Available online freely at www.isisn.org

Bioscience Research

Print ISSN: 1811-9506 Online ISSN: 2218-3973

Journal by Innovative Scientific Information & Services Network

RESEARCH ARTICLE BIOSCIENCE RESEARCH, 2020 17(1): 327-346. **OPEN ACCESS**

Exploring the Physiological and Molecular Mechanism of the Gum arabic (*Acacia senegal*) Based on Gene Expression Microarray

Omaima Nasir[1]

[1]Department of Biology, Turabah University College, Taif University, **Saudi Arabia.**

***Correspondence: dahaboma@yahoo.com, o.saeeed@tu.edu.sa** **Received 22-01-2019, Revised: 16-02-2020, Accepted: 20-02-2020 e-Published: 01-03-2020**

To investigate the differential expression of genes after Gum Arabic (*Acacia senegal*) administration by microarray study.The microarray was performed using colonic tissue of BALB/c s at 8 weeks of age treated with10% (w/w) GA dissolved in drinking water and control had a normal tap water for 4 days. A total 100 genes were analyzed by the pathway, gene ontology (GO) enrichment analysis, construction of protein-protein interaction (PPI) network, module analysis, construction of target genes—miRNA interaction network, target and genes-transcription factor (TF) interaction. We discuss key issues pertaining to experimental design, data preprocessing, and gene selection methods. Common types of data representation are illustrated. A total of 100 differentially miRNAs were screened and identified by microarray according to fold change the top genes which were significantly 59 genes with up-regulation and 41 genes down regulation, after Gum Arabic administration for 4 days. The data may unravel the future molecular mechanisms of Gum arabic by applying various bio-informatical approaches, we have revealed top score upregulation genes were 23, and down regulated genes with top score were 38. To the best of our knowledge we are the first to apply Microarray of several genes expression with their top functions after Gum arabic administration. These studies also highlighted that several additional, and as of yet unidentified, gene interactions may be responsible for the multiple beneficial effects of GA. The aim of our current study was to identify novel regulated genes, gene networks and pathways in Colonic tissue of BALB/c mice by applying microarray gene expression analysis subsequent to 4 days GA treatment.

Keywords: Acacia senegal, microarray, genes expression, pathways,

INTRODUCTION

Medicinal plants enriched with active compounds has many therapeutic properties. Various groups of people identified many medicinal plants to treat various diseases over time (Aye, M. M., *et al*., 2019). Since the advent of medicines, natural products, especially herbal products, have been used to support human health. From time immemorial, traditional medicine has been well known and used by the people over the course of history (Mahomoodally, M. F. 2013). Plants have been a source of medicines since ancient times. Plant products have attracted researchers from all over the world for many years because of their low side effects and positive effects on human health (Ekor, M. 2014). Gum Arabic (GA) is an edible dry sticky exudate, rich in non-viscous soluble fibre, made from Acacia senegal. It is complex mixture of glycoproteins and polysaccharides predominantly consisting of arabinose and galactose (Patel, S., & Goyal, A. 2015). GA is typically used as an emulsifier and preservative in food and pharmaceutical industries (Ahmed, A. *et al*.,2016).

It has been used by various communities in North Africa and the Middle East for century as an oral hygiene agent. (Al Za'abi, M. *et al.,* 2015) GA is used in Arabic folk medicine in patients with chronic renal failure to minimize both frequency and need of hemodialysis. (Ali, B. H., *et al.,* 2013). It has good antioxidant properties and is used against gentamicin and cisplatin to mitigate experimental nephrotoxicity (Ahmed, A. *et al*.,2016) Improve cardiovascularity (Babiker, R., et al.,2018) In addition, oxidative and adenine inflammational reduction of the chronic renal insufficiency in rats is reported in GA and Enhanced diabetic rat kidney functions (Al Za'abi, M., et al., 2018). This the pharmacological use of GA has greater effects on clinical applications.

The study of the differentiation of cells and tissues in gene expression has become an important tool in medicine. Microarray experiments allow a description of changes in health and disease expression across the genome (Tarca, A. L., *et al*., 2006). Expression profiling offers great opportunities to identify new molecular goals, to discover drugs, to improve them and to verify them. (Youns, M., et al., 2009). Our approach provides a new framework for research into the mode of action and protection and can also be used to establish a technique for standardizing herbal medicines. These resources can facilitate further gene function studies toward key bioactive natural products that define the medicinal properties of this traditional medicinal plant.

This study shows the role of GA in disease prevention and treatment through the control of different biological and physiological pathways. The studies based on animal model established that GA plays pivotal role in disease management through the modulation of various molecular pathways. This study summarizes the role of GA in the disease's prevention and treatment through the modulation of various biological pathways with upregulation and down regulation of genes

MATERIALS AND METHODS

. Methods

2.1. Experiment

Gum Arabic used in this study was 100% natural extract powder Acacia Senegal without any additive, purchased from Savanna Sudanese Gum (SSG), Khartoum, Sudan (www.ssgums.com).BALB/c mice of both sexes (n=5/group) were housed, food intake, body weight were maintained under controlled environment condition with 24°C, 50-70% humidity and a 12-h light/dark cycle at 8 weeks of age, the mice were allowed free access to with standard pelleted food (C1310, Altromin, Heidenau, Germany), the animal were divided into two group one control had a normal tap water, other group were treated with10% (w/w) GA dissolved in drinking water for 4 days, all mice were anesthetized with ether and sacrificed after 4 days of treatment prior to experimental procedures. All animal experiments were conducted according international law for the care and welfare of animals and were approved by local authorities.

2.2. RNA extraction

Colonic tissue of BALB/c mice were chosen for RNA extraction from control and treated samples, Total RNA was isolated from the last 5 cm of the distal part of large intestine using the Qiagen RNeasy Fibrous Tissue Mini Kit following manufacturers recommendations (Qiagen, Hilden, Germany) and purified with RNasey Mini Kit (Qiagen). ND-1000 (Thermo). The integrity and quality of the RNA was detected by agarose gel electrophoresis.

2.3. Microarray analysis

RNA samples used in microarray analysis were used for cDNAs synthesized with commercially available kit (Invitrogen Life Technologies, Rockville, MD) and oligo d (T) T7 primer (Barton DP,1997), cDNA was generated using biotin-labeled cytidine 5'-triphosphate (CTP) and uridine 5'-triphosphate (UTP) by in vitro transcription using a T7 promoter-coupled double-stranded cDNA as template and the T7 RNA transcript labeling kit (ENZO Diagnostics, Farmingdale, NY). The cRNA was fragmented and hybridized to the mouse genome MOE430A oligonucleotide array chip (Affymetrix, Santa Clara, CA). The array chips were then stained using phycoerythrin-conjugated streptavidin (Molecular probes, Invitrogen Life Technologies) and the fluorescence intensities were determined using a laser confocal scanner (Affymetrix). intensity of the scanned images was analyzed using Microarray Suite Version 5 (Affymetrix). Global scaling was applied to all arrays, such that the mean intensity of each array was equivalent. In global scaling, the raw signal value of each probe cell was multiplied by a scaling factor. Genes whose expression significantly varied with a signal log ratio of 0.5 were identified using Data Mining Tool (Affymetrix).

Sample name	Sample name MFT	RIN
1GA	1GAI6R_058a01	9.4
2GA	2GAI6R_058a02	9.6
3GA	3GAI6R_058a03	9.5
4GA	4GAI6R_058a04	9.4
5GA	5GAI6R_058a05	9.5
6cont	6contI6R_058b01	6.9
7cont	7contI6R_058b02	8.9
8cont	8contI6R_058b03	9.4
9cont	9contI6R_058b04	9.0
10cont	10contI6R_058b05	9.0

Table 1: Shows the sample name and identification number for evaluation of RNA

RESULTS

Data Preprocessing

3.1.1 List of differentially expressed genes

Quality Control and Normalization of the Array Data Quality Control used the Expression Console program (Affymetrix). For this, the raw data of the. CEL files were read out via MAS5. From the generated report the Scaling Factor (SF), the Present Call Rate (% P) and Mean Signal Intensity (Signal (P)) and the 3 '/ 5' Ratios of Internal Housekeeping Controls and added Spike-In RNAs were assessed the array quality and comparability (Fig,1).

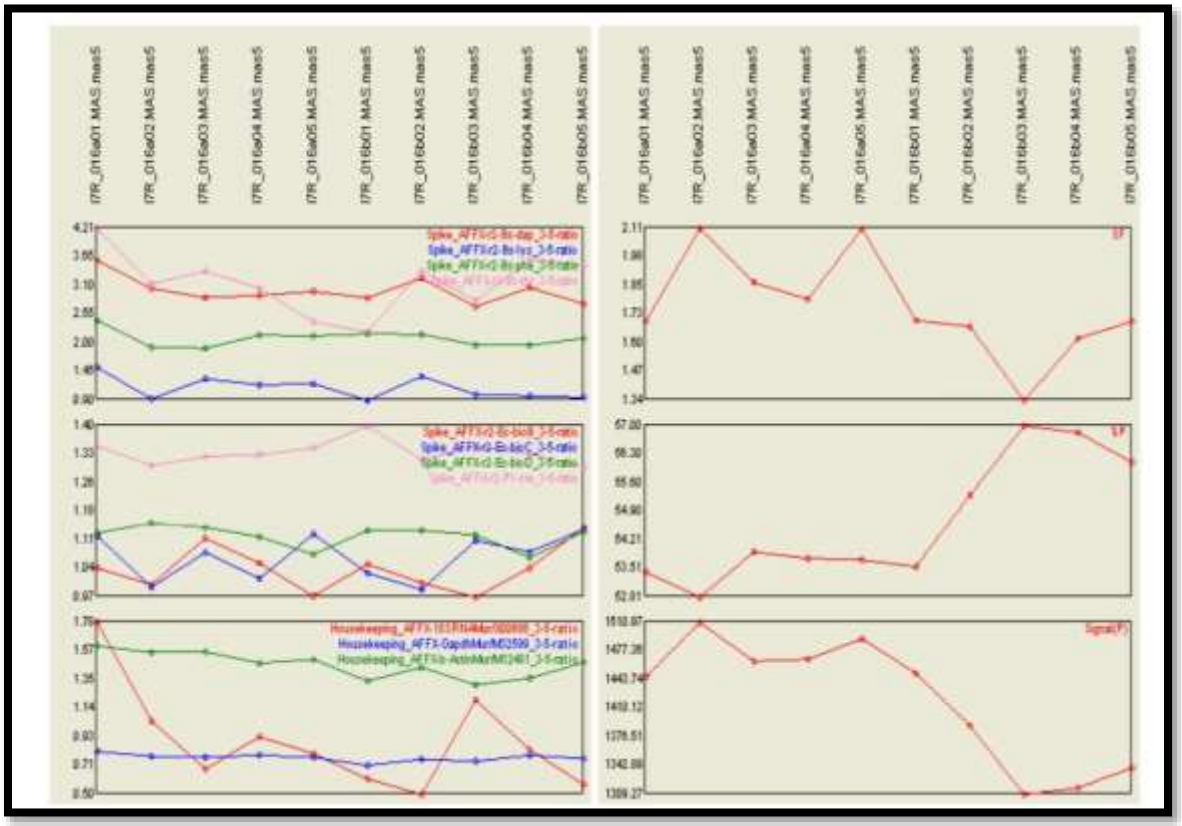


Figure 1: Quality parameters according to MAS5 Analysis of the arrays. All values are in the normal range and indicate good data quality.

The raw data of the arrays (CEL-files) were imported into Genespring 7.3. The extraction of data, background correction, normalization and calculation of the signal values per transcript ("gene level summary") was carried out via GC-RMA. Details are given in the file "GC-RMA Normalization.pdf". Subsequently, the data for base 2 were logarithmic, which is important for the later statistical evaluation. The quality of hybridizations and the quality of the normalization were checked by boxplots of the normalized arrays (Fig 2). The distribution of the signals of all

arrays is plotted in the boxplots. So that arrays can be compared, the distributions should be similar. The signal distribution of the probes before normalization already shows that no strong fluctuations occur within the data set, which speaks for a very good comparability of the data. Accordingly, the signal distributions of the sample sets after normalization and summation are almost identical for all arrays of the experiment.

3.1.2 Determine differentially expressed genes

In order to identify differentially expressed transcripts, the 5 hybridizations of the experimental group (GA) against the 5 arrays of the control group (C) were compared. First, the fold change was calculated for all transcripts. In a first analysis, only transcripts with a mean change of at least factor 2 up or down were considered for statistical analysis (58 sample sets). Subsequently, the p-value for an unpaired unequal-variance t-test (Welch's t-test) was determined and corrected for Benjamini-Hochberg1 for multiple testing.

A total of 36 transcripts with a corrected p-value of ≤ 0.05 (and a fold change of ≥ 2) were designated as differentially expressed (Fig 3). Since the number of significant transcripts was very small, the analysis was repeated with a fold change cut-off of 1.5. Out of 710 transcripts, 456 were significantly regulated. Both gene lists were linked to the annotations from NetAFFX2 and sorted by Fold Change in the file "I7R_016_genelists.xls". Table 1 explains the content of each column.

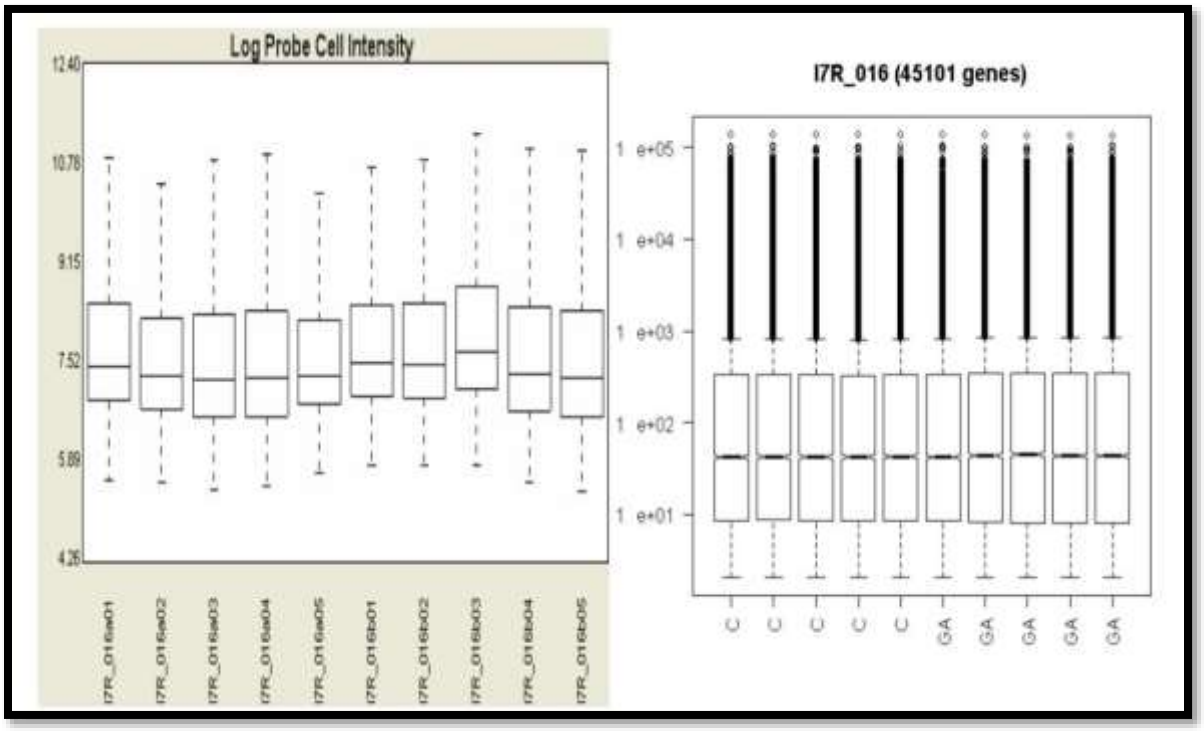
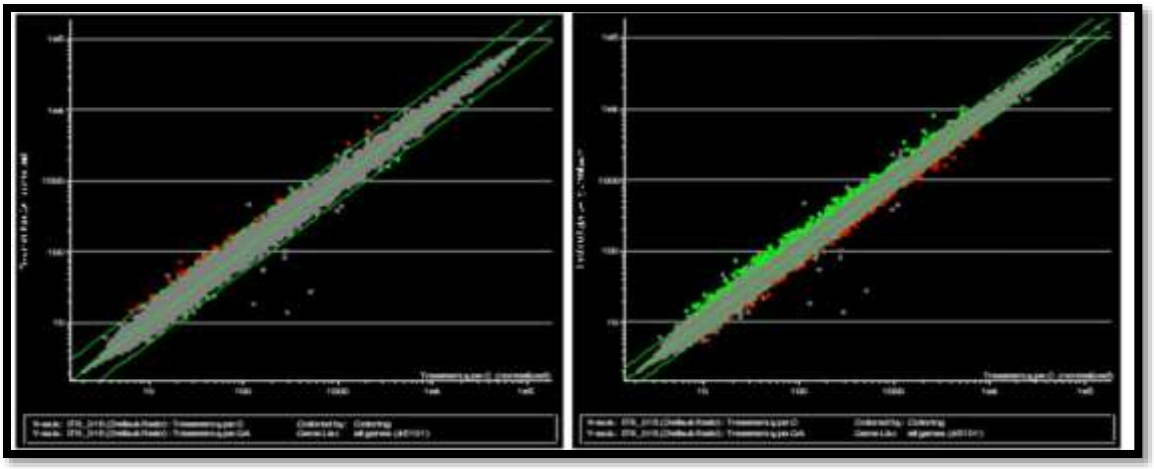


Figure 2: Box-and-Wiskerplots of the signals of the individual arrays before (left) and after (right) G



C-RMA normalization.

Figure 3: Scatter plots of the two significance analyzes with a fold change cut-off of 2 (left) and 1.5 (right). The signals of treated samples (GA) are plotted against those of control samples (C). Transcripts with significant up regulation are red, down regulated transcripts are green.

Table 1: Description of the columns in the list of regulated transcripts

Sample set ID	***Affymetrix Transkript Identifier***
Fold Change	Specifies the amount of expression change (mean) between the two conditions
Gene Title	Brief description of the gene product
Gene Symbol	Abbreviation for gene product (without aliases)
UniGene ID	Accession of the latest Unigene cluster
Chromosomal Location	Location of the gene in the genome indicating the cytoplasm
Ensembl	Ensemble Gene ID (www.ensembl.org)
Entrez Gene	NCBI Gene ID
RefSeq Transcript ID	Accession for Refseq RNA database
Gene Ontology Biological Process	Functional annotation of transcripts in gene ontology (GO) categories broken down by biological processes, molecular function, and cellular compartment (see, e.g., http://www.ebi.ac.uk/ego/index.html)
Gene Ontology Cellular Componen	
Gene Ontology Molecular Function	

3.1.3. Pathway Enrichment Analysis

3.1.3.1 Analysis of changed networks and pathways

For the functional analysis of the modified transcripts, the gene lists of the two analyzes were analyzed for interactions between the regulated genes and possible changes in known signaling and metabolic pathways using the Ingenuity Pathway Analysis software. The analysis is based on a literature and interaction database, which is controlled by postgraduate scientists after automatic text mining, whereby the quality of the information is consistently high. An assignment of the Affymetrix probeset IDs to the genes used by the Ingenuity database can be found in the file "gene summary.xls". The data is

analyzed in three ways:

3.1.3.2-Network analysis:

The database is examined for known interactions (also indirect) between the examined transcripts. These interactions are then displayed graphically in so-called networks. An overview of the networks and the genes involved gives the file "Networks_overview.xls". Tabulated here are the networks, the genes involved and the score of the network. The score is calculated from the number of focus genes, strength and direction of the change. The individual networks are stored in the files "NetworkX.Fig.4", the genes involved in the file "NetworkX_Identifier.xls". An explanation of the symbols and designations can be found in the file "IPA Legend.pdf". If a transcript occurs in more than one network, you can see it in the "Overlapping Networks.pdf".

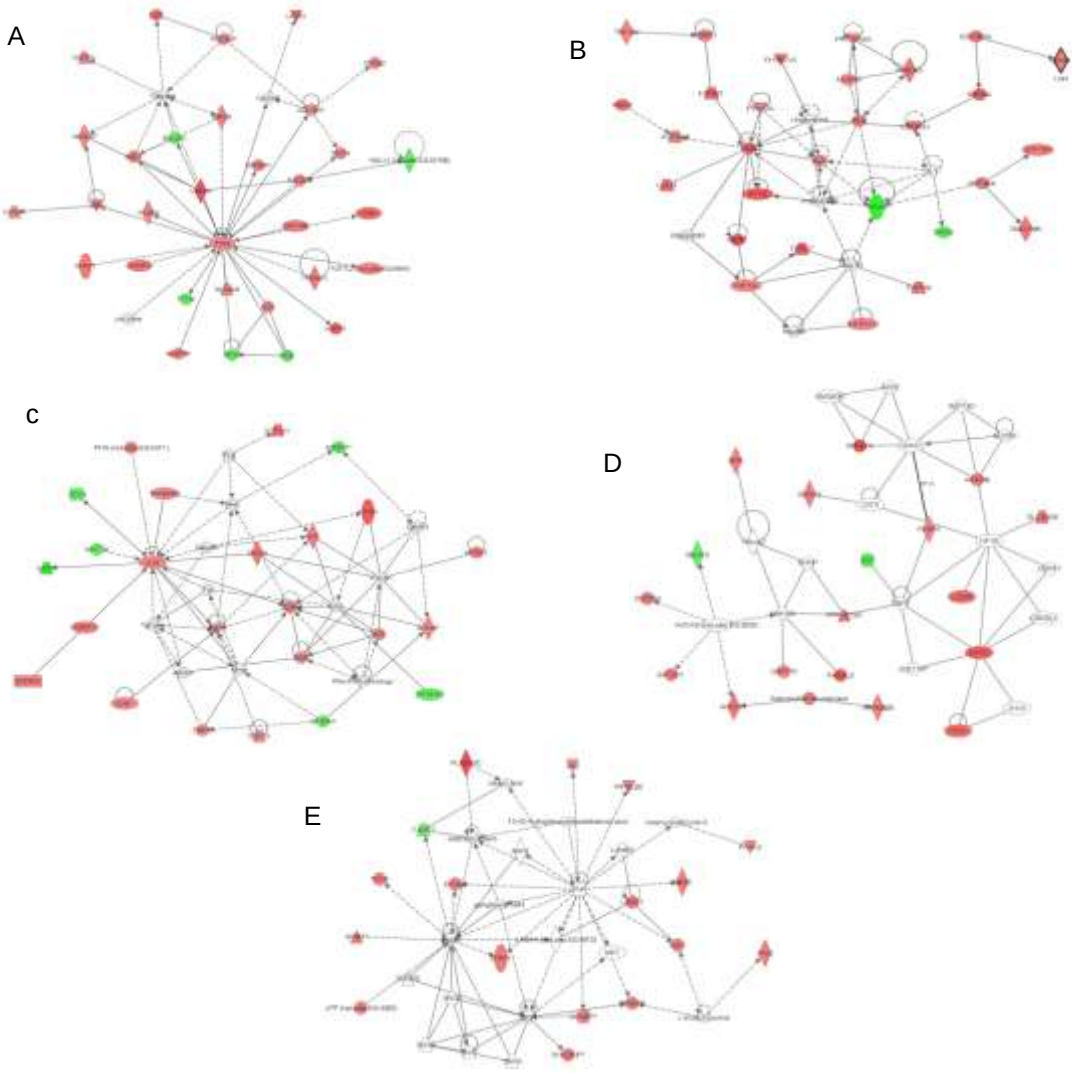


Figure 4: The networks and the different genes involved and its interactions between the Gum arabic and control transcripts in A, B, C, D and E .

3.1.3.3. Functional annotation:

The examined genes are assigned to certain functional categories based on information in the database. Furthermore, a pValue3 determines whether there is a significant accumulation of members of this category (example: in two categories each 10 genes show a different expression.) Category A comprises 12, category B 500 genes significant p-value results, whereas the changes in category B can be considered random and a high p-value results). An overview of all functional categories, the genes involved and the significance level can be found in the file "functions_overview.xls". A graphic representation of the functional categories ordered by decreasing significance is given in the figures "function molecular and cellular functions.Fig.5-A", "functions disease and disorder. Fig.5-B" and "functions_ physiological system development. Fig.5-C".

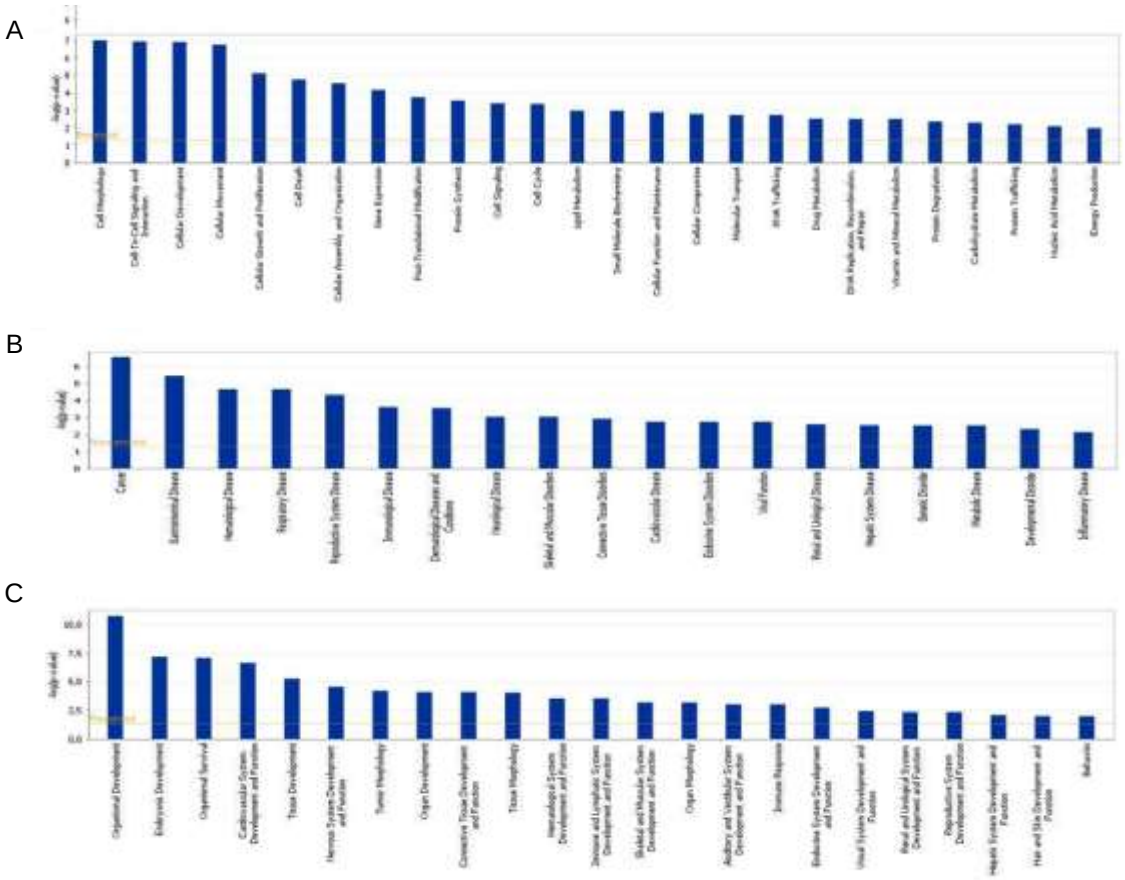
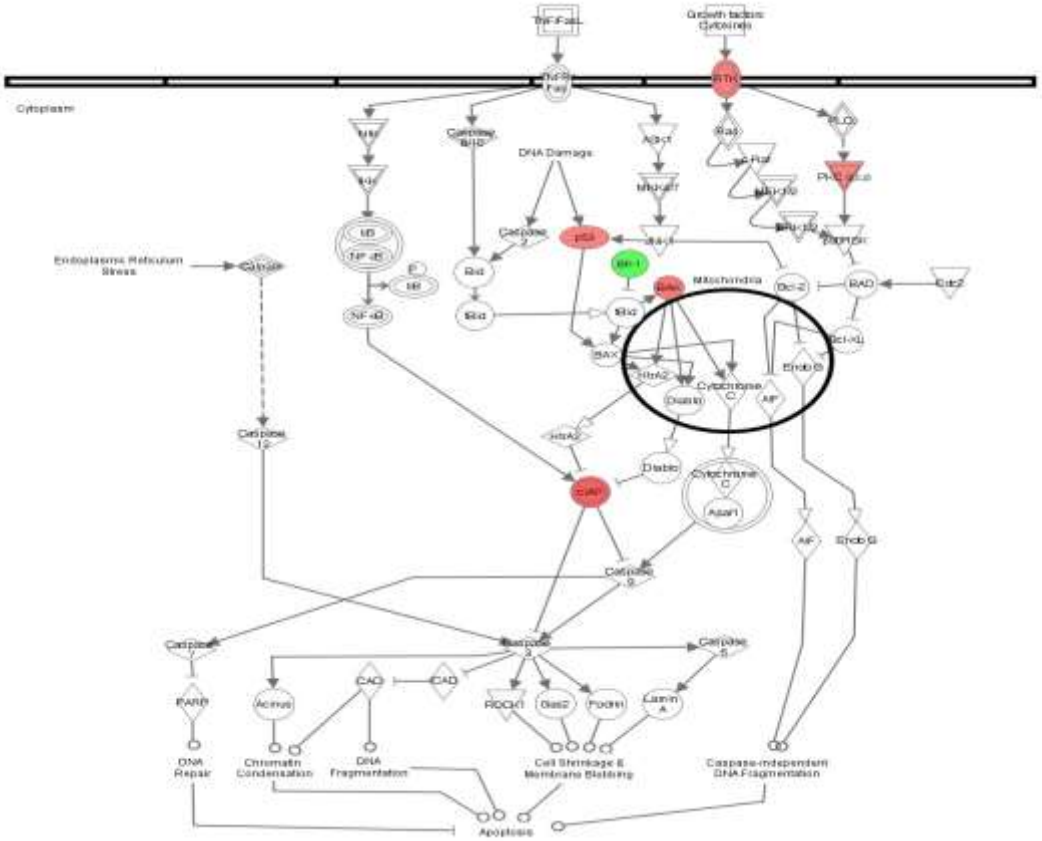


Figure 5: An overview of all functional categories, of the genes involved and the significance functions molecular and cellular functions.Fig.5-A", "functions disease and disorder. Fig.5-B" and "functions_ physiological system development. Fig.5-C".

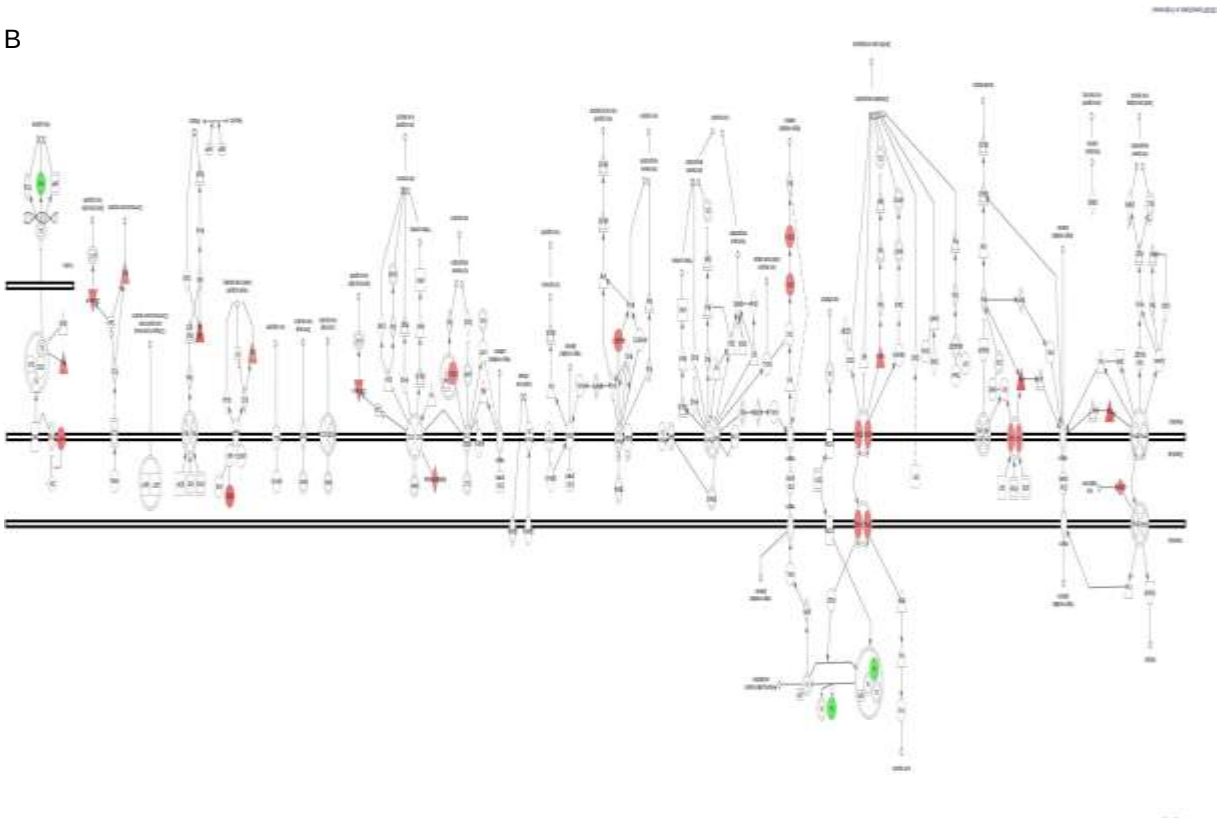
3.1.3.4. Pathway analysis:

As a third analysis, the regulated transcripts were analyzed for membership in manually generated signaling and metabolic pathways. Again, a p-value is calculated analogously as for the functional annotation. All pathways were listed by p-value in the files "metabolic pathways.jpg" and "signaling pathways.jpg". The modified transcripts that were assigned to the respective pathways listed in the files "metabolic pathways.xls" and "signaling pathways.xls". The pathways with the highest significance were additionally shown in detailed illustrations, Fig-6.

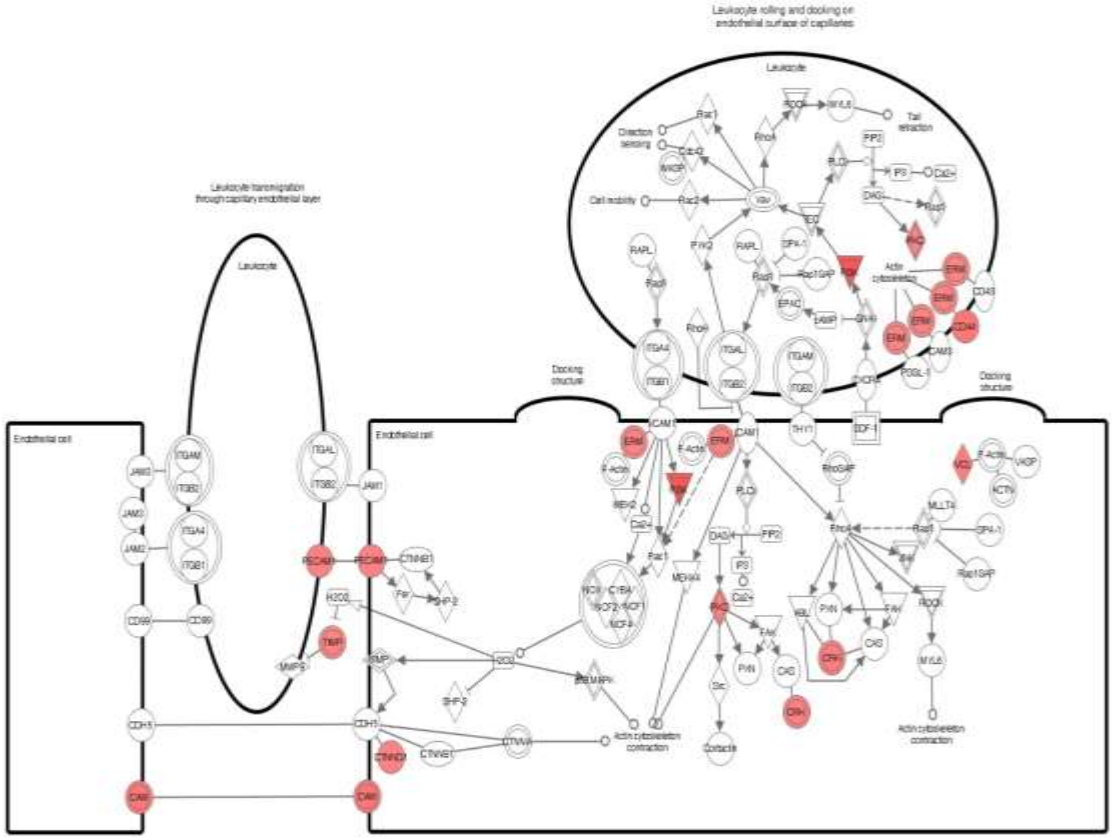
A



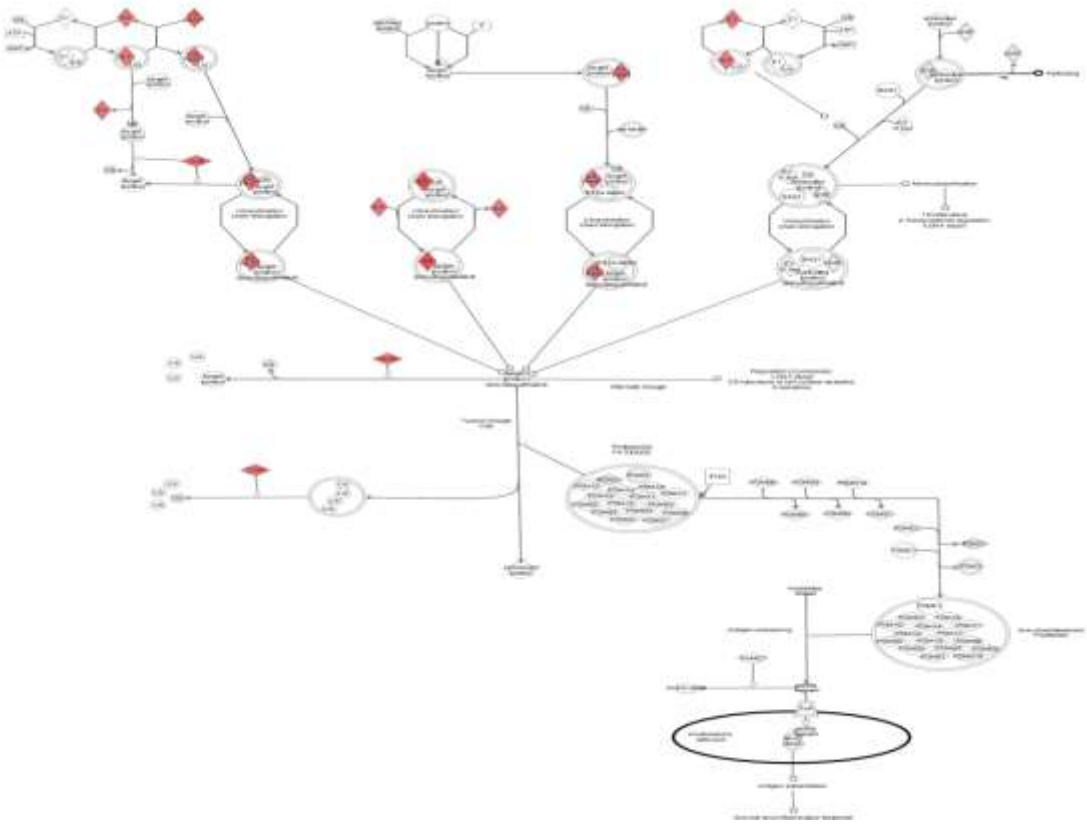
B



C



D



E

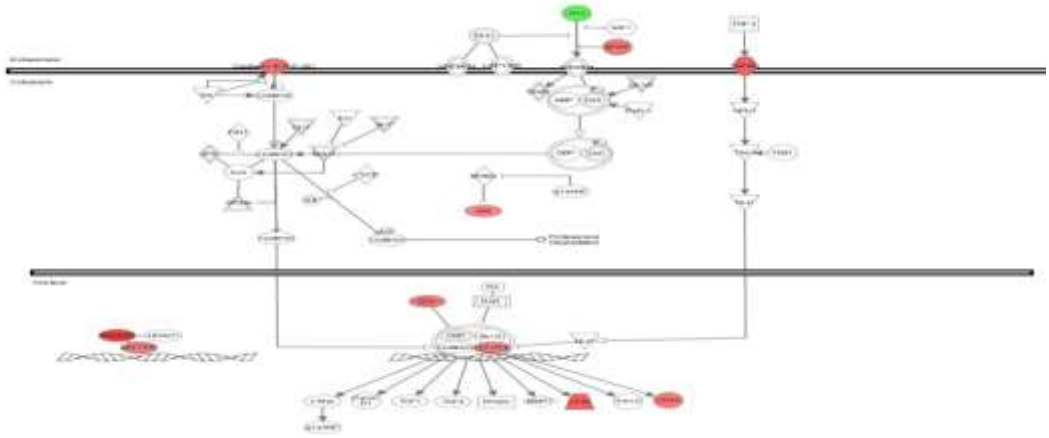


Figure 6: The pathways with the highest significance difference between Gum Arabic and control samples in detailed illustrations as, pathway apoptosis signaling A, pathway Axonal guidance signaling B, pathway Leukocyte extravasation signaling-3 C, pathway protein ubiquitination-5 D and pathway Wnt-beta catenin signaling-7 E .

3.1.3.2 Analysis of Gene interaction regulation:

Analysis of target genes-miRNA interaction network (up-regulated) were shown in Table 2 & Fig.7, also down-regulated genes were shown in Table 3 & Fig. 8 and, according to the fold change with their top function as shown in Table 4.

Table 2: Several genes expression mean and SD up-regulated by Gum arabic (Acacia senegal).

No	Gene Title	Control Mean &SD	GA Mean &SD	P-value	Fold Change
1	RIKEN cDNA 1300007C21	3.451±0.772	5.558±0.199	0.030	4.31
2	cytochrome P450, family 2, subfamily d, polypeptide 9	8.666±0.367	10.396±0.198	0.003	3.32
3	stomatin	5.773±0.409	7.421±0.163	0.006	3.13
4	PREDICTED	5.947±0.395	7.547±0.264	0.010	3.03
5	ubiquitin specific peptidase 12	4.646±0.468	6.205±0.187	0.015	2.95
6	stomatin	5.463±0.342	6.960±0.127	0.003	2.82
7	expressed sequence AI316828	7.648±0.528	9.082±0.109	0.029	2.70
8	UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 5	7.857±0.512	9.283±0.110	0.026	2.69
9	pyruvate carboxylase	4.130±0.461	5.524±0.138	0.020	2.63
10	stomatin	5.572±0.217	6.965±0.165	0.001	2.63
11	RIKEN cDNA 2610205E22 gene (2610205E22Rik), mRNA	4.243±0.138	5.613±0.569	0.047	2.59
12	carboxypeptidase D	3.788±0.465	5.158±0.360	0.048	2.58
13	CD38 antigen	7.785±0.264	9.131±0.096	0.001	2.54
14	RIKEN cDNA 9030612M13 gene	5.778±0.525	7.106±0.160	0.042	2.51
15	RIKEN cDNA 2310035C23 gene	5.533±0.400	6.856±0.121	0.013	2.50
16	aquaporin 4	7.978±0.183	9.259±0.095	0.000	2.43
17	RIKEN cDNA 4632427E13 gene	3.938±0.389	5.197±0.255	0.027	2.39
18	O-linked N-acetylglucosamine (GlcNAc) transferase	5.230±0.461	6.489±0.202	0.037	2.39
19	ADP-ribosylation factor 3	4.280±0.367	5.526±0.049	0.010	2.37
20	beta galactoside alpha 2,6 sialyltransferase 1	6.615±0.450	7.860±0.064	0.025	2.37
21	SH3 domain protein D19	4.791±0.277	6.020±0.118	0.004	2.34
22	cytochrome P450, family 2, subfamily d, polypeptide 10	8.932±0.392	10.148±0.134	0.019	2.32
23	RIKEN cDNA 5830411G16 gene	4.297±0.339	5.499±0.132	0.011	2.30
24	Cullin 4A (Cul4a), mRNA	7.022±0.252	8.195±0.163	0.004	2.26
25	membrane-bound transcription factor peptidase, site 1	5.557±0.439	6.726±0.194	0.041	2.25
26	low density lipoprotein receptor	5.593±0.387	6.758±0.174	0.025	2.24
27	RIKEN cDNA 4921513D23 gene	5.883±0.345	7.046±0.074	0.011	2.24
28	RIKEN cDNA 2310010I16 gene	6.783±0.184	7.945±0.046	0.000	2.24
29	hypothetical protein E130307C13	4.193±0.393	5.354±0.136	0.023	2.24
30	fucosyltransferase 2	4.799±0.249	5.956±0.183	0.006	2.23
31	RIKEN cDNA 4833439L19 gene	7.111±0.306	8.263±0.119	0.008	2.22
32	Ribosomal protein S6 kinase polypeptide 3 (Rps6ka3), mRNA	4.505±0.400	5.651±0.257	0.042	2.21
33	lin 7 homolog c (C. elegans)	7.652±0.345	8.789±0.048	0.011	2.20
34	vacuolar protein sorting 33A (yeast)	4.682±0.363	5.810±0.123	0.019	2.19
35	amyloid beta (A4) precursor-like protein 2	8.011±0.416	9.136±0.092	0.030	2.18
36	Cullin 4A (Cul4a), mRNA	6.929±0.261	8.049±0.137	0.005	2.17

37	glia maturation factor, beta	5.994±0.372	7.111±0.093	0.020	2.17
38	SM-11044 binding protein	5.484±0.325	6.601±0.097	0.011	2.17
39	glia maturation factor, beta	7.475±0.297	8.582±0.099	0.008	2.15
40	Rab40c, member RAS oncogene family	5.631±0.386	6.737±0.104	0.025	2.15
41	suppressor of Ty 16 homolog (S. cerevisiae)	6.120±0.280	7.207±0.123	0.007	2.12
42	cytochrome P450, family 2, subfamily f, polypeptide 2	8.576±0.443	9.658±0.119	0.046	2.12
43	glucuronidase, beta	5.858±0.273	6.926±0.089	0.006	2.10
44	tripeptidyl peptidase II	5.967±0.440	7.019±0.067	0.046	2.07
45	Rap guanine nucleotide exchange factor (GEF) 1	2.248±0.130	3.298±0.205	0.003	2.07
46	microtubule-associated protein 7	4.245±0.279	5.295±0.149	0.011	2.07
47	X-linked myotubular myopathy gene 1	8.268±0.301	9.316±0.070	0.010	2.07
48	interleukin 18	10.436±0.413	11.481±0.158	0.046	2.06
49	vav 3 oncogene	4.782±0.386	5.823±0.100	0.031	2.06
50	solute carrier family 26, member 3	12.171±0.380	13.210±0.072	0.028	2.05
51	xenotropic and polytropic retrovirus receptor 1	5.656±0.370	6.685±0.076	0.026	2.04
52	solute carrier family 39 (metal ion transporter), member 8	5.549±0.281	6.572±0.125	0.010	2.03
53	solute carrier family 7 (cationic amino acid transporter, y+ system), member 9	6.642±0.342	7.662±0.230	0.038	2.03
54	LIM and senescent cell antigen-like domains 1	6.428±0.239	7.447±0.056	0.003	2.03
55	sphingosine phosphate lyase 1	6.029±0.319	7.045±0.084	0.015	2.02
56	mesoderm induction early response 1 homolog (Xenopus laevis	7.193±0.197	8.209±0.153	0.004	2.02
57	Gene model 608, (NCBI) (Gm608), mRNA	4.332±0.395	5.346±0.105	0.038	2.02
58	protein kinase, cAMP dependent, catalytic, beta	6.161±0.288	7.164±0.084	0.010	2.00
59	adenylate kinase 3 alpha-like 1	3.626±0.245	4.626±0.131	0.007	2.00

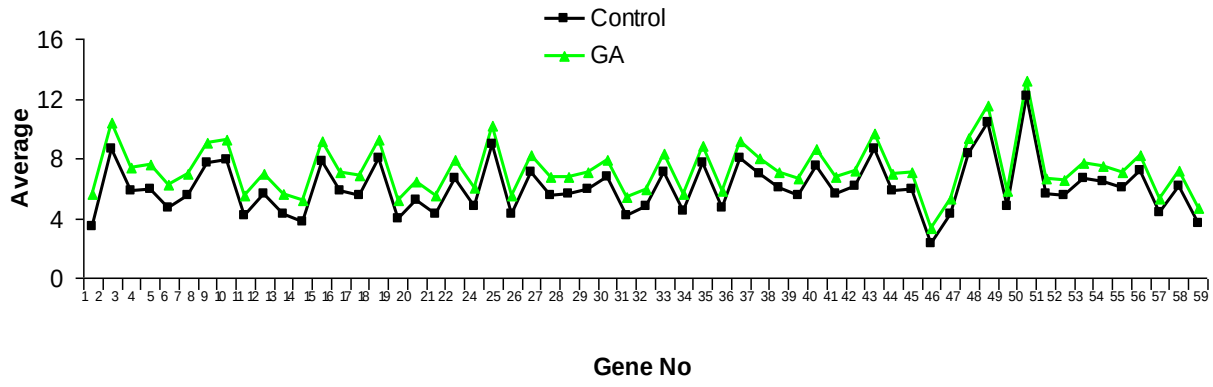


Figure 7: Several genes expression up-regulated by Gum arabic (Acacia senegal)

Table 3: Several gene expression down-regulated by Gum Arabic (Acacia senegal).

NO	Gene Title	Control Mean &SD	GA Mean &SD	P-value	Fold Change
1	Immunoglobulin heavy chain 6 (heavy chain of IgM), mRNA (cDNA clone MGC:18788 IMAGE:4189350)	7.040±0.103	6.026±0.298	0.012	-2.02
2	CD79B antigen	7.344±0.319	6.309±0.139	0.018	-2.05
3	CD3 antigen, delta polypeptide	4.060±0.388	3.020±0.114	0.033	-2.06
4	CD3 antigen, delta polypeptide	6.317±0.335	5.277±0.208	0.030	-2.06
5	serine (or cysteine) preptidase inhibitor, clade A, member 1b	7.048±0.174	6.006±0.286	0.014	-2.06
6	RIKEN cDNA 9130022K13 gene /// RIKEN cDNA 2210421G13 gene /// hypothetical protein LOC193676	7.214±0.364	6.166±0.121	0.026	-2.07
7	Monoclonal antiidiotypic antibody IgK (hypervariable region) mRNA	5.849±0.350	4.798±0.197	0.031	-2.07
8	immunoglobulin heavy chain 6 (heavy chain of IgM)	8.633±0.326	7.580±0.169	0.021	-2.07
9	DENN/MADD domain containing 2A	3.927±0.378	2.856±0.044	0.023	-2.10
10	sulfatase 1	4.760±0.075	3.689±0.156	0.000	-2.10
11	coronin, actin binding protein 1A	9.014±0.257	7.935±0.179	0.009	-2.11
12	T-cell receptor alpha chain /// RIKEN cDNA A430107P09 gene /// similar to T-CELL RECEPTOR ALPHA CHAIN C REGION /// similar to T-cell receptor alpha-chain precursor	4.472±0.399	3.381±0.100	0.029	-2.13
13	RIKEN cDNA 0610025L06 gene	8.460±0.260	7.346±0.188	0.008	-2.17
14	Fas apoptotic inhibitory molecule 3	6.908±0.196	5.779±0.225	0.005	-2.19
15	regulator of G-protein signaling 4	6.150±0.204	4.997±0.381	0.028	-2.22
16	CD79A antigen (immunoglobulin-associated alpha)	7.737±0.316	6.560±0.287	0.025	-2.26
17	RIKEN cDNA 0610025L06 gene	5.761±0.273	4.578±0.135	0.005	-2.27
18	membrane-spanning 4-domains, subfamily A, member 1	7.228±0.374	6.038±0.258	0.031	-2.28
19	tumor necrosis factor receptor superfamily, member 13b	5.123±0.310	3.931±0.129	0.008	-2.28
20	ubiquitin D	7.356±0.421	6.149±0.236	0.037	-2.31
21	Ras association (RalGDS/AF-6) domain family 5	5.719±0.267	4.492±0.129	0.003	-2.34
22	histocompatibility 2, class II antigen E beta	10.788±0.526	9.523±0.145	0.049	-2.40
23	chemokine (C-X-C motif) ligand 14	6.308±0.498	5.040±0.091	0.037	-2.41
24	RIKEN cDNA 2010001M09 gene	8.001±0.399	6.711±0.231	0.023	-2.45
25	chemokine (C-X-C motif) ligand 14	5.726±0.414	4.392±0.107	0.014	-2.52
26	interleukin 1 beta	5.100±0.561	3.737±0.123	0.045	-2.57
27	immunoglobulin kappa chain variable 28 (V28)	7.622±0.236	6.158±0.554	0.041	-2.76
28	RIKEN cDNA 1200013B08 gene	5.384±0.331	3.872±0.386	0.018	-2.85
29	expressed sequence AI987692	12.689±0.511	11.167±0.189	0.023	-2.87
30	melanoma-derived leucine zipper, extra-nuclear factor	9.567±0.413	8.044±0.213	0.011	-2.87
31	membrane-spanning 4-domains, subfamily A, member 4B	5.800±0.482	4.254±0.324	0.029	-2.92
32	immunoglobulin heavy chain 6 (heavy chain of IgM)	8.338±0.566	6.665±0.258	0.027	-3.19
33	resistin like alpha	8.514±0.627	6.739±0.100	0.023	-3.42
34	RIKEN cDNA 9030605I04 gene	13.347±0.532	11.455±0.254	0.012	-3.71
35	granzyme A	6.927±0.747	4.811±0.305	0.031	-4.33
36	chemokine (C-C motif) ligand 5	5.946±0.746	3.820±0.231	0.026	-4.37
37	angiogenin, ribonuclease A family, member 1	5.712±0.823	3.542±0.304	0.039	-4.50
38	angiogenin, ribonuclease A family, member 4	13.619±0.593	10.601±1.020	0.034	-8.10
39	immunoglobulin heavy chain 4 (serum IgG1)	7.154±1.195	4.090±0.426	0.042	-8.37
40	immunoglobulin heavy chain 4 (serum IgG1)	7.671±1.156	4.305±0.350	0.024	-10.31
41	angiogenin, ribonuclease A family, member 4	11.586±0.786	7.921±1.129	0.029	-12.68

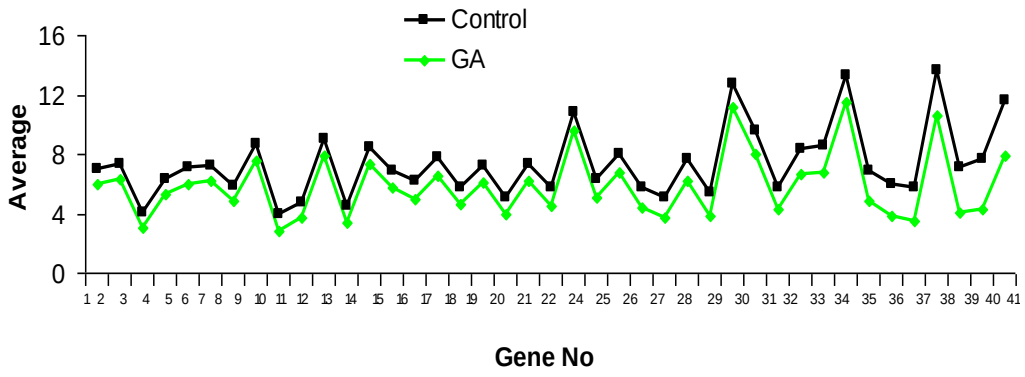


Figure 8: Several genes expression down-regulated by Gum arabia (Acacia senegal)

Table 4: Microarray of Sseveral genes expression with their top functions after Gum arabic (Acacia senegal) administration.

ID	Genes	Score	Focus Genes	Top Functions
1	**ANG,** CSAR1, **CD3D,** **CD79A,** **CD79B,** CIITA, GBP2, GBP3, **GZMA,** **HLA-DMB,** **HLA-DRB1,** IFIT1L, IGH-3, IGH-8, **IGH-1A,** **IGHG1*,** IGHG2, IGHG3, IGHG4, **IGHM*,** IGKC, IGL@, IGLL1, IL2, IL4, IL6, MOG, **MS4A1,** **RETNLA,** SAMSN1, SEMA4D, **SLC26A3,** **STOM*,** **TNFRSF13B,** VPREB1 (includes EG:7441	25	15	Immune Response, Hematological System Development and Function, Immune and Lymphatic System Development and Function
2	AQP2, **AQP4,** ATF4, CDKN1A, CNKSR3, CREB3, CTNNB1, **CYP2D9,** DLG1, GDF15, GH1, HDC, HMGB2, HSPA1A, KCNJ4, KLF10, **LIN7C,** MAZ, **MBTPS1,** MET, **MI-ER1,** MUC2, **OGT,** PLK2, **RAB40C,** **RPS6KA3 (includes EG:6197),** SGK, **SLC7A9,** SP1, SSRP1, **SULF1,** **SUPT16H,** TP53, **VPS33A,** WT1	18	12	Cancer, Cell Death, Reproductive System
3	ABCD3, ASS, ATF6, CASP9, CAT, **CD38,** **CORO1A,** CRP, CXCL5, CXCL9, **CYP2D10,** **CYP2F1,** DPP4, FN1, GCLC, GLA, **GMFB*,** **H2AFJ,** IFNG, LEP, MMP11, MOG, NFYB, OGG1, **PACAP,** PCSK2, PECAM1, PHLDA1, RAB3C, RFX5, SEPP1, **SLC39A8,** **ST6GAL1,** **TUG1 (includes EG:544752),** **UBD**	16	11	Metabolic Disease, Cell-To-Cell Signaling and Interaction, Hematological System Development and Function
4	ADAM17, ALCAM, **ARF3,** ARG1, BDKRB1, COLEC2, **CPD,** **CXCL14*,** DUSP6, EGF, GBP2, GM2A, **GUSB,** HAS1, HMGN2, HSD11B1, IER2, IGK@, IL8, IL1R2, **MTM1*,** MYC, P4HB, PENK1, PMP2, PNPT1, **PRKACB,** PRL, PSME2, PTAFR, **RGS4,** **SH3D19,** TNF, **TPP2,** **VAV3**	14	10	Lipid Metabolism, Small Molecule Cellular Development
5	ALCAM, APBB1, **APLP2,** **B3GALT5,** **CCL5,** CCR4, CCRL2, CD163, CORT, CTSZ (includes EG:1522), DUSP6, ECGF1, ENPP1, HRAS, **IL18,** IL18BP, **IL1B,** **LDLR,** **LIMS1,** MAPK8, MUC2, P4HB, PBEF1, PIGR, **RAPGEF1,** **RASSF5,** SCYE1, **SERPINA1,** SERPINB2, SERPINB9, SLC10A1, SLC10A2, SQLE, TAP2, TCF1	14	10	Cellular Movement, Dermatological Diseases and Conditions, Inflammatory Disease
6	**AK3L1,** TCOF1 (includes EG:6949	2	1	Developmental Disorder, Genetic Disorder, Gene Expression
7	**MAP7,** TRPV4, YWHAG	2	1	Cell Morphology, Cell Signaling, Cellular Assembly and Organization
8	CHMP4A, CHMP4B, **CHMP4C,** PDCD6IP, VPS4A	2	1	Cell Morphology, Cellular Assembly and Organization, Cancer

Indicates up regulation of gene expression indicates down regulation of gene expression

DISCUSSION

In the last decade, advances in DNA sequence technology have dramatically influenced the transcriptome and genome sequencing. Micro-arrays and SAGE have enabled large-scale transcriptome analysis from numerous plants. These techniques, however, can only be used for model plants with known genome sequences. EST sequence was successfully used in non-model plants to analyze transcriptome. Deep EST sequence using capillary sequencing involving cDNA cloning and individual DNA preparations is time consuming and expensive for each clone. Transcriptome analysis by using the Illumina sequencing technology has recently been applied to several species that lack genomic sequence data and are one of the most popular tools for gene discovery. (Wang, B., et al.,2019). The results of the current study also indicated that microarray can be effectively assembled and used for novel genes discovery with their functions. In our study RNAs were assessed the array quality and comparability according to MAS5 Analysis of the arrays. All values are in the normal range and indicate good data quality.

The genes expression up-regulated by Gum Arabic were 59 (Table 2, Fig. 6) and genes down-regulated by Gum Arabic. were 41 (Table 3, Fig. 7) including large number of genes involved in different metabolic functions, cover various biological processes and molecular functions, Analysis of target genes-miRNA interaction network, analyzed according to fold change 51 up-regulated genes shown in (Table 2 & Fig.6), and down-regulated genes is shown in (Table 3 & Fig.7) well described according to their biological function is shown in (Table 4).The up- regulated genes by Gum Arabic had fold change above 2.00, whereas down- regulated genes by Gum Arabic had fold change below 2.00

Genes after administrating GA, showed that 15 Genes were focused with score of 25, out of which 13 are up regulated with known function and found in gene bank is given below (Table 4) ANG, This gene is an extremely powerful mediator of the formation of new blood vessels. It hydrolyzes tRNAs that lead to lower protein synthesis and is similar to pancreatic ribonuclease, the mature peptide has antimicrobial activity against some bacteria and fungi, including S. pneumoniae and C. albicans. [provided by RefSeq, Aug 2014] https://www.genecards.org/cgi-bin/carddisp.pl?gene=ANG**).** CD3D The protein encoded in this gene is part of the complex T-cell / CD3 (TCR / CD3) receptor and is involved in the development and transduction of T-cell signal. Defects in this gene are a cause of severe combined immunodeficiency autosomal recessive T-cell-negative/B-cell-positive/NK-cell-positive (SCIDBNK) [provided by RefSeq, Feb 2009 https://www.genecards.org/cgi-bin/carddisp.pl?gene=CD3D].CD79 The B lymphocyte antigen receptor is a multimeric complex comprising the specific antigen component called surface immunoglobulin (Ig), Surface Ig non-covalently associates with two other proteins, Ig-alpha and Ig-beta, which are necessary for expression and function of the B-cell antigen receptor[provided by RefSeq, Jul 2008] https://www.genecards.org/cgi-bin/carddisp.pl?gene=CD79A.CD79B , it is The B lymphocyte antigen receptor, non-covalently associates with two other proteins, Ig-alpha and Ig-beta, which are necessary for expression and function of the B-cell antigen receptor. This gene encodes the Ig-beta protein of the B-cell antigen component. [provided by RefSeq, Jul 2008] https://www.genecards.org/cgi-bin/carddisp.pl?gene=CD79B).GZMA, function as a common component necessary for lysis of target cells by cytotoxic T lymphocytes and natural killer cells https://www.genecards.org/cgi-bin/carddisp.pl?gene=GZMA),HLA-DMB, plays a central role in the peptide loading of MHC class II molecules by helping to release the CLIP (class II-associated invariant chain peptide) molecule from the peptide binding siteThey are expressed in antigen presenting cells (APC: B lymphocytes, dendritic cells, macrophages). [provided by RefSeq, Jul 2008] https://www. genecards. org/cgi-bin/carddisp.pl?gene=HLA-DMB, HLA-DRB1 It plays a central role in the immune system by presenting peptides derived from extracellular proteins. Present in the peptide binding specificities. [provided by RefSeq, Jul 2008] https://www .genecards . org/cgi-bin/carddisp.pl?gene=HLA-DRB1,IGH-1A Immunoglobulins recognize foreign antigens and initiate immune responses such as phagocytosis and the complement system. [provided by RefSeq, Dec 2017] https://www.genecards.org/cgi-bin/carddisp .pl?gene= IGH . IGHG1 (Immunoglobulin Heavy Constant Gamma 1 (G1m Marker)) is a Protein Coding gene. Among its related pathways are Role of phospholipids in phagocytosis and Creation of C4 and C2 activators. Gene Ontology (GO) annotations

related to this gene include *antigen binding*. An important paralog of this gene is IGHG3. https://www.genecards.org/cgi-bin/carddisp.pl?gene=IGHG1),IGHM , gene encodes the C region of the mu heavy chain, which defines the IgM isotype. secreted Ig forms that act as antibodies can be produced by alternative RNA processing of the heavy chain C region sequences. (summary by Janeway et al., 2005).[supplied by OMIM, Aug 2010, https://www.ncbi.nlm.nih.gov/gene/3507,MS4A1, this gene encodes a B-lymphocyte surface molecule which plays a role in the development and differentiation of B-cells into plasma cells. https://www.genecards.org/cgi-bin/carddisp.pl?gene=MS4A1.RETNLA it is Probable hormone. Plays a role in pulmonary vascular remodeling https://www.uniprot.org/uniprot/Q9EP95.TNFRSF 13B , provides instructions for making a protein called TACI. Through interactions with other proteins, TACI promotes cell signaling, plays a role in B cell survival and maturation, and is involved in the production of antibodies. https://www.ncbi.nlm.nih.gov/gene/23495 . Genes after administrating GA, showed that 15 Genes were focused with score of 25, out of which 2 are down regulated.SLC26A3 this gene is Chloride/bicarbonate exchanger. Mediates the efficient absorption of chloride ions in the colon, participating in fluid homeostasis. Plays a role in the chloride and bicarbonate homeostasis during sperm epididymal maturation and capacitation. https: // www.uniprot.org/uniprot/P40879. STOM This gene codes an integral membrane protein in a highly conserved family, The encoded protein is located on the red blood cell membrane and other type of cells where it may regulate ion channels and transporters. https://www.genecards.org/cgi-bin/carddisp.pl?gene=STOM ,

Genes after administrating GA, 12 Genes were focused with score 18 (Table 4) the 1 upregulated genes and 11 genes with score 25 were down regulated with known function and found in gene bank is given below:-

SULF1, this gene shows upregulation with GA administration, is involved in cell signalling, https://www.ncbi.nlm.nih.gov/gene/55959. AQP4, this gene shows downregulation with GA administration, This protein is the predominant aquaporin found in brain and has an important role in brain water homeostasis. https://www.genecards. org/cgi-bin/carddisp.pl?gene= AQP4. CYP2D9, this gene shows downregulation with GA administration . The CYP2C9 enzyme breaks down (metabolizes) compounds including steroid hormones and fatty acids. https://ghr.nlm.nih.gov/gene/CYP2C9. LIN7C, this gene shows downregulation with GA administration Forms membrane-associated multiprotein complexes that may regulate delivery and recycling of proteins to the correct membrane domains. https://www.genecards.org/cgi-bin/carddisp.pl? gene= LIN7C . MBTPS1, this gene shows downregulation with GA administration,regulates cholestrol or lipid homeostasis, https://www.genecards.org/cgi-bin/carddisp.pl? gene= MBTPS1. MI-ER1, this gene shows downregulation with GA administration, protein functions as a transcriptional regulator. https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIER1. OGT, this gene shows downregulation with GA administration, can regulate their cellular processes like glycosylation and phosphoryltion. https://ghr.nlm.nih.gov/gene/OGT. RAB40C , this gene shows downregulation with GA administration, induces metabolism of proteins, https://www.genecards.org/cgi-bin/carddisp.pl?gene=RAB40C. RPS6KA3 (INCLUDES EG:6197), this gene shows downregulation with GA administration, these proteins help regulate the activity of certain genes and are involved in signaling within cells. https://ghr.nlm.nih.gov/gene/RPS6 KA3. SLC7A9, this gene shows downregulation with GA administration, this protein absorbs particular protein into the blood. https://ghr.nlm.nih.gov/gene/SLC7A9. SUPT16H, this gene shows downregulation with GA administration, facilitates chromatin transcription provided by RefSeq, Feb 2009, https://www.genecards.org/cgi-bin/carddisp.pl?gene=SUPT16H. VPS33A this gene shows downregulation with GA administration, Plays a role in vesicle-mediated protein trafficking to lysosomal compartments https://www.genecards.org/cgi-bin/carddisp.pl?gene=VPS33A .

Genes after administrating GA, showed that 11 Genes were focused with score of 16, out of which 3 are up regulated. UBD genes is involved in many cellular processes, caspase-dependent apoptosis, formation of aggresomes, mitotic regulation, and dendritic cell maturation https://www.genecards.org/cgi-bin/carddisp.pl?gene=UBD. CORO1A, involved in cell cycle progression, signal transduction, apoptosis, and gene regulation

https://www.genecards.org/cgi-bin/carddisp.pl?gene=CORO1A. PACAP, include regulation of proliferation, differentiation, and apoptosis in some cell populations https://www.ncbi.nlm.nih.gov/pubmed/11133067 .

Genes after administrating GA, showed that 11 Genes were focused with score of 16, out of which 8 are down regulated, CD38, catalyzes the synthesis and hydrolysis of cyclic ADP-ribose (cADPR) from NAD^+ to ADP-ribose https://www.genecards.org/cgi-bin/carddisp.pl?gene=CD38 . CYP2D10, in liver microsomes, this enzyme is involved in an NADPH-dependent electron transport pathway https://www .uniprot .org /uniprot / P24456. CYP2F1, are monooxygenases which catalyze many reactions involved in drug metabolism and synthesis of cholesterol, steroids and other lipids https://www.genecards.org/cgi-bin/carddisp.pl?gene=CYP2F1. GMFB, causes differentiation of brain cells, stimulation of neural regeneration, and inhibition of proliferation of tumor cells https://www.genecards.org/cgi-bin/carddisp.pl?gene=GMFB. H2AFJ, these are histone proteins responsible for the nucleosome structure of the chromosomal fiber in eukaryotes https://www.genecards.org/cgi-bin/carddisp.pl?gene= H2AJ . SLC39A8 gene acts as a transporter of several divalent cations, including manganese (Mn), zinc (Zn), cadmium (Cd), and iron (Fe), across the plasma membrane (Boycott et al., 2015 and Park et al., 2015).ST6GAL1 Catalyzes the transfer of sialic acid from CMP-sialic acid to galactose-containing substrates. https://www . genecards.org/cgi-bin/carddisp.pl?gene=ST6GAL1.TUG1(INCLUDES EG: 544752), functions in the epigenetic regulation of transcription https://www.genecards.org/cgi-bin / carddisp.pl?gene=TUG1.

4 Genes after administrating GA, showed that 10 Genes were focused with score of 14, out of which 2 are up regulated, CXCL14, proteins involved in immunoregulatory and inflammatory processes https://www.genecards.org/cgi-bin/carddisp.pl?gene=CXCL14. RGS4, regulatory molecules that act as GTPase activating proteins (GAPs) for G alpha subunits of heterotrimeric G proteins. https://www.genecards.org/cgi-bin/ carddisp.pl ? gene=RGS4.

Genes after administrating GA, showed that 10 Genes were focused with score of 14, out of which 8 are down regulated, ARF3, stimulate the ADP-ribosyltransferase. Involved in protein trafficking; https://www.genecards.org/cgi-bin/carddisp.pl?gene= ARF3. CPD, a hepatitis B virus-binding protein https://www.genecards.org/cgi-bin/carddisp.pl ? gene = CPD . GUSB, The *GUSB* gene provides instructions for producing an enzyme called beta-glucuronidase (β-glucuronidase https://ghr.nlm.nih.gov/gene/GUSB. MTM1, provides instructions for producing an enzyme called myotubularin https:// ghr .nlm . nih.gov/gene/MTM1.PRKACB, protein is a catalytic subunit of cAMP (cyclic AMP)-dependent protein kinase, https://www.genecards.org/cgi-bin/carddisp.pl? gene= PRKACB. SH3D19 , May play a role in regulating A disintegrin and metalloproteases (ADAMs) in the signaling of EGFR-ligand shedding https://www. Uniprot .org/ uniprot/Q5HYK7. TPP2, functions for some MHC class I antigen presentation. https:// www.genecards.org/cgi-bin/carddisp.pl?gene=TPP2. VAV3 activate pathways leading to actin cytoskeletal rearrangements and transcriptional alterations. https:// www. genecards.org/cgi-bin/ carddisp.pl?gene=VAV3 .

Genes after administrating GA, 4 Genes were focused with score 10 showed up regulation, CCL5, is chemotactic for T cells, eosinophils, and basophils, and plays an active **role** in recruiting leukocytes into inflammatory sites https://www .genecards. org/cgi-bin/carddisp.pl?gene=CCL5 .IL1B, promotes B-cell activation and antibody production, and fibroblast proliferation and collagen production https://ghr. nlm.nih. gov/gene/IL1B. RASSF5, It functions as a tumor suppressor, and is inactivated in a variety of cancers. https://www.genecards.org/cgi-bin/carddisp.pl?gene=RASSF5. SERPINA1 Serpins help control several types of chemical reactions by blocking (inhibiting) the activity of certain enzymes https://ghr.nlm.nih.gov/gene/SERPINA1.

Genes after administrating GA, 6 Genes were focused with score 10 showed down regulation, APLP2, couples retina development https:// www.ncbi. nlm.nih. gov/ gene/11804. B3GALT5, protein is involved in the pathway protein glycosylation, https://www.uniprot.org/uniprot/Q9Y2C3. IL18, The protein encoded by this gene is a proinflammatory cytokine that augments natural killer cell activity in spleen cells, and stimulates interferon gamma production in T-helper type I cells. https://www. genecards. org/cgi-bin/carddisp.pl?gene=IL18 . LDLR, instructions for making a protein called a low-density lipoprotein

receptor. https://ghr.nlm.nih.gov/gene/LDLR . LIMS1, it is involved in growth factor receptor kinase signaling pathways https://www.genecards. org/cgi-bin/carddisp.pl?gene=LIMS1. RAPGEF1 involved in apoptosis, integrin-mediated signal transduction, and cell transformation. https://www.genecards.org/cgi-bin/carddisp.pl?gene=RAPGEF1 .

Genes after administrating GA, 3 Genes were focused with score 2 shows downregulation, AK3L1, Adenylate kinases regulate the adenine and guanine nucleotide compositions within a cell by catalyzing the reversible transfer of phosphate group among these nucleotides. https://www.genecards.org/cgi-bin/carddisp.pl?gene= AK4. MAP7, Microtubule-stabilizing protein that may play an important role during reorganization of microtubules during polarization and differentiation of epithelial cells. involved in the function of cell morphogy, cell signaling, cellular assembly and organization. https://www.genecards.org/cgi-bin/carddisp.pl?gene=MAP7 . CHMP4C, The role of CHMP4C in the formation of stable kinetochore-microtubule attachments during the cell cycle https://www.ncbi.nlm.nih.gov/gene/92421

CONCLUSION

It was noteworthy that many genes were identified which is involved in the upstream and downstream metabolic pathways, A better understanding of molecular pathways involved in different cellular mechanism. These valuable gene candidates could prove beneficial for producing larger quantities of such bioactive compounds for medical applications. This study may help close the gap between traditional knowledge and current practices in therapeutic industry.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

ACKNOWLEGEMENT

The author acknowledged the help of Prof Florian Lang Physiology Institute-1, Prof Dr.med Ferruh Artunc, University Hospital Tubeingen. Microarray Facility, Tubingen University, Germany,

AUTHOR CONTRIBUTIONS

Omaima Nasir associated with whole project administration, methodology, review, editing and writing original draft.

REFERENCES

Ahmed, A. A., Fedail, J. S., Musa, H. H., Musa, T. H., & Sifaldin, A. Z. (2016). Gum Arabic supplementation improved antioxidant status and alters expression of oxidative stress gene in ovary of mice fed high fat diet. Middle East Fertility Society Journal, 21(2), 101-108.

Al Za'abi, M., Al Busaidi, M., Yasin, J., Schupp, N., Nemmar, A., & Ali, B. H. (2015). Development of a new model for the induction of chronic kidney disease via intraperitoneal adenine administration, and the effect of treatment with gum acacia thereon. American journal of translational research, 7(1), 28.

Ali, B. H., Al-Husseni, I., Beegam, S., Al-Shukaili, A., Nemmar, A., Schierling, S.& Schupp, N. (2013). Effect of gum Arabic on oxidative stress and inflammation in adenine–induced chronic renal failure in rats. PloS one, 8(2), e55242.

Aye, M. M., Aung, H. T., Sein, M. M., & Armijos, C. (2019). A Review on the Phytochemistry, Medicinal Properties and Pharmacological Activities of 15 Selected Myanmar Medicinal Plants. Molecules, 24(2), 293.

Babiker, R., Elmusharaf, K., Keogh, M. B., & Saeed, A. M. (2018). Effect of Gum Arabic (Acacia Senegal) supplementation on visceral adiposity index (VAI) and blood pressure in patients with type 2 diabetes mellitus as indicators of cardiovascular disease (CVD): a randomized and placebo-controlled clinical trial. Lipids in health and disease, 17(1), 56.

Barton DP, Cai A, Wendt K, Young M, Gamero A, et al.: Angiogenic protein expression in advanced epithelial ovarian cancer. Clin Cancer Res 3, 1579–1586, 1997.

Boycott, K. M., Beaulieu, C. L., Kernohan, K. D.,

Gebril, O. H., Mhanni, A., Chudley, A. E. & Tetreault, M. (2015). Autosomal-recessive intellectual disability with cerebellar atrophy syndrome caused by mutation of the manganese and zinc transporter gene SLC39A8. The American Journal of Human Genetics, 97(6), 886-893.

Ekor, M. (2014). The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. Frontiers in pharmacology, 4, 177.

https://ghr.nlm.nih.gov/gene/CYP2C9
https://ghr.nlm.nih.gov/gene/GUSB
https://ghr.nlm.nih.gov/gene/IL1B
https://ghr.nlm.nih.gov/gene/LDLR
https://ghr.nlm.nih.gov/gene/MTM1
https://ghr.nlm.nih.gov/gene/OGT
https://ghr.nlm.nih.gov/gene/RPS6KA3
https://ghr.nlm.nih.gov/gene/SERPINA1
https://ghr.nlm.nih.gov/gene/SLC7A9
https://www.genecards.org/cgi-bin/carddisp.pl?gene=AK4
https://www.genecards.org/cgi-bin/carddisp.pl?gene=ANG
https://www.genecards.org/cgi-bin/carddisp.pl?gene=AQP4
https://www.genecards.org/cgi-bin/carddisp.pl?gene=ARF3
https://www.genecards.org/cgi-bin/carddisp.pl?gene=CCL5
https://www.genecards.org/cgi-bin/carddisp.pl?gene=CD38
https://www.genecards.org/cgi-bin/carddisp.pl?gene=CD3D
https://www.genecards.org/cgi-bin/carddisp.pl?gene=CD79A
https://www.genecards.org/cgi-bin/carddisp.pl?gene=CD79B
https://www.genecards.org/cgi-bin/carddisp.pl?gene=CORO1A
https://www.genecards.org/cgi-bin/carddisp.pl?gene=CPD
https://www.genecards.org/cgi-bin/carddisp.pl?gene=CXCL14
https://www.genecards.org/cgi-bin/carddisp.pl?gene=CYP2F1
https://www.genecards.org/cgi-bin/carddisp.pl?gene=GMFB
https://www.genecards.org/cgi-bin/carddisp.pl?gene=GZMA
https://www.genecards.org/cgi-bin/carddisp.pl?gene=H2AJ
https://www.genecards.org/cgi-bin/carddisp.pl?gene=HLA-DMB
https://www.genecards.org/cgi-bin/carddisp.pl?gene=HLA-DRB1
https://www.genecards.org/cgi-bin/carddisp.pl?gene=IGH
https://www.genecards.org/cgi-bin/carddisp.pl?gene=IGHG1
https://www.genecards.org/cgi-bin/carddisp.pl?gene=IL18
https://www.genecards.org/cgi-bin/carddisp.pl?gene=LIMS1
https://www.genecards.org/cgi-bin/carddisp.pl?gene=LIN7C
https://www.genecards.org/cgi-bin/carddisp.pl?gene=MAP7
https://www.genecards.org/cgi-bin/carddisp.pl?gene=MBTPS1
https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIER1
https://www.genecards.org/cgi-bin/carddisp.pl?gene=MS4A1
https://www.genecards.org/cgi-bin/carddisp.pl?gene=PRKACB
https://www.genecards.org/cgi-bin/carddisp.pl?gene=RAB40C
https://www.genecards.org/cgi-bin/carddisp.pl?gene=RAPGEF1
https://www.genecards.org/cgi-bin/carddisp.pl?gene=RASSF5
https://www.genecards.org/cgi-bin/carddisp.pl?gene=RGS4
https://www.genecards.org/cgi-bin/carddisp.pl?gene=ST6GAL1
https://www.genecards.org/cgi-bin/carddisp.pl?gene=STOM
https://www.genecards.org/cgi-bin/carddisp.pl?gene=SUPT16H
https://www.genecards.org/cgi-bin/carddisp.pl?gene=TPP2
https://www.genecards.org/cgi-bin/carddisp.pl?gene=TUG1
https://www.genecards.org/cgi-bin/carddisp.pl?gene=UBD
https://www.genecards.org/cgi-bin/carddisp.pl?gene=VAV3
https://www.genecards.org/cgi-bin/carddisp.pl?gene=VPS33A
https://www.ncbi.nlm.nih.gov/gene/11804
https://www.ncbi.nlm.nih.gov/gene/23495
https://www.ncbi.nlm.nih.gov/gene/3507
https://www.ncbi.nlm.nih.gov/gene/55959
https://www.ncbi.nlm.nih.gov/gene/92421
https://www.ncbi.nlm.nih.gov/pubmed/11133067
https://www.uniprot.org/uniprot/P24456
https://www.uniprot.org/uniprot/P40879
https://www.uniprot.org/uniprot/Q5HYK7
https://www.uniprot.org/uniprot/Q9EP95

https://www.uniprot.org/uniprot/Q9Y2C3

Mahomoodally, M. F. (2013). Traditional medicines in Africa: an appraisal of ten potent African medicinal plants. Evidence-Based Complementary and Alternative Medicine, 2013.

Park, J. H., Hogrebe, M., Grüneberg, M., DuChesne, I., Ava, L., Reunert, J., ... & Innes, A. M. (2015). SLC39A8 deficiency: a disorder of manganese transport and glycosylation. The American Journal of Human Genetics, 97(6), 894-903.

Patel, S., & Goyal, A. (2015). Applications of natural polymer gum arabic: a review. International Journal of Food Properties, 18(5), 986-998.

Tarca, A. L., Romero, R., & Draghici, S. (2006). Analysis of microarray experiments of gene expression profiling. American journal of obstetrics and gynecology, 195(2), 373-388.

Wang, B., Kumar, V., Olson, A., & Ware, D. (2019). Reviving the Transcriptome Studies: An Insight Into the Emergence of Single-Molecule Transcriptome Sequencing. Frontiers in genetics, 10.

Youns, M., Efferth, T., & Hoheisel, J. D. (2009). Microarray analysis of gene expression in medicinal plant research. Drug discoveries & therapeutics, 3(5).