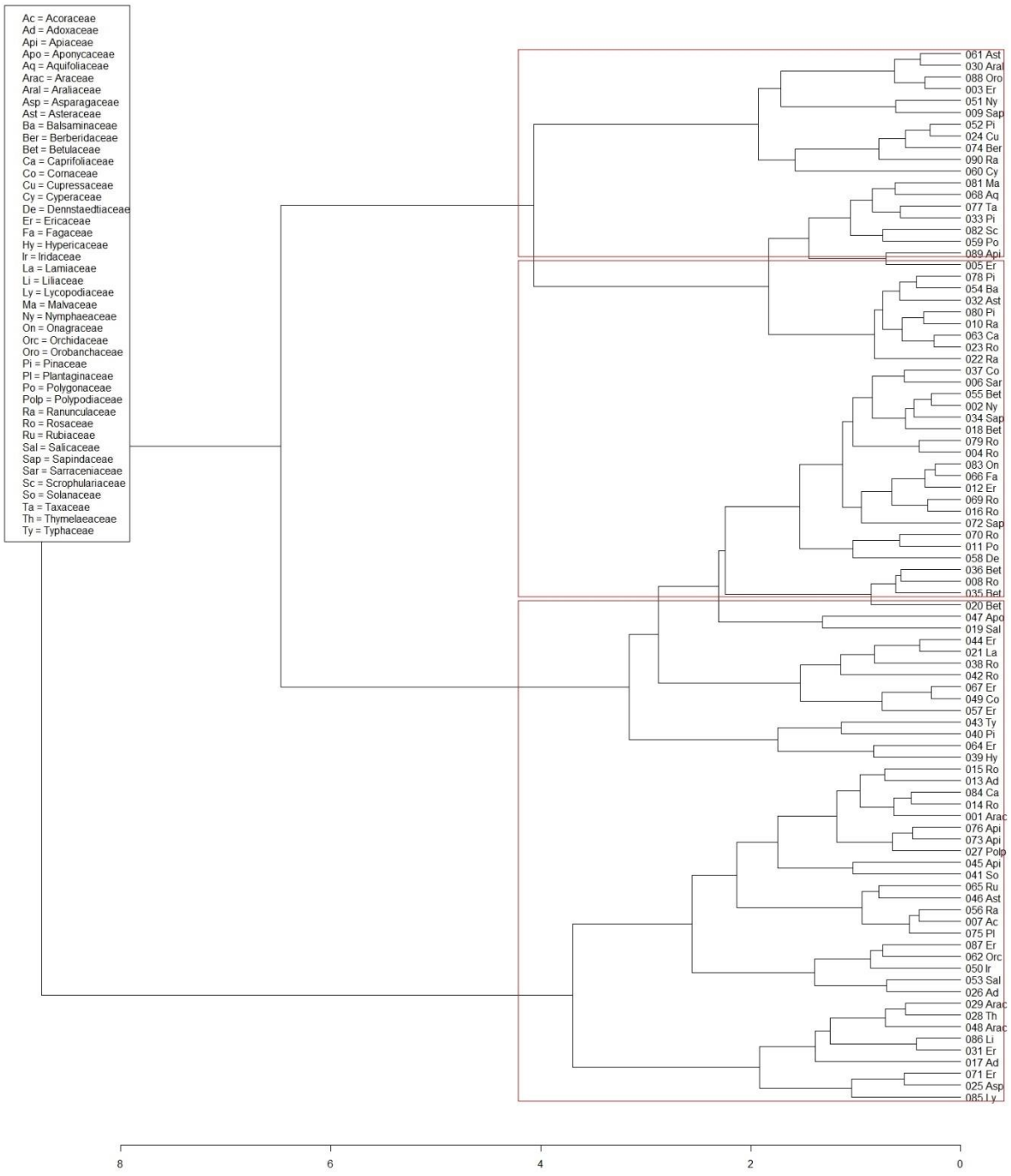

Figure 19. Hierarchical cluster analysis (Euclidean distance, Ward's method) of bioactivity profiles of Canadian medicinal plants extracts using the M2 data, and labeled with the extracts' family, where k was found to be three.

Appendix I: R output for pvclust

```
> result<- pvclust(BOE, method.hclust="ward.D2", method.dist = "euclidean",
nboot=10000)
Bootstrap (r = 0.5)... Done.
Bootstrap (r = 0.5)... Done.
Bootstrap (r = 0.62)... Done.
Bootstrap (r = 0.75)... Done.
Bootstrap (r = 0.88)... Done.
Bootstrap (r = 1.0)... Done.
Bootstrap (r = 1.0)... Done.
Bootstrap (r = 1.12)... Done.
Bootstrap (r = 1.25)... Done.
Bootstrap (r = 1.38)... Done.
Warning message:
In a$p[] <- c(1, bp[r == 1]) :
  number of items to replace is not a multiple of replacement length
 > BOE2 <- t(BO2)
 > result2<- pvclust(BOE2, method.hclust="ward.D2", method.dist = "euclidean",
 nboot=10000)
 Bootstrap (r = 0.5)... Done.
 Bootstrap (r = 0.5)... Done.
 Bootstrap (r = 0.62)... Done.
 Bootstrap (r = 0.75)... Done.
 Bootstrap (r = 0.88)... Done.
 Bootstrap (r = 1.0)... Done.
 Bootstrap (r = 1.0)... Done.
 Bootstrap (r = 1.12)... Done.
```

```
Bootstrap (r = 1.25)... Done.

Bootstrap (r = 1.38)... Done.

Warning message:

In a$p[] <- c(1, bp[r == 1]) :

  number of items to replace is not a multiple of replacement length

>
```

Appendix J: P-values plot

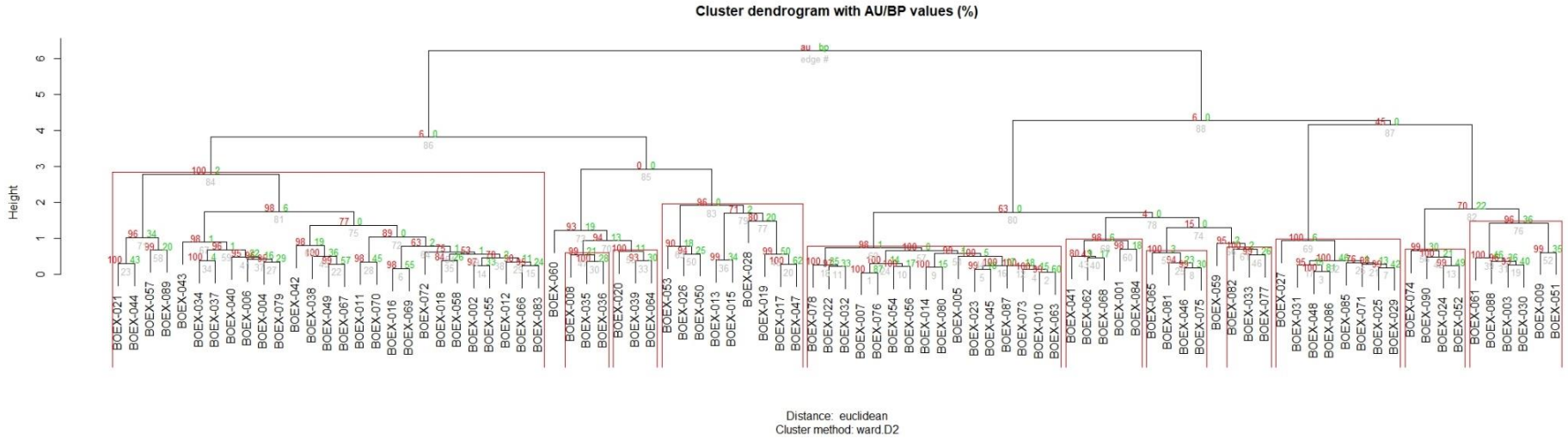

Figure 20. Hierarchical cluster analysis (Euclidean distance, Ward's method) of bioactivity profiles of Canadian medicinal plants extracts using the M1 data, with each node labeled with AU (red) and BP (green) values, where the nodes with an alpha greater or equal 0.95 are outlined in red boxes.

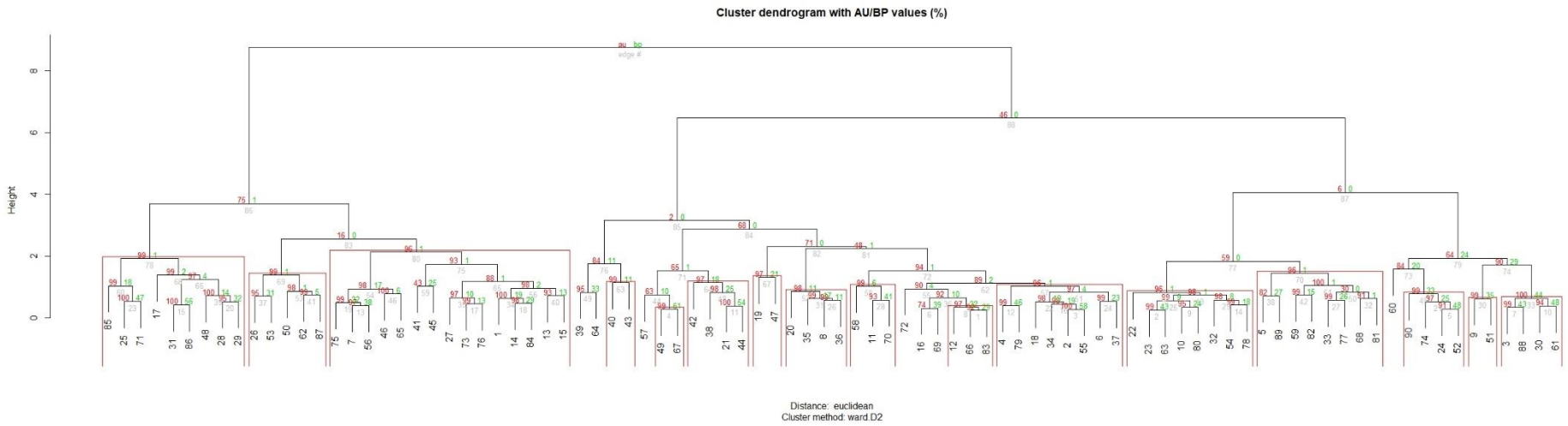

Figure 21. Hierarchical cluster analysis (Euclidean distance, Ward's method) of bioactivity profiles of Canadian medicinal plants extracts using the M2 data, with each node labeled with AU (red) and BP (green) values, where the nodes with an alpha greater or equal 0.95 are outlined in red boxes.

Appendix K: MDS plots

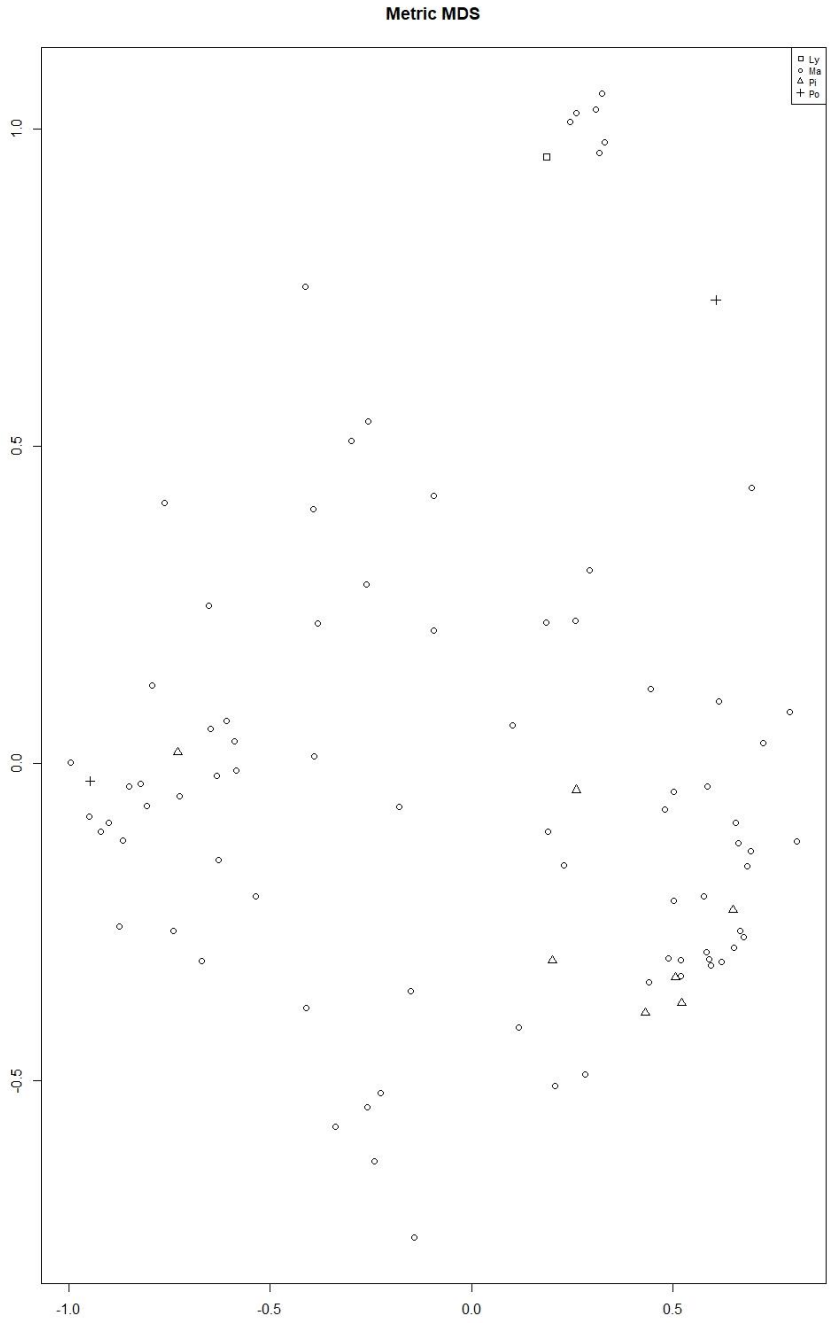

Figure 22. Output from MDS analysis of bioactivity profiles obtained from Canadian medicinal plant extracts from M1 dataset, with the extracts' class labeled.

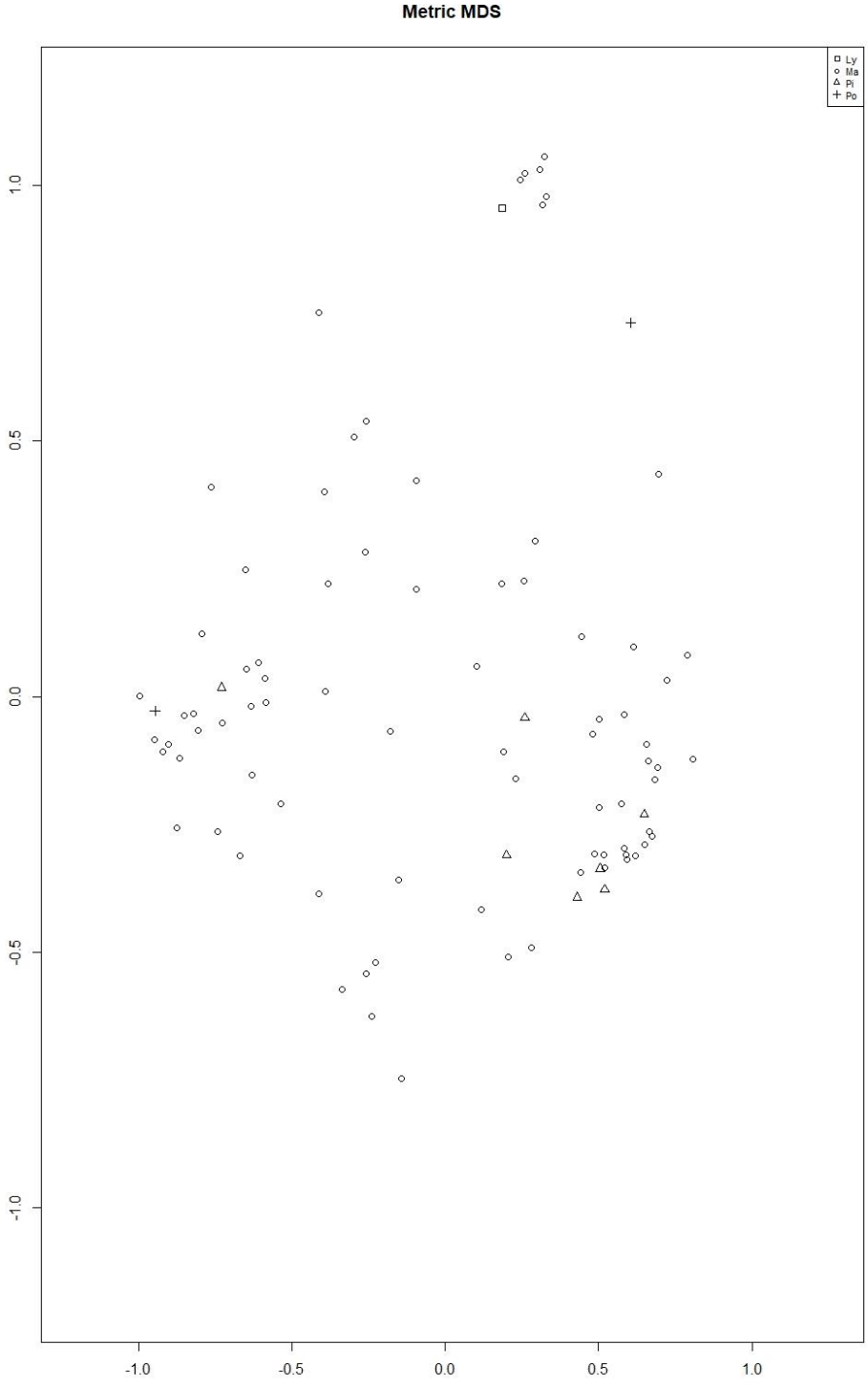

Figure 23. Output from MDS analysis of bioactivity profiles obtained from Canadian medicinal plant extracts from M2 dataset, with the extracts' class labeled.

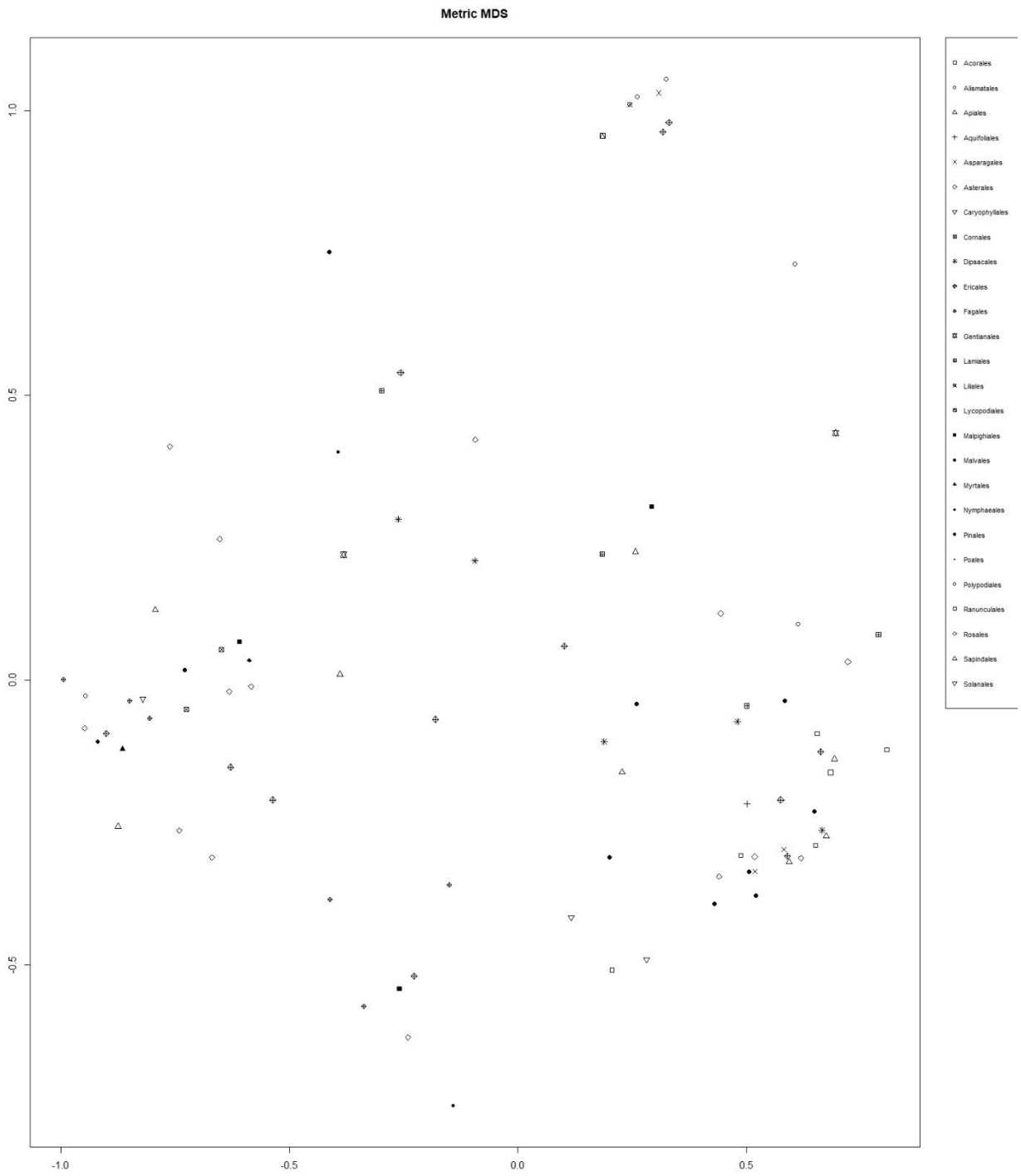

Figure 24. Output from MDS analysis of bioactivity profiles obtained from Canadian medicinal plant extracts from M1 dataset, with the extracts' order labeled.

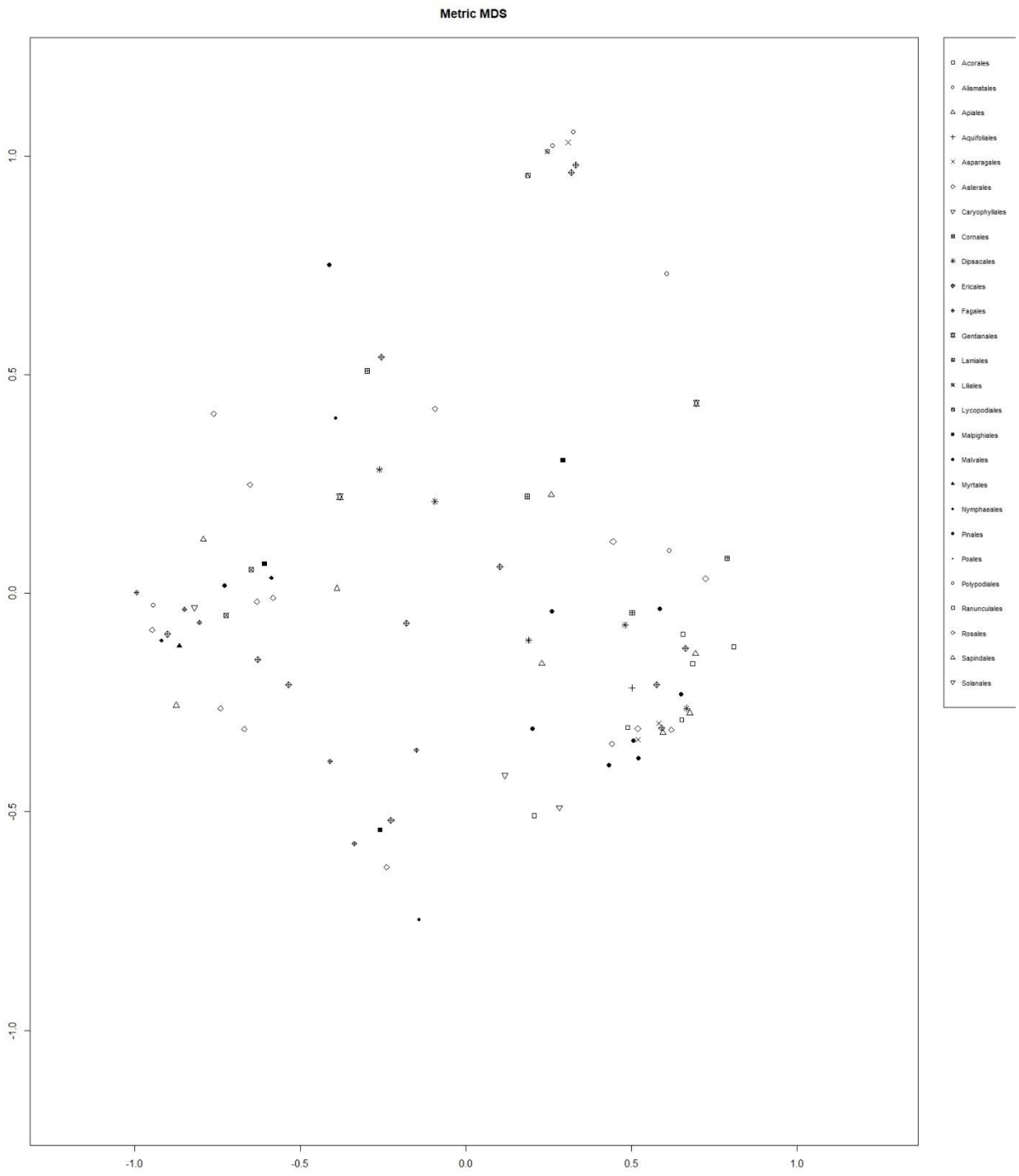

Figure 25. Output from MDS analysis of bioactivity profiles obtained from Canadian medicinal plant extracts from M2 dataset, with the extracts' order labeled.

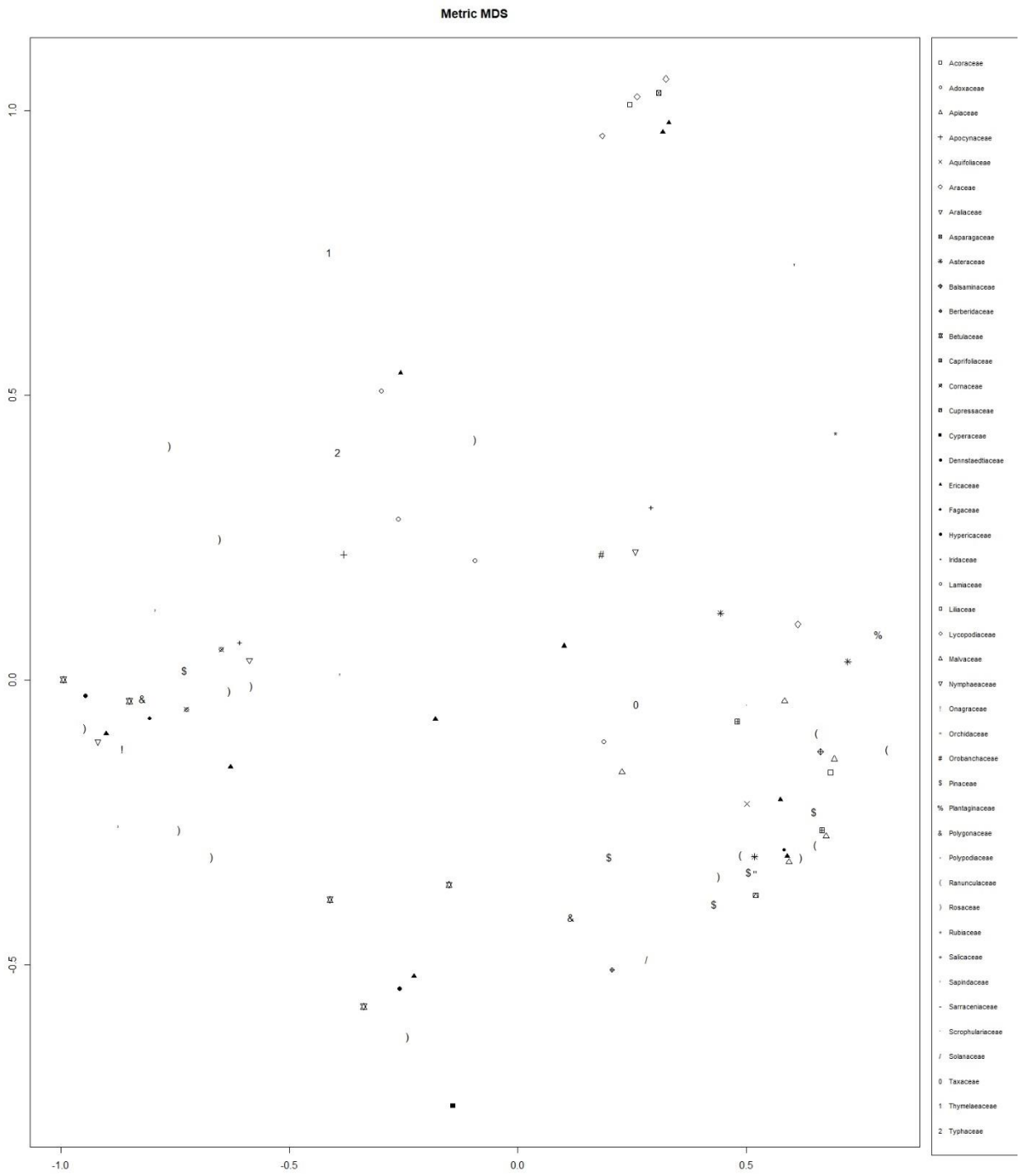

Figure 26. Output from MDS analysis of bioactivity profiles obtained from Canadian medicinal plant extracts from M1 dataset, with the extracts' family labeled.

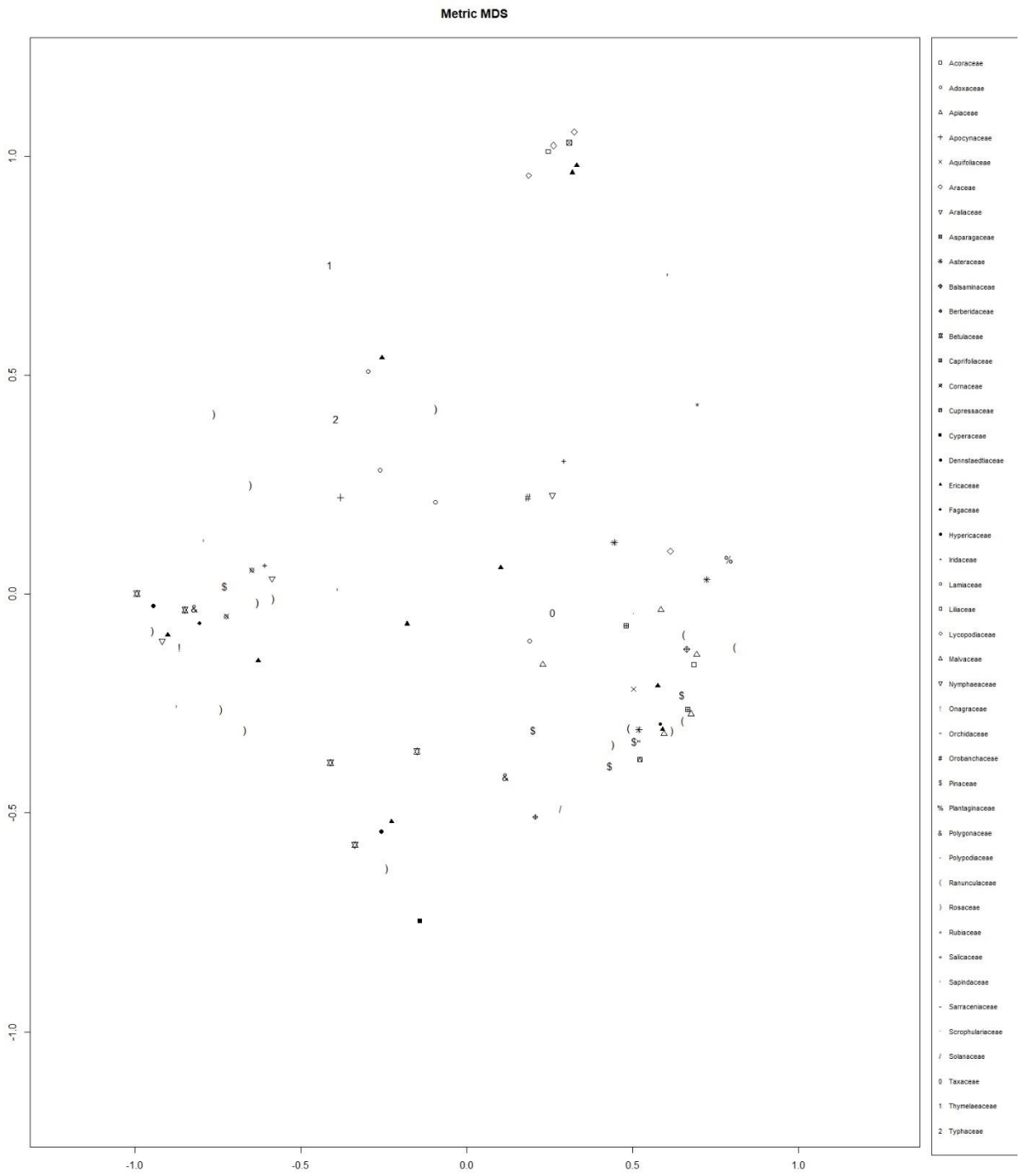

Figure 27. Output from MDS analysis of bioactivity profiles obtained from Canadian medicinal plant extracts from M2 dataset, with the extracts' family labeled.

Appendix L: Summary tables

Table 5. Summary table of clusters observed (from the top to the bottom of the figure) in Figure 7 for the hierarchical clustering of the antibiotic activity of extracts from Canadian medicinal plants using M1, according to the extract's class.

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	Cluster 6	Cluster 7	Total
Lycopodiopsida	0	1	0	0	0	0	0	1
Magnoliopsida	8	6	25	9	7	21	4	80
Pinopsida	2	0	4	0	0	1	0	7
Polypodiopsida	0	1	0	0	0	1	0	2
Total	10	8	29	9	7	23	4	90

Table 6. Summary table of clusters observed (from the top to the bottom of the figure) in Figure 8 for the hierarchical clustering of the antibiotic activity of extracts from Canadian medicinal plants using M2, according to the extract's class.

	Cluster 1	Cluster 2	Cluster 3	Total
Lycopodiopsida	0	0	1	1
Magnoliopsida	14	26	40	80
Pinopsida	4	2	1	7
Polypodiopsida	0	1	1	2
Total	18	29	43	90

Table 7. Summary table of clusters observed (from the top to the bottom of the figure) in Figure 9 for the hierarchical clustering of the antibiotic activity of extracts from Canadian medicinal plants using M1, according to the extract's order.

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	Cluster 6	Cluster 7	Total
Acorales	0	0	1	0	0	0	0	1
Alismatales	0	2	1	0	0	0	0	3
Apiales	1	0	3	0	0	0	1	5
Aquifoliales	0	0	1	0	0	0	0	1
Asparagales	0	1	1	1	0	0	0	3
Asterales	1	0	2	0	0	0	0	3
Caryophyllales	0	0	1	0	0	1	0	2
Cornales	0	0	0	0	0	2	0	2
Dipsacales	0	0	2	3	0	0	0	5
Ericales	1	2	3	0	1	3	2	12
Fagales	0	0	0	0	3	3	0	6
Gentianales	0	0	1	1	0	0	0	2
Lamiales	1	0	2	0	0	0	1	4
Liliales	0	1	0	0	0	0	0	1
Lycopodiales	0	1	0	0	0	0	0	1
Malpighiales	0	0	0	2	1	0	0	3
Malvales	0	0	1	1	0	0	0	2
Myrtales	0	0	0	0	0	1	0	1
Nymphaeales	1	0	0	0	0	1	0	2
Pinales	2	0	4	0	0	1	0	7
Poales	0	0	0	0	1	1	0	2
Polypodiales	0	1	0	0	0	1	0	2
Ranunculales	2	0	3	0	0	0	0	5
Rosales	0	0	2	1	1	7	0	11
Sapindales	1	0	0	0	0	2	0	3
Solanales	0	0	1	0	0	0	0	1
Total	10	8	29	9	7	23	4	90

Table 8. Summary table of clusters observed (from the top to the bottom of the figure) in Figure 10 for the hierarchical clustering of the antibiotic activity of extracts from Canadian medicinal plants using M2, according to the extract's order.

	Cluster 1	Cluster 2	Cluster 3	Total
Acorales	0	0	1	1
Alismatales	0	0	3	3
Apiales	2	0	3	5
Aquifoliales	1	0	0	1
Asparagales	0	0	3	3
Asterales	1	1	1	3
Caryophyllales	1	1	0	2
Cornales	0	1	1	2
Dipsacales	0	1	4	5
Ericales	1	4	7	12
Fagales	0	5	1	6
Gentianales	0	0	2	2
Lamiales	2	0	2	4
Liliales	0	0	1	1
Lycopodiales	0	0	1	1
Malpighiales	0	0	3	3
Malvales	1	0	1	2
Myrtales	0	1	0	1
Nymphaeales	1	1	0	2
Pinales	4	2	1	7
Poales	1	0	1	2
Polypodiales	0	1	1	2
Ranunculales	2	2	1	5
Rosales	0	7	4	11
Sapindales	1	2	0	3
Solanales	0	0	1	1
Total	18	29	43	90

Table 9. Summary table of clusters observed (from the top to the bottom of the figure) in Figure 11 for the hierarchical clustering of the antibiotic activity of extracts from Canadian medicinal plants using M1, according to the extract's family.

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	Cluster 6	Cluster 7	Total
Acoraceae	0	0	1	0	0	0	0	1
Adoxaceae	0	0	0	3	0	0	0	3
Apiaceae	0	0	3	0	0	0	1	4
Apocynaceae	0	0	0	1	0	0	0	1
Aquifoliaceae	0	0	1	0	0	0	0	1
Araceae	0	2	1	0	0	0	0	3
Araliaceae	1	0	0	0	0	0	0	1
Asparagaceae	0	1	0	0	0	0	0	1
Asteraceae	1	0	2	0	0	0	0	3
Balsaminaceae	0	0	1	0	0	0	0	1
Berberidaceae	1	0	0	0	0	0	0	1
Betulaceae	0	0	0	0	3	2	0	5
Caprifoliaceae	0	0	2	0	0	0	0	2
Cornaceae	0	0	0	0	0	2	0	2
Cupressaceae	1	0	0	0	0	0	0	1
Cyperaceae	0	0	0	0	1	0	0	1
Dennstaedtiaceae	0	0	0	0	0	1	0	1
Ericaceae	1	2	2	0	1	2	2	10
Fagaceae	0	0	0	0	0	1	0	1
Hypericaceae	0	0	0	0	1	0	0	1
Iridaceae	0	0	0	1	0	0	0	1
Lamiaceae	0	0	0	0	0	0	1	1
Liliaceae	0	1	0	0	0	0	0	1
Lycopodiaceae	0	1	0	0	0	0	0	1
Malvaceae	0	0	1	0	0	0	0	1
Nymphaeaceae	1	0	0	0	0	1	0	2
Onagraceae	0	0	0	0	0	1	0	1
Orchidaceae	0	0	1	0	0	0	0	1
Orobanchaceae	1	0	0	0	0	0	0	1
Pinaceae	1	0	3	0	0	1	0	5
Plantaginaceae	0	0	1	0	0	0	0	1
Polygonaceae	0	0	1	0	0	1	0	2
Polypodiaceae	0	1	0	0	0	0	0	1
Ranunculaceae	1	0	3	0	0	0	0	4
Rosaceae	0	0	2	1	1	7	0	11
Rubiaceae	0	0	1	0	0	0	0	1
Salicaceae	0	0	0	2	0	0	0	2
Sapindaceae	1	0	0	0	0	2	0	3

(Table 9 continued)

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	Cluster 6	Cluster 7	Total
Sarraceniaceae	0	0	0	0	0	1	0	1
Scrophulariaceae	0	0	1	0	0	0	0	1
Solanaceae	0	0	1	0	0	0	0	1
Taxaceae	0	0	1	0	0	0	0	1
Thymelaeaceae	0	0	0	1	0	0	0	1
Typhaceae	0	0	0	0	0	1	0	1
Total	10	8	29	9	7	23	4	90

Table 10. Summary table of clusters observed (from the top to the bottom of the figure) in Figure 12 for the hierarchical clustering of the antibiotic activity of extracts from Canadian medicinal plants using M2, according to the extract's family.

	Cluster 1	Cluster 2	Cluster 3	Total
Acoraceae	0	0	1	1
Adoxaceae	0	0	3	3
Apiaceae	1	0	3	4
Apocynaceae	0	0	1	1
Aquifoliaceae	1	0	0	1
Araceae	0	0	3	3
Araliaceae	1	0	0	1
Asparagaceae	0	0	1	1
Asteraceae	1	1	1	3
Balsaminaceae	0	1	0	1
Berberidaceae	1	0	0	1
Betulaceae	0	4	1	5
Caprifoliaceae	0	1	1	2
Cornaceae	0	1	1	2
Cupressaceae	1	0	0	1
Cyperaceae	1	0	0	1
Dennstaedtiaceae	0	1	0	1
Ericaceae	1	2	7	10
Fagaceae	0	1	0	1
Hypericaceae	0	0	1	1
Iridaceae	0	0	1	1
Lamiaceae	0	0	1	1
Liliaceae	0	0	1	1
Lycopodiaceae	0	0	1	1
Malvaceae	1	0	0	1
Nymphaeaceae	1	1	0	2
Onagraceae	0	1	0	1
Orchidaceae	0	0	1	1
Orobanchaceae	1	0	0	1
Pinaceae	2	2	1	5
Plantaginaceae	0	0	1	1
Polygonaceae	1	1	0	2
Polypodiaceae	0	0	1	1
Ranunculaceae	1	2	1	4
Rosaceae	0	7	4	11

(Table 10 continued)

	Cluster 1	Cluster 2	Cluster 3	Total
Rubiaceae	0	0	1	1
Salicaceae	0	0	2	2
Sapindaceae	1	2	0	3
Sarraceniaceae	0	1	0	1
Scrophulariaceae	1	0	0	1
Solanaceae	0	0	1	1
Taxaceae	1	0	0	1
Thymelaeaceae	0	0	1	1
Typhaceae	0	0	1	1
Total	18	29	43	90