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D w " v g | " R e n , w m o n e u g " © p k x g t u k v g u k " D k n k o u g n  
v c t c h 2019 E E 018 p q n w " r t q l g " k n g " f g u v g m n g p o k v k t

Dw" v g | k p " v c u e t , o , . " j e | , t n e p o e u , . " { Ã t Ã v  
x g " d w n i w n e t , p , p " c p e n k m n g g k p f n g m d k n k n u g n " ¼  
g f k n f k k p k = " d w " ± c n , o c p , p " f q t w f c p " d k t k p e  
x g " o c v g t { c n n g t k p " d k n k o u g n " g v k g " w { i w p " q  
{ c r , n e p " ± c n , o c n e t c " c v h g f k n f k k p g " d g { c p " g

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Uqp " { , n n c t f c " ± q w " k p u c p . " m k o { v e u c n " o  
m e t u k p q l g p k m " g v m k n g t k p k p " i k f g t k n o g u k p f g " x  
c l c p n c t " q n c t c m " d k v m k u g n " r t g r c t c v n c t , " x g  
h k v q m k o { c u c n n c t , " u , m n , m n e " m w n n c p o c m v c f , t r  
g v m k n g t k " p g f g p k { n g f q m c c p p u g t { k g p n " " 3/4 p v n d k p n o g g t u k k p p f f g  
c t c v , t o c e , p , p " k n i k u k p k " ± g m o k v k t 0 " [ c r , n  
c u k v n g t k p " m c p u g t " j Ñ e t g n g t k p k p " e c p n , n , , p  
f Ñ | g p n x g g o " g c f r g q r v q | w " k p f Ñ m n g o g f g " 3/4 p g o n k " d k t "

Dw" v g | " ± c n , o c u , p f c " k p u c p n c t , p " u , m " u , r  
d k v m k n g t k p " { c r , u , p f c " { c { i , p " d k t " g m k n f g " o  
kumarik asit, ferulim " c u k v ø k p " F P C " o g v k n c u { q p w p c " q n c p  
m c p u g t k " j Ñ e t g " j c v v , p f c m k " g v m k n g t k " c t c v , t  
j Ñ e t g " j c v v , p f c " \* J g r I 4 + " f g k k - k u m a f i k a s i t n c t f c "   
w { i w n c o c u , " k p r , f n q o | , n c . t " , " g v B u g f e n o l i k n m a p d e l e r i n , v , t 0  
DNMT3A, DNMT3B, TET1, HDAC1, HDAC3 ve HAT1 mRNA ve protein  
seviyelerine olan etkileri Western Blot ve qRT-R \ T " k n g " d g k a f e i k a s i g p o k v k  
ferulik asit ve o-m w o c t k m " c 5 0 u d d z n d ' u t k , ± " k e p u " , G M , 3 . l " n M O v 2 5 4 m i M o  
d w n w p o k a f e i k a s i t , f e r u l i k a s i t v e o - k u m a r i k a s i t i n E C 5 0 d o z u n u n H e p G 2  
j Ñ e t g n g t k p g " w { i w n c p o c u , " u q p w e w p f c " F P O V 3  
HDAC1. " J F C E 5 " x g " J C V 3 " o T P C " u g x k { g n g t k p f g " c p  
Buna em " q n c t c m " F P O V " g p | k o " V c Ñ m v " k d x v k " v g q k w ± 3/4 m c t Ñ n  
c u k v n g t k p " g r k i g p g v k m " f g k k o t m . g t , f p g . p " q t n v c p  
m q { o w v w t 0 "

C P C J V C T " M G N : O G N G T k m " c u k v n g t . " J g r I 4 " j Ñ e t g  
metilasyonu, DNA asetilasyonu

## ABSTRACT

### INVESTIGATION THE EFFECTS OF PHENOLIC ACIDS ON DNA METHYLATION

MSc THESIS

P G X P " MC [ C " F M E

PAMUKKALE UNIVERSITY INSTITUTE IF SCIENCE

BIOLOGY

(SUPERVISOR: PROF. DR. SEVKI ARSLAN)

F G P \ ÖR T 2021

In recent years, most people have frequently used herbal preparations or phytochemicals, which are components of their normal diets, to eliminate toxic, mutagenic and carcinogenic effects of chemical substances and as a protective agents against different disease factors. In this context, phenolic acids have attracted the attention of many researchers because they have potential in the prevention of cancer due to their antioxidant effects. According to the results of the researches, phenolic acids have shown that they play an important role in reducing the viability of cancer cells, changing and regulating of the cell cycle and inducing apoptosis.

In this thesis study, the effects of phenolic acids namely caffeic acid, o-coumaric acid, ferulic acid commonly found in medicinal plants on DNA methylation were investigated on human liver cancer cell line. In this context, various doses of caffeic acid, ferulic acid and o-coumaric acid were administered in human liver cancer cell line (HepG2) and their effective doses were calculated. The effects of these phenolic substances on DNMT3A, DNMT3B, TET1, HDAC1, HDAC3 and HAT1 mRNA and protein levels were determined by Western Blot and qRT-PZR. EC<sub>50</sub> doses for caffeic acid, ferulic acid and o-coumaric acid were found to be 1.02 mM, 3.1 mM and 5 mM, respectively. As a result of the administration of the EC<sub>50</sub> dose of caffeic acid, ferulic acid and o-coumaric acid to HepG2 cells, it was observed significant decreases in DNMT1, DNMT3A, DNMT3B, TET1, HDAC1, HDAC3 and HAT1 mRNA levels. In addition, DNMT enzyme activity was measured. All these results revealed that phenolic acids decreased DNA methylation, which is one of the epigenetic changes.

**KEYWORDS:** Phenolic acids, HepG2 cell line, epigenetic, DNA methylation DNA acetylation.

# ¥ P F G M N G T

## Sayfa

“ \ G.V.....	i
<b>ABSTRACT.....</b>	<b>ii</b>
<b>¥ P F G M N G T.....</b>	<b>iii</b>
GM N " N ..U.V.G.II.....	v
VCDNQ " N ..U.V.G.II.....	vii
UGODQN " N ..U.V.G.II.....	viii
“ P U “ \.....	x
<b>1. I T.....</b>	<b>1</b>
1.1 Epigenetik .....	1
<b>2. I G P G N " D N I.....N.G.T.....</b>	<b>7</b>
2.1 Fenolik Asitler .....	7
2.1.1 Hidroksisinamik Asitler.....	9
2.2 H g p q n k m " C u k v n g t k p " H k  ...k.m.u.g.n..."x10 " Mk o { c u c	10
2.2.1 Kafeik Asit.....	10
2.2.2 Ferulik Asit.....	11
2.2.3 o-Kumarik Asit.....	13
2.3 Fenolik Asitlerin Biyolojik Etkileri.....	14
2.4 DNA Metilasyonu.....	15
2.5 Tezin Amac,.....	20
<b>3. [ " P V G.O.....</b>	<b>20</b>
3.1 Materyal .....	22
3.1.1 ¥ c n , o c f c " M w n n c p , n c . p . " . M k . o . { . c . 22 c n n c t " x g	22
3.1.2 ¥ c n , o c f c " M w n . n . c . p . . n . c . p . " . E . k . j . c .   . 21 c t	21
3.1.3 ¥ c n , o c f c " M w n . n . c . p . . n . c . p . " . R . t . k . o . g . 21 n g t	21
3.2 Metod.....	24
3.2.1 J Å e t g " M Ñ n v Ñ t . Ñ " ¥ . c . n . . . . . o . c . n . c . t . . . . . 22	22
3.2.1.1 Kafeik Asit, Ferulik Asit ve o-Kumarik Asit	
Mq p u c p v t c İ Ÿ ğ p n n . c . p . p . ç . p . " .....	23
3.2.2 J Å e t g " E c p n , n , . . . . . p . . . . . p . " . U . c . r . v . c . p . o . 23 u ,	23
3.2.2.1 V t k r c p " O c x k " D q { c o c " V g u v k " k n g " J Å e t g	
U c r v c . p . o . c . u . . . . . 23	23
3.2.2.2 J Å e t g " E c p n , neyanKİstMlgViyolek... * . O . V . 25	25
3.2.3 V q v c n " T P C " . . . . .   . . q . n . c . u . { . q . p . w . . . . . 27	27
3.2.3.1 T P C ø p , p " U r g m v t q . h . q . v . q . o . g . v . t . k . n 28 C p c n k   k	28
3.2.3.2 V q v c n " T P C ø p , p " C i c t q   " L g n " 28 n g m v t q h q	28
3.2.4 cDNA Sentezi.....	29
3.2.5 o T P C " F Ñ k p f g " G m u r t g u { q p . n . c . t . . . . . 30 , p " M c p v k v	30
3.2.5.1 I g t ± g m " \ c o c p n , " R q n k . o . g . t . c .   . . . . . 30 k p e k t " T g	30
3.2.6 R t q v g k p " F Ñ   g { k p f g " G m u r t g . u . { . 31 p " U g x k { g	31
3.2.6.1 T R C " V c o r q p w   ħ n g . ù . R . t . q . w . g . k . p . " 32	32
3.2.6.2 D k m k p m q p k p k m " C u k v " * D E C . + . . . . . [ 32 p v g o k " k n	32
3.2.6.3 F P C " O g v k n c u { q p w p f c " I ¾ t g x " C n c p " F P O V	
Aktivitesinin Belirlenmesi.....	34
3.2.6.4 SDS-PAGE Elektroforezi .....	35
3.2.6.5 Western Blot Analizi.....	38

3.2.6.6	u v c v k m u g . n . " . C . p . c . n . k .   . n . g . t .	39
<b>4.</b>	<b>BULGULAR</b>	<b>40</b>
4.1	Sitotoksisite Analizi	40
4.2	Western Blot Analizi	42
4.3	o T P C " F Ã   g { k p f g " G m u r t g u { q p n c t , p , p " V c { k \ c o c p n , " R q n k o g t c .   . " . \ . k . p . e . k . t . " . T . g . c . 4 8 u k { q p w	48
4.3.1	V q v c n " T P C " . . . .   . . q . n . c . u . { . . q . p . w	48
4.3.2	mRNA Ekspresyon Analizleri	49
4.4	DNMT Enzim Aktivitesinin Belirlenmesi	555
<b>5.</b>	<b>V C T V K ..O.C</b>	<b>55</b>
<b>6.</b>	<b>U Q P W ¥ " X G " ..P.G.T</b>	<b>65</b>
<b>7.</b>	<b>KAYNAKLAR</b>	<b>69</b>
<b>8.</b>	<b>" \ I G ¥ O</b>	<b>77</b>



# GM N " N U V G U

## Sayfa

g m k n G' 3 0 3 p g v k m " o g m c p k .   . . . o . c . n . c . t . . . * . [ . . . q . . . w . . . " 4 2 3 5 -	36
g m k n H' 3 0 4 a g n " x g " g r k i g p g v k m . . . h . c . m . v . . . t n g t " * U g c	36
g m k n Hidrolik Asit . . . . .	8
g m k n Silah Asit . . . . .	9
g m k n M' 4 0 6 m " c u k f k p . . . { . c . r . . . u . c . n . . . h . q . t . o . . . } . . .	10
g m k n H' 4 0 7 k m " c u k f k p . . . { . c . r . . . u . c . n . . . h . q . t . o . . . } . . .	11
g m k n o-Kumarik Asit . . . . .	12
g m k n F' P 4 0 9 g v k n c u { q p w " x g " . . . g . v . m . k . n . g . t . k . . . } . . .	17
g m k n d' k 4 0 9 q p " o q f k h k m c u { q p n c t . . . . . x . g . . . } . . .	19
g m k n v' j 5 0 3 < n c o , p f c m k " m c t g n g t k p . . . i . . .	23
g m k n H' q 5 0 4 < c p f c " O V V " k p f k t i g o . g . u . k . . .	25
g m k n Stép On Real-Time PZR Sistemi . . . . .	30
g m k n d' g 5 0 6 < j Ä e t g " j c v v , p f c " D E C " { . . . } . . .	34
g m k n F' 6 0 8 0 8 m " m q p u m k p' H t g t w h k p m i' C t u f k v ø k p " j Ä e t g " e c p n . . . n . . . . . p . c . . . g . v . m . k . u . k . . .	39
g m k n F' 6 0 8 0 4 m " m q p u c p v t c u { q p n c t f c m k " M e h g k m " j Ä e t g " e c p n . . . n . . . . . p . c . . . g . v . m . k . u . k . . .	40
g m k n F' 6 0 8 0 5 m " m q p u c p M w t c u k p' C a k f v ø k m k " q j Ä e t g " e c p n . . . n . . . . . p . c . . . g . v . m . k . u . k . . .	40
g m k n Kafele Asit Beralik asit ve o-Kumarik asitin k p u c p " m c t c e k g t " m c p u g t k " j Ä e t g " * J g r I 4 seviyesine olan etkisií í í í í í í í í í í í í í í í í . . . í	42
g m k n Kafele Asit Beralik asit ve o-Kumarik asitin k p u c p " m c t c e k g t " m c p u g t k " j Ä e t g " * J g r I 4 seviyesine olan etkisi . . . . .	43
g m k n Kafele Asit Beralik asit ve o-Kumarik asitin k p u c p " m c t c e k g t " m c p u g t k " j Ä e t g " * J G R I 4 seviyesine olan etkisi . . . . .	44
g m k n Kafele Asit Beralik asit ve o-Kumarik asitin k p u c p " m c t c e k g t " m c p u g t k " j Ä e t g " * J G R I 4 seviyesine olan etkisi . . . . .	45
g m k n Kafele Asit Beralik asit ve o-Kumarik asitin k p u c p " m c t c e k g t " j n c p v g p k ç j Ä e t g " * J G R I 4 seviyesine olan etkisi . . . . .	46
g m k n " M 0 5 0 3 0 3 < u k v " w { i w n c p c p " J g r I 4 " j Ä e t g u k g n f g " g f k n g p " T P C ø p , p " ' 3 . ø . n . k . m . . . } . . .	48
g m k n " K 0 5 0 3 0 4 < c u k v " w { i w n c p c p " J g r I 4 " j Ä e t g u T P C ø p , p " ' 3 ø n k m " c i . c . t . q . . . . . l . . . g . n . . . } . . .	49
g m k n " M 0 5 0 3 0 5 m " c u k v " w { i w n c p c p " J g r I 4 " j Ä e t g g f k n g p " T P C ø p , p " ' 3 ø n k . m . . . c . i . c . t . . . } . . .	49
g m k n " Kafele Asit Beralik asit ve o-Mwo c t k m " c u k v ø k p " k p u c p " m c t c e k g t " m c p u g t k " j Ä e t g " * J g r I 4 seviyesine olan etkisi . . . . .	51

<b>g m k n "</b>	<b>Ka<del>6</del>0<del>5</del>0<del>4</del>0<del>4</del></b>	likasit ve o-Mwo c t k m" c u k v ø k p "	
		k p u c p " m c t c e k g t " m c p u g t k " j Ñ e t g " * J g r I 4	
		seviyesine olan etkisi.....	50
<b>g m k n "</b>	<b>Ka<del>6</del>0<del>5</del>0<del>4</del>0<del>5</del></b>	likasit ve o-Mwo c t k m" c u k v ø k p "	
		k p u c p " m c t c e k g t " m c p u g t k " j Ñ e t g " * J g r I 4	
		seviyesine olan etkisi.....	51
<b>g m k n "</b>	<b>Ka<del>6</del>0<del>5</del>0<del>4</del>0<del>6</del></b>	likasit ve o-Mwo c t k m" c u k v ø k p "	
		k p u c p " m c t c e k g t " m c p u g t k " j Ñ e t g " * J g r I 4	
		seviyesine olan etkisi.....	51
<b>g m k n "</b>	<b>Ka<del>6</del>0<del>5</del>0<del>4</del>0<del>7</del></b>	likasit ve o-Mwo c t k m" c u k v ø k p "	
		k p u c p " m c t c e k g t " j m c p u g p f k ç ' j Ñ e v 3 " ø T D C ' I 4	
		seviyesine olan etkisi.....	52
<b>g m k n "</b>	<b>Ka<del>6</del>0<del>5</del>0<del>4</del>0<del>8</del></b>	likasit ve o-Mwo c t k m" c u k v ø k p "	
		k p u c p " m c t c e k g t " m c p u g t k " j Ñ e t g " * J g r I 4	
		seviyesine olan etkisi.....	52
<b>g m k n "</b>	<b>Ka<del>6</del>0<del>5</del>0<del>4</del>0<del>9</del></b>	likasit ve o-Mwo c t k m" c u k v ø k p "	
		k p u c p " m c t c e k g t " m c p u g t k " j Ñ e t g " * J g r I 4	
		seviyesine olan etkisi.....	53
<b>g m k n "</b>	<b>Ka<del>6</del>0<del>6</del>0<del>3</del>0<del>3</del></b>	likasit ve o-mwo c t k m" c u k v k p r e k p u c p " m c t	
		j c v v , p f c " * J g r I 4 + " F P C " o g v k n c u { q p w p c " g v m k u k	

# VCDNQ" N UVGU

## Sayfa

<b>Tablo 1:</b> U g ± k q m d k p " i g p n g t " k ± k p " v . c . p . . . . . o . n . c . 2 p c p " r t k o g	
<b>Tablo 2:</b> M w { w e w m n c t c " { Ñ m n g p g p " T P C " ¾ t p 2 g m n g t k " x g	
<b>Tablo 3:</b> e F P C " u g p v g   " m c t . . . . . o . . . . . x . g . . . . . r . t . q . 3 0 q m q n Ñ	
<b>Tablo 4:</b> T K R C " v c o r q p w p . w . p . . . . . j . c .   . . . . . t . n . c . p . . . . .	33
<b>Tablo 5:</b> D E C " U q n . Ñ . u . { . q . p . w . . . . .	35
<b>Tablo 6:</b> T g c m u k { q p . . . . . m . c . t . . . . . o . . . . .	36
<b>Tablo 7:</b> C { t , o c " x g " u , m , v , t . o . c . . . . . l . g . n . n . g . t 3 k p k p " j c   ,	
<b>Tablo 8:</b> EC <sub>50</sub> F g g t . n . g . t . k . . . . .	40

# U G O D Q N " N U V G U

**à ECe**lius derecesi

**M:** Molaritre

**EC<sub>50</sub>:** Etkili konsantrasyon

**mg:** Miligram

**ml:** Mililitre

**mM:** Milimolar

**µg:** Mikrogram

**µl:** Mikrolitre

**µM:** Mikromolar

**dH<sub>2</sub>O:** Distile su

**rpm:** F c m k m c f c m k " f g x k t " u c { , u ,

**SDS:** U q f { w o " f q f g u k n " u Ñ n h c v

**BSA:** Bovine serum albumin

**BCIP:** 5-bromo-4-kloro-indol-fosfat

**ATCC:** C o g t k m c " v k r k " m Ñ n v Ñ t " m q n g m u k { q p w

**RIPA:** Radyo-k o o Ñ p q r t g u k r k v c u { q p " f g p g { k

**PBS:** H q u h c v " v c o r q p n w " v w | " ± ¾ | g n v k u k

**PAGE:** Poliakrilamid jel elektroforezi

**ALP:** Alkalen Fosfataz

**TEMED:** Tetrametilendiamin

**DMSO:** Dimetilsulfoksit

**FBS:** H g v c n " u , , t " u g t w o w

**DMEM:** Dulbecco Modifiye Eagle Medyum

**cDNA:** Komplementer DNA

**dNTP:** 2'-f g q m u k p Ñ trifosfatq | k f " 7 )

**EDTA:** Etilen diamin tetra asetik asid

**EtBr:** G v k f { w o " d t q o Ñ t

**mRNA:** o g u c l e , " T P C

**NaCl:** U q f { w o " M n q t Ñ t "

**qRT-PZR:** I g t ± g m " | c o c p n , " m c p v k v c v k h " r q n k o g t " | k

**RNA:** T k d q p Ñ m n g k m " c u k v "

**DNA:** F g q m u k t k d q p Ñ m n g k m " c u k v

**TAE:** Tris-Asetik asit-EDTA

**CO<sub>2</sub>:** Karbondioksit

**DNMT:** DNA metil transferaz

**TET:** tet metilozin dioksijenaz

**GAPDH:** gliseraldehit-3-fosfat dehidrogenaz

**HDAC:** histon deasetilaz

**HAT:** histon asetiltransferaz

“ P U ” \

Gr k i g p g v k m " v g o g n n k " j c u v c j n c m a n c t , p " f v Æ | f g  
k n c ± n c t " u q p " { , n n c t f c " m w n n c p , n o c { c " d c n c  
f g | c x c p v e l , " { c p " g v m k n g t k f k t 0 " D w " { Æ | f g p " { c  
{ c m n c , o n c t , p " c t c v , t , n o c u , . " a r g e t k i m e s a h i g t k p k p "  
± q m " j g f g h n k " g v m g p " o c f f g n g t k p " v g u r k v " g f k  
m e r u c o , p f c " c p v k m e k t u m a r k p a s i t l i l e o n k u n l a " b e z e r k i m y a s a l p k " q  
{ c r , { c " u c j k r " m e h g k m " x g " h g t w n k m " c u k v n g t k  
m e t i l a u { q p w p c " q n c p " g v m k n g t k " d g n k t n g p o k v k t 0 "  
g v m k n g t k " m e r u c o n , " q n c t c m " k p u c p " m e t c e k g t "

D w " v g | " ± c n , o c u , p f c " g n f g " g f k n g p " j g t " u  
d g p k æ " b ± d d g " f g k n . " f g g t n k " j q e c n c t , o , p " x g  
u c { g u k p f g " i g t ± g m n g v k k p k " d g n k t v o g m " k u v g t

[ Æ m u g m " n k u c p u " g k v k o " j c { c v , o " d q { w p e c "  
m e f c t " { c t f , o n c t , p , " g u k m k g ö g { g m v ü v g p t Æ d g g g  
j q e c o " R t q h 0 " F t 0 " g x m k " C T U N C P ø c .

¥ c n , o c n c t , o " u Æ t g u k p e g . " | c o c p " c { , t c  
g f k p k n o g u k p f g " ¾ p g o n k " m e v m , n c t , " q n c p " f g g  
F Q C P ø c .

R t q l g p k p " o c f f k " c p f " g u R v g w k m p k c " n g u " c © p d { x g t u k  
C t c v , t o c " R t q l g n g t k " M q q t f k p c u { q p " D k t k o k ø p

D e p c " j g o " f g p g { " ± c n , o c n c t , o f c " j g o " f g "  
n e d q t c v w x c t " q t v c o , p , " r c { n c v , , o " u g x i k r  
D Q \ D G [ Q N W " M C T X ø c ' . P C H K T N K ø { c . " F q w m c p " O  
[ K N F K T K O ø c .

V g | k o k " { c | o c " u Æ t g e k o f g " d g p k " u Æ t g m n k " f  
g k o " O Æ o k p " F M E ø { g .

C t c o , | c " v g | " c c o c n c t , o , p " u q p " f ¾ p g o n g t l  
m e { p œ v g i l i m , | , o " O k j t c " F M E ø { g . "

C t c n c t , p f c " q n o c m v c p " o w v n w n w m " f w { f w w o  
F M E " x g " D g { | c " F M E ø { g .

Ve son olarak her zaman arkamda olan maddi, m e p g x k " f g u v g k p k " g  
rahmetli d c d c o " O g j o g v " M C [ C ø { c . " f w c n c t , { n c " j g t  
u g x i k n k " c p p g o " G u o c " M C [ C ø { c " x g " d g p k " j g r " d  
C { g " C N R ø g " v g g m m Æ t n g t k o k " u w p c t , o 0 "

# 1. I T

## 1.1 Epigenetik

F P C ø p , p " { c r , u , p , p " x g " k n g x k p k p " c { f , p n c  
{ g p k " d k t " m c r , " c ± , n o c u , p , " u c n c f , 0 " I g p g v k  
etkeni olan bir genin genomdaki yer k " v g u r k v " g f k n g t g m " v g f c  
d g n k t n g p o g u k " ± c n , o c n e t , p c " { c t f , o e , " q n o c r  
f g " i g p " f ã | g p n g p o g u k p k p " c n v , p f c " { c v c p " o g  
j c u v c n , , p " i g n k k o " u ã t g e k p k k s i k l i k c e p i g e n e t i k p " c ± , r  
c n c p , " k n g " c { f , p n c v , n o c m v c f , t " \* C { c | " x g " f k

n m " m g | " 3 ; 7 2 ø n k " { , n n e t f c " Y c f f k p i v q p "  
i ã p ã o ã | f g " õ F P C " f k | k u k p f g m k " f g k k o n g t n g "  
d ¾ n ã p o g " k n g " m e n , v , { n q c p d w k p n f k c p n g k p " . " f g i g k p " k n h n q k p m  
v c p , o n c p o c m v c f , t 0 " U q p " { , n n e t f c " g r k i g p g  
k p e g n g p f k k p f g . " g r k i g p g v k m " q n c { n e t , p " e c  
e c p n , n e t f c + " q n f w m ± c " g v m k n k " q n g w e w " p n g n c k y  
i g n k k o " u ã t g e k p f g m k " j ã e t g " h e t m n , n c o c n e t  
f g k k m n k m n g t f g " ¾ p g o n k " t q n " q { p c o c m v c f , t 0  
h e t m n , " g r k i g p g v k m " { c r , n e t f c m k " h e t m n , " m t  
± , m o c m v c f , t 0 " G r k i g p g v k m " h g p q o g p k p " ã | g t k p  
d k t d k t k { n g " d c n , " x g " i g t k " f ¾ p ã ã o n ã " q n  
o q f k h k m c u { q p n e t , f , t " \* Q t e c p . " 4 2 2 8 + 0

I ã p ã o ã | f g " { c r , n c p " d k t " f k g t " g r k i g p g v k  
f g k k m n k m n g t g " u g d g r " q n c p " m e n , v , n e d k n k t " c  
o g m e p k | o c n e t " i g p q v q m u k m " o g m e p k | o c n e t , p " v c  
i g p " k h c f g " u g x k { g u k p k " f ã | g p n g o g m v g f k t 0 " G r k  
ilgk p ± " ¾ | g n n k k " v g t u k p k t " q n o c u , f , t 0 " [ c p k " d k  
x g " d w " r t q h k n k " i g n g e g m " p g u k n n g t g " c m v c t c d k n

Grki gpgvkm" qnc { nct , p " gvmkn gt kpkp " mg h  
ogmcpk | oc p n g p p g uf kAp fggmk " jcvcnct fcp " fqnc { ,  
Qt icpk | oc p , p " uc n , mn , " dkt " godtk { qpkm " ignl  
dkt dkt k { ng " w { wonw " gvmkn g k o k " xg " f ã | gp ng p  
i gp ng t k p " hctmn , c' f { gg 't g' f xkn " o | gcuokc " p v n g m " f d k' tk " h j ã e t  
vkrkpkp " qnw ocu , p , " uc nc oc mvcf , t 0 " D<sup>3/4</sup> { ng e  
grki gpgvkm" ogmcpk | oc nct , p " dgnktnk " i gp ng t  
i gp ng t k p " khcf gukpk " dk n mg n k ò c ù u v g t g h g m h n g " ã  
qtvc { c " ± , mo cu , p , " uc nct nct 0 " Dw " u , t c f c " og r  
{ c " f c " f ã | gp uk | nk m . " i gp ng t k p " khcf guk p f g " c  
grki gpgvkm" mc { pc mn , " l ã nu g t c ' h x gn ' h R g { p' lo t g d f c p r w

Grki gpgvkm" fg k kmnk mng t k p " cnv , p f c " { cv  
gp " k { k " dknkpgp ng t k " FPC " ogvkn cu { qp w . " j l  
f ã | gp ng og uk p f g " i <sup>3/4</sup> t g x n k " mqfnc poc { cp " TPC " \*  
epiggpgvkm" ogmcpk | oc nct f c " i gt ± g mng g d k n g e g m  
rgm " ± q m " j c u v c n , m n c " d e n c p v , n , f , t 0 " " | g n n k n  
gm | qp " f k | k n g o g " ± c n , o c n c t , p f c . " d w " f k | k n g t  
mutau { qp c " w t c f , gen'etik-~~h~~ u p v g g t k h g n l o m h g u k ' 0 h G p k v g c  
i gp " mqpv t q n " ogmcpk | oc nct , p , p " d c , p f c " q n f  
mc pug t " q n w w o w p w " uc nc { cp " ± q m " uc { , f c " { q n  
i gp g v k m " j g o " f g " grki gpgvkm" u ã t g ± n g t f g m k " f  
rgm " ± q m " q c f w , c f p c " p m c t o c , m " d k t " j c u v c n , m v , t 0 " ã  
v ã o <sup>3/4</sup> t " d c u m , n c { , e , " i gp ng t k p " k n g x k p k " mc { d  
ogvcuv c | " { c r c d k n o g " <sup>3/4</sup> | g n n k k " i <sup>3/4</sup> u v g t g p " mc p  
q n o c m v c f , t 0 " M c f p , u o g f t c k p p " q n g w n " c ± p q " m m c t o c , m " d k t  
q p m q i g p n g t " x g " v ã o <sup>3/4</sup> t " d c u m , n c { , e , " i gp ng t f  
grki gpgvkm" fg k kmnk mng t " uc nc oc mvcf , t " \* C

Mc pug t . " f ã p { c " i gp gnk p f g " <sup>3/4</sup> n ã o " n ã o f g p n g  
orc p n c <sup>3/4</sup> p ã o ã | 20-6 2n'k { iki kafta daha h c | n c " q n o c u , r' d g m n g p  
I gp gn " q n c t c m " v ã o <sup>3/4</sup> t " d ã { ã o g u k . " j g o " grki gpg  
q n c p " i gp g v k m " u c r o c n c t n c " k n k m k n k f k t 0 " C { t  
p g q r n c ukvok " mg " t i n g g n p k " h c | n c t x , g p " f m <sup>3/4</sup> v o ã g " { j f w p r w " i v t n d k p u  
v g x k m " g v o g f g " m k c { t g , n c j k r t " c q k h w t w " g <sup>3/4</sup> p g t k n



o g m c p k | o c n c t , " j g f g h n g o g m " m c p u g t k p "  $\frac{3}{4}$  p n g p o  
j c u v c n , m n c t " k  $\pm$  k p " , w o f w , v t "  $\frac{3}{4}$  g m k p c k g "  $\frac{3}{4}$  p k t g " p { , c p m n c " "  
uygun ya da dengeli beslenme, f  $\tilde{A}$  | fiziksel aktivite ile  $\frac{3}{4}$  p n g p g d k n k t 0 " D w " o  
d k { q n q l k m " q m d k t n g m " g p m y k k p k p f d  $\tilde{A}$  {  $\tilde{A}$  m "  $\pm$  q w p n w  
q n c t c m " d g n k t n g p o g o n k c p " u q g t u " c q ' n f w e " w d o w w ' p d c ' k ' n n g c t k m n "  
u c j k r v k t 0 " D w " d k a g v k m h g t y d  $\frac{3}{4}$  t p g m  $\frac{3}{4}$  s i t l e r i g e t k m " u g r  
flavonoidler, retinoidler, izotiyosiyanatlar ve alil b k n g i l e i l i r f i t o k i m y a s a l l a r  
verilebilir. Meyve ve sebzelerce | g p i k p " f k { g v n g g k k p v  $\tilde{A}$  g n g k k k o  
j g o " d c n c p i , e , p ,  $\frac{3}{4}$  p j g g o n " k f "  $\frac{3}{4}$  n k B u s t e g e g d e g c u n l u p k 4 2 3 7 -

U q p " { , n n c t f c " d k n k o " k p u c p n c t , " v c t c h , p f  
{  $\frac{3}{4}$  p v g o n g t k " i g n k v k t g o d c k n c o t g f m " " k m c k p p u " g { k p , " n v c  $\tilde{A}$  p o "  
\* d c n c p i ,  $\pm$  . " i g n k k o " x g " o g v c u v c | " g x t g n g t k  
 $\pm$  c n , o c n c t " u , t c u , p f c "  $\frac{3}{4}$  | g n n k m n g " F P C " o g  
o q f k h k m c u { q p w p f c " f g k k o n g t g " p u g a n d a g l u " q n c p "  
c l c p n c t , p " m n k p k m "  $\pm$  c n , o c n c t , " { c r , n o c m v c f  
c o c e , { n c " {  $\tilde{A}$  t  $\tilde{A}$  v  $\tilde{A}$  n g p " k n c  $\pm$  " c t c v , t o  $\tilde{A}$  m ' x j g , " i ' g n k  
m c | c p o , v , t 2019 C { c | " x g " f k 0 .

Kanser ve DNA metilasyonu c t c u , p k i i d k m l a r a k R n k 5 " { , n , p f c " m  
j  $\tilde{A}$  e t g n g t k p k p " i g p q o n c t , p , p ' i  $\frac{3}{4}$  q v g t k g f k i  $\frac{3}{4}$  k p g f " g j  
 $\pm$  , m o , J k r , q 0 g v k n c u { q p " v  $\tilde{A}$  o  $\frac{3}{4}$  t " j  $\tilde{A}$  e t g n g t k "  $\frac{3}{4}$  p e  
d  $\frac{3}{4}$  n i g n g t k p f g p " o g , v k n c ' u x g p v  $\tilde{A}$  o  $\frac{3}{4}$  t d , p  $\tilde{A}$  e t l g n g t k p l  
q n c p " i g p q o k m " m e t c t u , | n , m " u q p w e w " q t v c { c "  $\pm$  ,

G r k i g p g v k m . " i g p q v k r " h e t m n , n , m n c t c " f c { c  
f w t w o n c t , " k h c f g " g f g t " x g " r q v c p u k { g n " q n c t c r  
u , t c u , p f c " i g p g n n k m n g " u v c d k n " d k t " g m k n f g "  
m e t c t n , " i g p " k h c f g u k p k p " h e t m n , " f w t w o n c t , f  
s o p " | c o c p n c t f c " q t v c { c "  $\pm$  , m o , v , t 0 " D k t  $\pm$  q m "  
o q f k h k m c u { q p w . " k n k m k n k " r t q v g k p " d k n g k o k  
E r I " f k p  $\tilde{A}$  m n g q v - k D N A g n e t i l a s y o f u g t o p l u d l a r a k a l t e r n a t i f d u r u m l a r  
q n w v w p ' b g v m h k n g k o g " i k t g t " \* N c k t f . " 4 2 2 7 + 0 "

G r k i g p g v k m . " F P C " u g m c p a d e s i n d e m e y d a n a g e l e m k n k " q  
m c n , v u c n " s i y e s i n d e s t a b i l k a l a b i l e m b i r m u l t i - m e v o c p n , " d k t " h g p

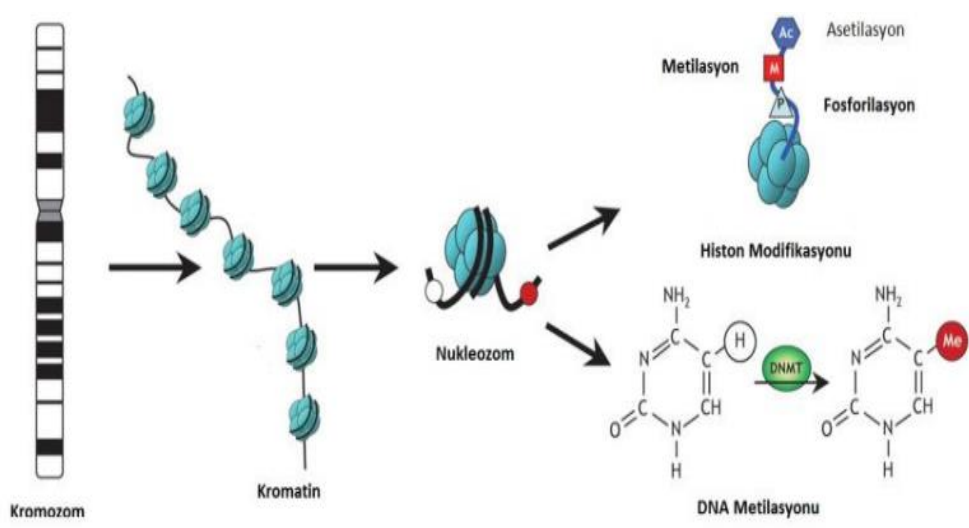
I g p " k h c f g u k p k " f ã | g p n g { g p " k n a m e d l a s y o r k u p e e k n " o q  
j k u v q p " o q f k h k m c p u g p h c ± t c , n f , , t o c n c t , " d c n c o , p  
g r k i g p g v k m " o g m c p k | o c n c t " c t c e , n , , { n c " c p n  
u c { , f c " v ã o ¾ t " d c u m , n c { , e , " i g p n g t " g r l k i g p g v  
olarak spesifik genlerin F P C ø p , p " i n q d c n " j k r q o g v l o r t a y a u { q p w  
± , m c t 0 " D w " h c t m n , " g v m k " k ± k p " u g d g r " ¾ | g n n k m  
c ± , m " g m k n f g " d k n k p o g o g m v g f k t " c p e c m " j c u  
d c n c p f , C ; p p c p ; B P g p | k o k " q n c t c m " F P O V ø p k p "  
k n k m k n k g q k n c m k k " n k m c ø " u g t " j ã e t F g P " O j v ç v k n p c j t k , v p ¾ t p n " g  
p16INK4a, RARE O6-metilguanin transferaz. " k p u c p " o w l v n g l u t a y o n q n q w  
S-transferaz-II f c j k n " q n o c k m " n ã | g t ã g " ¾ ± g u w r t g u ¾ t " i g p n  
c f c e , m n c t , p , p " f g o g v k n c u { q p w p c " u g d g r " q n w t "

C { t , e c . " g r k i g p g v k m " o g m c p k | o c n c t " j g o " j  
i k d k " j g o " f g " v g f c x k " u ã t g e k p f g " m w o m u n v e p , n c d k  
j k u v q p " o q f k h k m c u { q p w " i k d k " g r k i g p g v k m " h c t  
g v m k n k " d k t " u v t c v g l k " k | n g p g d k n g e g k " i ¾ u v g  
± q m " r t q v g k p " k n g " F P C " o g v k n c u { q p w p w p i r " m q p v t c  
m , u o , " ã | g t k p f g " { g p k " k n c ± n c t , p " i g n k v k t k n  
i ã p ã o ã | f g " ¾ | g n n k m n g " j g o c v q n q l k m " m c p u g t " v  
x g " f g u k v c d k p 0 " D w " d k n g k m n g t . " { c r , u e c n " q n c  
F P C " o g v k n " v t c p u h g t c | " g p | k o n g t k p k p " k p j d  
o g m c p k | o c n c t f c p " k n j c o " c n , p c t c m " i g n k v k t k n  
õ T q o k f g r u k p ö " i k d k " c p v k " m c p u g t " g v m k u k "  
k p j k d k v ¾ t n 2013 k f k t " \* | o k t n k .

G r k i g p g v k m " k n c ± n c t . " v g m " d c n c t , p c " { c "  
d k t n k m v g " m w n n c p , n c t c m " d q | w n o w " j u g v g g q ã t q o  
i g p n g t k p " x g l x g { c " j ã e t g p k p " p q t o c n " h q p m u k { q  
c m v k x c u { q p w p w " u c n c w m t c g 0 ¾ t " t i p g p k p t k p v ã x o ¾ t  
o g m c p k | o c n c t , p , p " { g p k f g p " c m v k x c u { q p w " u c n  
gelebilir ve sop t c u , p f c " d c m c " d k t " { ¾ p v g o n g " v g f c x k  
2006).

Grki gpgvk m" qnc { nct , p " r q v c p u k { g n " v g t u l  
u w u v w t w n o w " v Ñ o ¾ t " u w r t g u ¾ t " i g p n g t k p " { g p k f  
k ± k p " h , α w c w w t c 0 " " F P C " o g v k n v t c p u h g t c | " { c " f c  
bloke edilmesi potansiyel q n c t c m" g r k i g p g v k m" u w u v w t o c " u Ñ t  
inhibe edebilir. F P C " o g v k n v t c p u h g t c | n c t " x g " j k u v q p "  
epigenetik inhibisyon i± k p " k m k " c p c " k n c ± " j g f g h n g t k f k t 0 "  
f g c u g v k n c | " k p j k d k v ¾ t n g t k p k p " m q o d k p c u { q p n  
{ g p k f g p " c m v k x g " q n o c u , " g v m k n k " g m k n f g " u k p  
d c n c o f c " m q o d k p Ğ m (alınan) k l a m e t n d i l m e y e d e n a m e t m e k t e d i r  
(Laird, 2005).

F P O V ø p k p " k ¾ j l g d h k u k { m q g w " F P O V 3 . " u w u v w t w n o v  
k h c f g " g f k n o g u k " x g " j k r g t o g v k n c u { q p w p " v g t  
u g p v g | n g p o k " F P C " | k p e k e n g e l e k e p e k t i r . j D N M T o g v k n  
k p j k d k v ¾ t n g t - a z a - 2 e f n g c q t m c u n k " u d k v r k k f p k g p " x 7 g " | g d w n c t k p  
i ¾ u v g t k n o k v k t 0 " D w " d k n g k m n g t k p " m c p u g t " .  
j Ñ e t g n g t k p k p " c r q r v q | w " w { c t f , , " x ¾ u h g t k n g  
\* H c p i " , 2003). f k

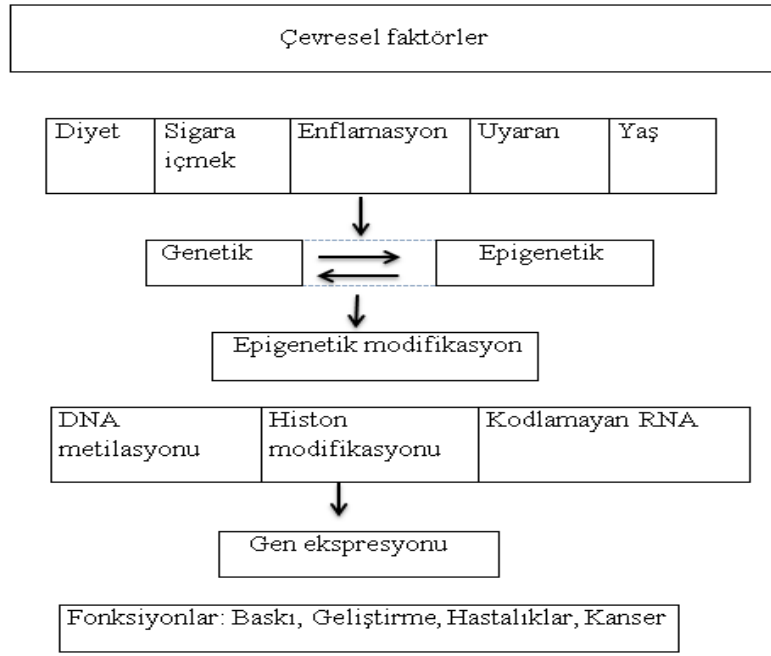


g m k 6 7 3 0 3 p g v k m" o g m c p k | o c n c t " \* [ q m w . " 4 2

R g m " ± q m " i m Ñ ± n u Ñ g " t Ğ p k v n k e , " m n k p k m " q n c t c m "  
m g o q v g t c r k m " k n c ± n c t , p " i g p g v e y a k e t i l e g e ' s a h i p Ñ ± n Ñ " j

q n f w w " d k n k p o g m v g f k t 0 " D w " p g f g p n g . " j g t j c p  
i Ñ ± n Ñ " c p p u v g k " k n c ± n c t , " q n f w m ± c " v g t e k j " g f k n k t

Mg o q v g t c r k " w " c p " k n g t c n j g c o " k j " g " f q g n h u n c k " " f v e g " f n e x p  
hala ¾ p n g p g o g { g p " m q o r n k m c u { q p n c t " x g " { c p " g v r  
c t c v , t o c n c t f c " { g p k " k n c ± n c t " d k n k o u g n " c n  
d q { w p e c " d k v m k u g n " m ¾ m g p n k " f q c n " Ñ t Ñ p n g t " .  
kaynak olarak kabun " g f k n o k v k t " \* M j c | g p f c t " x g " f k 0 . "



g m k Ñ ğ 3 0 4 a g n " x g " g r k i g p g v k m " h c m v ¾ t n g t " \* U g

¥ g x t g u g n " g v m g p n g t . " u v t g u " x g " v c p , o n c p  
g r k i g p g v k m " o g m c p k | o c n c t f c " o g { f c p c " Ñ " g n g p " f  
q n w c d k n \* o g g m k o n " k t o m g p " v g j k u " x g " v g f c x k f g m  
t c o g p . " m c p u g t " d Ñ v Ñ p " f Ñ p { c f c " u c n , m " r t  
q n w v w t o c m v c f , t 0 " F Ñ p { c f c " x g " V Ñ t m k { g ø f g " ± q  
gibi geleneksel tedax k n g t k " m w n n c p o c m v c f , t 0 " M c p u g t " v g  
{ ¾ p v g o " m g o q v g t c r k f k t 0 " H e m e v " i g t g m " { c p " g  
x g t o g n g t k p f g p " f q n c { , " k p u c p n c t " { g p k " x g " t  
c t c o c m v c f , t n c t 0 " G u k v i c g p g n k m , p ğ o g f n k ' k d w " j ±

f Ñ | g n v g p " k n c ± n c t " u q p " { , n n c t f c " m w n n c p , n o c  
c | c n v , n o c u , " k ± k p " f q c n " i g n g p g m u g n " { c m n c  
m q p w n o c u , " x g " f c j c " c defli etken p i a d g e l e r i n k e s p i g e d i l m e s i j k r " ± q  
u q p " f g t g e g " ¾ p D g w o " ± n c n | , c p o c c , " m v c , r t u 0 c o , k u f m a r i k m e h g k n  
c u k v n g t k p " c p v k m e t u k p q l g p k m " g v m k u k p k " g r k i g  
o g v k n c u { q p w p c " g v m k n g t k " b u g m a d k e l e m i n g e p i g e t i k v k t 0 " D  
g v m k n g t k " m e r u c o n , " q n c t e m " k p u c p " m e t c e k g t '  
k n g t k m k " ± c n , o c n c t " k n g " m w n n c p , n c p " o c f f g n .  
j c u v c n , m n c t , p " v g f c x k u k p f g r " h a m a l a r a k e k o n o m i k o c " r q v  
{ ¾ p f g p " Ñ t Ñ p n g t k p " Ñ t g v k n o g u k " u c n c p c d k n g e g

## 2.1 GP GN " D NI NGT

### 2.1 Fenolik Asitler

I  $\tilde{A}p \tilde{A}o \tilde{A}| g " m c f c t " \{ c r , n o , " \pm c n , o c n c t " k$   
7 2 2 2  $\emptyset f g p " h c | n c " h k v q m k o \{ c u c n " d g n k t n g p o k$   
w p n c t f , t = " h g p q n k m " c u k v n g t . " h n c x q p q k f n g  
kumarinler, lignanlar, kinonn c t " i k d k " h c t m n , " d k n g k m n g t " i  
d k n g k m n g t " \* g p " x g " f k 0 . " 4 2 3 7 + 0

H g p q n k m " d k n g k m n g t " k p u c p " f k { g v k p k p "  $\frac{3}{4} p g$   
u , m " i  $\frac{3}{4} t \tilde{A} n g p n g t k " h g p q n k m " c u k v n g t " x g " h n c x c p$   
 $\frac{3}{4} p n g \{ k e k " g v m k n g r t t k q \{ v n g g k " p k n g k t k m " k x n g k " f d k t p 0 " g " t [ c c n p n k g t k$   
f q n i c , { f , c n c t , p " g b t k h k g d k p k , k t t x \* g [ k c u p k i p " f x " g c " | f e k n v 0 . " 4 2 2

V  $\tilde{A}o \frac{3}{4} t " j \tilde{A} e t g n g t k \{ n g " \{ c r , n c p " d k t \pm q m " \pm c$   
etkisinin bulunmas, " p g f g p k { n g " m c p u g t k p " v g f c x k u k p f g "  
d k n f k t \* K T n c o q k " x v g k " t f k 0 . " 4 2 2 9 +

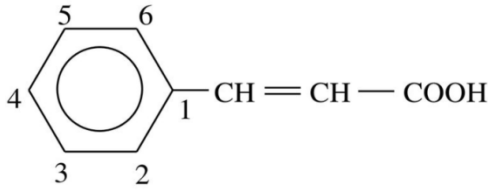
H g p q n k m " d k n g k m n g t . " d k v m k n g t k p "  $\pm g k v n k$   
k m k o c v " x g " h g p k n r t q r c p q k f " t g c m u e k d i f . B u p n c t , "  
d k n g k m n g t . " g p "  $\pm q m " \{ c \{ i , p " q n c t c m " q n w c p " h$   
h k | { q n q l k m "  $\frac{3}{4} p g o g " u c b i t k i m g k f 0 " d i \tilde{A} p t \tilde{A} g o o g h f " x g " k f n , g$   
h c m v  $\frac{3}{4} t n g t g " m c t , " \frac{3}{4} p d g k o m n g k " k d a l e r j k , t a n t u " a n t e r o j e n i k p c t 0 " H$   
anti-enflamatuar, anti-mikrobiyal, antioksidan, anti-trombotik, kardiyoprotektif ve  
f c o c t " i g p k n g v k e k " g v m k n g t " i k d k "  $\pm q m " \pm g k v$   
x g " f k 0 . " 4 2 2 8 + 0

H k v q m k o { c u & n̄ ndcktt , " p  $\tilde{A} \{ \frac{3}{4} p u g k o " n q n c p " h g p q n k m " c$   
q n c t c m " d w n w p c p . " d k v m k n g t k p " t g p i k . " m q m w u  
c p v k q m u k f c p " o c f f g n g t f k t 0 " I g p g n n k m n g " f q c t  
d k t " i t w d w " j c t k  $\pm + 0 " D w " f v k n k " \alpha p v k q m u k f d g p i k p t n , g$   
t g p i k p k . " m q m w u w p w . " d g u k p " f g g t k p k " x g " m c n k  
w | c v , e , " m q t w { w e w " o c f f g " q n c t c m " m w n n c p , o , "

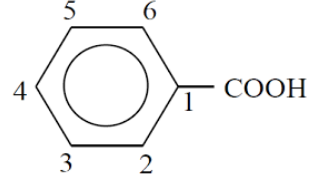
± q w " d k v m k " d c | , " j c u d k n ; m g m k n p ' g v g n f w a n k p k p f (2008).

Genel olarak serbest halde bulunmayan fenolik asitler; hidrokisisinamik asitler

\* g m k n " 4 0 3 + " x g " j k f t q m u k d g p | q k m " c u k v n g t " \*  
 D w " d k n g O H k v m i O C J t 5 g " i t w r n c t , " d c n c p c t c m " ¾ p g o n  
 q n w o c m v c f , t " \* M q n c ± " x g " f k 0 . " 4 2 3 9 + 0



**g m k Hidroksisinaamik asit**

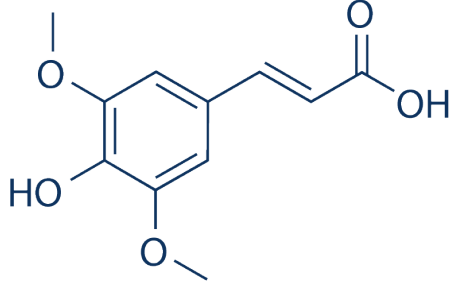
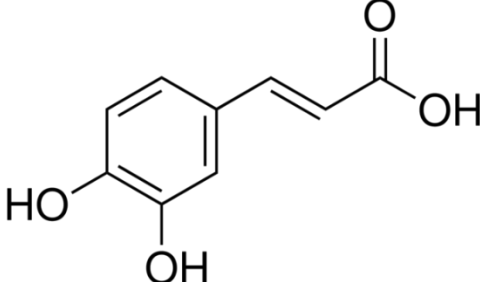
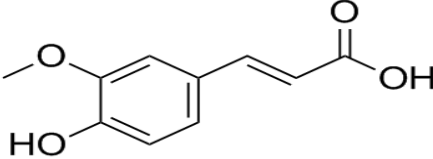
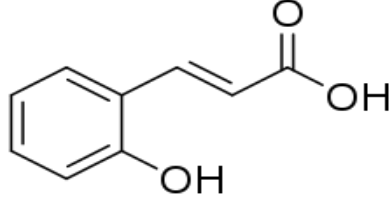


**g m k Hidrobenzoik asit**

H g p q n k m " c u k v n g t . " o g m c p k | o c n c t , " j c n c " v  
 m c p ç p v k m c p u g t "deşeklemektir. Ancak fenolik "asitlerin serbest  
 radikalleri temizlemek, ksenobiyotiklerin o g v c d q n k | o c u , p f c " { g t " c  
 k p f Ñ m n g o g m . " i g p " k h c f g u k p k p " f Ñ | g p n g p o g u k p  
 o q f Ñ n c u { q p w . " F P C " j c u c t , " q p c t , o , . " j Ñ e t g "  
 k ± g t g d k n k t 2016) T q u c " x g " f k 0 .

### 2.1.1 Hidroksisinaamik Asitler

Fenilr t q r c p " j c n m c u , p c " d c n c p c p " j k f t q m u k n '  
 ¾ | g n n k k " f g k g p " j k f t q m u k u k p c o k m " c u k v n g t  
 kafeik asit, o-m w o c t k m " c u k v " x g " u k p c r k m " c u k v v k t " \*  
 halinde olsalar f c " ± q m " c | " o k m v c t n c t f c " u g t d g u v " j c n f g

 <p>Sinapik asit</p>	 <p>Kafeik asit</p>
 <p>Ferulik asit</p>	 <p>o- Kumarik asit</p>

**g m k Sifat dan Sifat**

[ c r , u , " h g t w n k m " c u k f i g v ± ù m è d g p e g { g p j m g h p c p g . " U g { n c p " v c t ± , p , . " c p c u q p . " m , t o , | , " d k v m k n g t f g " d w n w p o c m v c f , t 0 " M e h g k p " i k d k " c p c u k v n g " d k t n k m v g " ± c n , d k t { c q m " g p k v g m k k " p j f ã e " t { g r t g " t c k n k r k f " r g t q m u k f c u { q p w " x g " f q m w " j c u c t , p c " m g p h n c o c v w x c t . " p g h t q r t q v g m v k h " c m v k x k v g " i ¾ u m , u , o f c " d w n w p c p " u k p c r k m " k a n s e r o j e n p v è a k t i a g " c p v k p h n c o c v w e t " g v m k " i ¾ u v g t f k k . " f k { c d g v k m " j { c r , n c p " ± c n , o c n e t n e " i ¾ u v g t k n o k v k t 0 " C { t , c u k v " o k m v c t n e t , p , p " c | c n o c u , p p c k . p " " v k q u r g n " c c o t " v r o t c u g d g r " q n f w w " q t v c { c " m q p o w v w t " \* M q n c ± " x g " f

MÃ ± ã m " d k t " u , p , h " m e d w n " g f k n g p " h g p q n k m " c d k t ± q m " ± c n , o c " f k m m e v n g t k " d w " i t w r " ã | g t k p { k { g e g m n g t m k p ± , { p c , r q , n u c , t p f m c d a h d q m v e p { o , c , u " , k p p u c p n e t " f \* f k { g v n g t k p " u g d | g . " o g { x g " j w d w d c v . " ± c { . o c f f g n g t f g p " i ã p f g " { c m n c , m " 4 7 " o i " k n g " 3 " i "

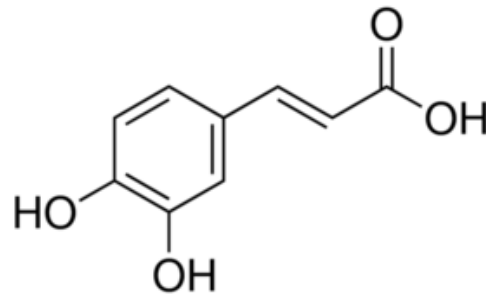


Hidroksisinasamik asitlerden kafeik, ferulik, m- ve p-kumarik asitler sahip  
 q n f w m n c t , " c p v k q m u k f c p . " c p v k h k d t ¾ | . " c p v k  
 u c { g u k p f g " d k n k o " f Ñ p { c u , k u f n a r i k a s i t i n f b i y o t o j i k " r q r Ñ  
 c m v k x k v g n g t k { n g " c n c m e n , " { t ' r \* , r g o , " x " g ± d f k " o | . " ±

## 2.2 H g p q n k m " C u k v n g t k p " H k | k m u g n " x g " M k o { c

### 2.2.1 Kafeik Asit

Kafeik asit (3,4-dihidroksi-u k p p c o k m " c u k v + " q t i c p k m " d k t  
 c p v k q m u k f c p f , t 0 " ¥ q m " ± g k v ñ k g m k n m k o g ± f g " f q



g m k M c 4 0 6 m " c u k f k p " { c r , u c n " h q t o Ñ n Ñ

Mc h g k m " c u k v " g p " { c { i , p " d w n w p c p " h g p q n k m  
 o g { x g n g t k p " d Ñ v Ñ p " m , u , o n c t , p f c " ¾ | g n n k m n g "  
 q t c p f c " d w n w p o c m v c f , t 0 " O g { x g f g m k " o k m v c t ,  
 i ¾ u v g t k t m g p . " v q r n c o " m e n k v g u k " k u g " o g { x g f g  
 k o o Ñ p " u k u v g o n g " k n k m k n k " c u v , o " x g " c n g t l k  
 n ¾ m q v t k g p n g t k p " u g p v g | k p k " u g ± k e k " q n c t c m "  
 c p v k v Ñ o k x k v g u k m " i ¾ u v g t k n o k v k t " \* D c t w v " x g " U

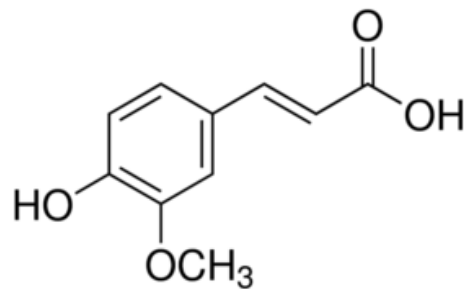
Mc j x g " r q n k h g p q n n g t k " m c h g k m " c u k v " x g " m n  
 d c | , " ¾ p g o n k " { q n n c t , p , p " c m v k x c g u { m k p " w i " ¾ u g v " g k t p  
 F c j c u , . " g r k f g o k { q n q l k m " ± c n , o c n c t . " { Ñ m u g  
 o g v c d q n k m . " u k p f k t k o " u k u v g o k . " j g r c v k m " x g  
 u , m n , , p , p " f c j c " f Ñ Ñ m " q n o c u , { n c " k n k m k r

polifenoln g t k p k p " c p v k v Å o ¾ t " g v m k u k . "nde Åeckhik " j Å e t g  
± c n , o c n c t f c " c t c v , t , n o , v , t 0 " M c h g k m " c u  
m c t u k p q o " j Å e t g M e l g t : k p k p ü c x p g " o U M c p q o c " m c p u g  
± q c n o c u , p , " k M e l j 4 k d ' g j " Å e f t g g t g . g " t l g M f u g ' t g u { q p w p w "  
F P C " o g v k n c u { q p w p 3 w 6 ' : c c t " v g m u t t e g m d ' { x c g p ' w p k w " k p f Å m n  
j Å e t g u k " d g p | g t k " j Å e t g n g t k p " ¾ | v e M D A M B n g t k p k '  
4 5 3 " k p u c p " o g o g " m c p u g t k q " p j w Å p e w " g d n c g u t n k , p n f c g t " " F \* P J C g " t  
f k 0 " 4 2 4 2 + 0

M c h g k m " c u k v - . B ' ( N F Å m d + g " g x g ' h c m w t ¾ k u 9 " ( M M P v c n q r t q  
9) aktiviterip k p " k p j k d k u { q p w " c t c e , n , , { n c " j g r c v q  
o g v c u v c | , p , \* E p j v k i l g x g . v b k 0 k t 4 2 2 6 +

### 2.2.2 Ferulik Asit

Ferulik asit (FA, 3-metoksi, 4-hidroksi sinamik asit), sebze ve meyvelerde  
u , m n , m n c " d w n w p c p . " h g p k n c n c p k p " x g " v k t q | k p  
d k n g \* k g n m k n " 4 0 7 +



g m k Ferulik 7 u < k f k p " { c r , u c n " h q t o Å n Å

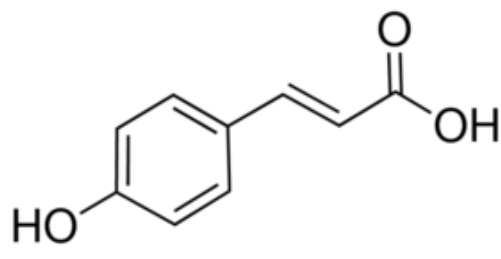
M k o { c u c n " { c r , u , " | g t f c ± c n g " u c t , " t g p i k p  
m w t m w o k p g " d g p | g o g m v g f k t 0 " " | g n n k m n g " v q j w o  
n k i p k p " i k d k " d k { q r q n k o g t n g t g " d c n e . " j { c w m f c h : d  
± c x f c t " i k d k " v c j , n n c t , p " m g r g m n g t k p f g . " m c x  
d w n w p o c m v c f , t 0 " W p f c m k " v q r n c o " h g p q n k m " c  
q n w v w t o c m v c f , t " \* V c p g t . " 4 2 2 9 + 0 "

H g t w n k m " c u k v . " h g p q m u k t c f k m c i o k ' s i d a n c r , u , p  
 r q v c p u k { g n g " u c j k r v k t 0 " G v m k m c k u " , d p k , t p " " u { g c t p d , g p u f v c "   
 Ñ n m g n g t f g " n k r k v " r g t q m u k f c u { q p w p w " g p i g n n g  
 k ± g t k k p f g " m e v m , " o c f f g u k " q n c t c m Ñ ± r g Ñ " d k n t o " c  
 o g o d t c p " c p v k q m u k f c p , " q n c t c m " g v m k " g v v k k " x  
 c n i , p n , , . " i t k r " x g " k p h n w g p | c { c " m e t , " m q t v  
 j k f t q m u k n " t c f k m c n k . " j k r q m n q t ¾ | g " p c " u v k Ñ v t " n x g g " k p  
 u Ñ r Ñ t Ñ e Ñ " g v m k n k f k t = " u g t d g u v " t c f k m c n " | k p e l  
 H C ø p , p " t c v n c t f c " r c p m t g c v k m " j Ñ e t g n g t f g " k  
 C p v k q m u k f c p " ¾ | g n n k m n g t k " t c v n k a t s i f o g e r e z e k o { c u c  
 x g " h c t g n g t f g " f g t k " v Ñ o ¾ t Ñ " q n w w o w p f c " f c " i ¾

H g t w n k m " c u k v k p " m e t c e k g t " m e p u g t k p g " \*  
 { ¾ p n g p f k t f k k " x g " c r q r v q | w " k p f Ñ m n g f k k " d k n

**2.2.3 o-Kumarik Asit**

[ c r , f c m k " j l k p w p t u l g " t k p w " d c n , " q n c t c m " q t  
 Ñ | g t g " Ñ ± " v c p g " k | q o g t k " d w n w p c p " m w o c t k m " c  
 d k n g \* k g n m k n " 4 0 8 +



g m k n - M 4 0 8 k ' m " c u k f k p " { c r , u c n " h q t o Ñ n Ñ

O q n g m Ñ n " H 4 O t . o ' Ñ m Ñ " g E n Ñ n " c , - 3 a f Ñ t 0 3 6 k 6 g " p d  
 4 3 2 " k n g " 4 3 5 " Å E " c t c u , p f c f , t 0 " R q t v e m e n . " m k t  
 U v t g u g " m e t , " m q t w o c " u c n c o c u , p , p " { c p , p f  
 F P C ø f c " q m u k f c v k h " ± j k c p u " c { t Ñ c m " u p g g n f " g o p k " m q v r e f t w a c w " f k c " c  
 q n o c m v - M w o c 0 k m " c u k v " ¾ | g n n k m n g " o k f g " m e p u g t  
 d k n f k t k n o k v k t " \* C m m e p . " 4 2 2 : + 0 "

o-Mw o c t k m" c u k v " m c j x g . " ± c { " m w t w { g o k " i k  
bulunan bir hidroksisinamik asittir. o-kumarik asidin antilipidemik, antioksidan ve  
c p v k m c t u k p q l g p k m" i k d k " h c t m n , " d k { q n q l k m" c  
U c f q y { " x g " f k 0 . " 4 2 3 7 + 0

### 2.3 Fenolik Asitlerin Biyolojik Etkileri

H g p q n k m" c u k v n g t . " d k v m k n g t k p " k ± g t k k p f g m k " h g p q n k m" c u k  
x g " u c f g e g " m ã ± ã m" d k t " i t w d w" f , , p f c " f q c f c  
o c f f g n g t k p k p " k ± k p f g " d w n w p c p " h g p q n k m" c u k  
m q m w u w p w . " d g u k p " f g g t k p k " x g " m e d e n k r a f g u k p k "  
¾ o t ã p ã " w | c v o c m" c o c e , { n c " i , f c n c t f c " m q t w {  
C { t , e c " h g p q n k m" c u k v " k ± g t g p " r g m" ± q m" d  
q n c t c m" m w n n c p , n o c m v c f , t " \* C u n c p . " 4 2 3 7 + 0

U q p " { , n n c t f c . " c p v k m c p u k p t c" p c , m v c k p x" k x v g g" u d k p v g k  
q n c t c m" d k n k p g p " h g p q n k m" c u k v n g t k p " i l g i c n , ,  
± g m o g n v N g k f" k x t g 0" f k 0 . " 4 2 2 ; + 0

[ c r , n c p " g r k f g o k { q n q l k m" ± c n , o c n c t f c . " u  
\* ± c { " x g " c t c r " d i g k u d k g p " g ã t " ã p k " d k n , g t t n f , g m m , c" p u g t " x  
m c t , " d k v m k n g t k p " k ± g t k k p f g m k " h g p q n k m"  
u ã t ã n o g m v g f k t 0 " R q n k h g p q n n g t k p " c p v k c n g t l  
antimikrobiyal, antibakteriyel, antiviral, antimw v c l g p k m . " c p v k m c t u k p q  
c p v k q m u k f c p " x g " c p v k v t q o d q v k m" g v m k " i k d k " r  
\* D c e c p n , . " 4 2 3 6 + 0

V ã o ¾ t " j ã e t g n g t k { n g " { c r , n c p " ± c n , o c n c t  
polifenollerin antikanserojen aktivitesi tesr k v " g f k n o k " q n w r " d w" d k  
v g f c x k u k p f g " { g t " c n c d k n g e g k " u ¾ { n g p o k v k t C  
i g n k k o k p k " ¾ p n g { g t g m" m c p u g t g " m c t , " m q t w {  
2014).

D k t ± q m " ± c n , o c " g g t k g " g p g g t v n k g m p " f o g ã f k c j k c m n g k p r  
q n w w o w p w " g p i g n n g { g G k k i g g p g k k m " i f ¾ u k g t k o n k k v  
m c p u g t " i g p k c k o g k t " m g p t ' c g u x , t g n g t f g " q t v c { c " ± ,  
f g k k m n k m n g t k p " g t m g p " f g k k o k a z a k a p i l i r . g { g t g m  
D w " { ã | f g p " g t m g p " c c o c f c m k " g r k i g n p v g v k m " o  
o g v c u v c | , p , p " R g m ' g v k p m k " g c k i g p g d k m k t f O g k v k  
q n c t c m " q n w w t " x g " f k { g v " d g u k p n g t k " q n c t c m "  
a r a u , p f c " r q n k h g p q n n g t " x g " h n c x c p q k f n g t . " g r  
m c { p c , " q n c t c m " w v a p p , n a m c f p o " , ± c v { k m d ' j x g " c n , o ,  
x c m e n e t , " c t c u , p f c m k " k n k m k { k " c p c n k | " g f g p  
h c t m n , " i n w g t ' f k n k h g p q " u x g ± n k " m e f , p n e t " ã | g  
c n , o , p , p " j c u v e n e t f c " o g o g " v ã o ¾ t ã " i g n k k o k  
u , m n , , p , " ¾ p g o n k " ¾ n ± ã f g " c | c n v v , , " d w n o w  
k a n s e r i i ¾ t ã n o g c " t u v , o ( S e l v a k u m a r " x g " f k . 0 . " 4 2 4 2 +

## 2.4 DNA Metilasyonu

F P C " o g v k n c u { q p w . " ¾ p e g n k m n g " u k v q | k p k p "  
u ã t g ± v g " h c t m n , n c o c . " i g p q o k m " d c u m , . " F P C "  
i f a d e s i n i e t k i l e r . D N A h i p e r m e t i l a y o n u , g e n e l l i k l e p r o m o v g t " E r I " c f c n e t  
o g { f c p c " i g n g p " i g p n g t k p " k h c f g u k p k " u w u v w t o  
\* H c p i " x g " f k 0 . " 4 2 2 9 + 0

F P C " o g v k n c u { q p w = " g o d t k { q p k m " i g n k k o . "  
f ã | g p n g p o g u k . " Z " m t q o q | q o w " k p c n k r o h o z o m u { q p w .  
u v c d k n k v g u k p k p " u c n c p o c u , " i k d k " d k t ± q m " j  
g r k i g p g v k m " o g m e p k | o c f , t 0 " O g v k n c u { q p w p " d w "  
k { k " d k t " g m k n f g " m q p v t q n " g f k n o g u k p k " i g t g  
e p k i g p g v k m " m q p v t q n " u k u v g o k p k p " f ã | i ã p " d k  
G r k i g p g v k m " o q f k h k m e u { q p n e t " f ã | i ã p " d k t " g n  
d w " u ã t g ± n g " k n i k n k " r e v q n q l k m " u q p w ± n e t " q t v  
2016)

DNA metilasyonu { q p w p w p " c p q t o c n " o q f g n n g t k " x g " f u , t c u , p f c " k n k m k n k " i g p k p " u w u v w t w n o c u , " m U r g u k h k m " q n c t c m " g r k i g p g v k m " ± g k v n k n k m . " d g f w { c t n , " i ¾ t Æ p o g ' m F P C k o g v D w c ' p g d g w ' h u Æ t g e k p k d k n g g p n g t k . " d g n k t n k " c p c j v c t " i g p n g t k p " q n w w o w p w " g v n o k g n m g t p o k | G o r c k n i c g t k g p k f i t e ¾ r k c v v k k m " o u g v m t c v i g n k " ¾ t F P O V o ñ g t k p " c g n p k k g m g ü k k j g f m k k h " d k v w { i w n c p o c u , " c n v g t p c v k h " m c p u g t " m g o q v g t c r k u (Li ve Tollefsbol, 2010).

U q p " c t c v , t o c n c t . " ± g k v n k " ± g x t g u g n " u v o g v c n n g t . " u q { w Æ m u ' g m w t c w n | n " , m ' c j x l g n " q n o c m " Æ | g u g x k { g n g t k p f g " f g k k m n k m n g t g " { q n " c ± v , , p f k t g p e k " k n g " k n k m k n k " F P C " o g v k n c u { q p w " v c t c

F P C " o g v k n c u { q p w p w p " g p " ± ¾ m g o n k ' o x g " Æ | Æ g t Æ K p d c | , " d ¾ n i g n g t f g " d w n w p c p - d ' g u v k v m u | k k v p q | d k c p | g , " p f , ¾ p " D g k p e k " d c | m e t i f s i t o z i n f ( 5 g o p E k + n " g o p q " f 7 k h k m c u { q p w " i g p g n f q n c t c m " f c " k u k s i o z i n g f o s f i t - g u a n k z i n - g 5 p o " " x f g k " p 7 Æ o n m g t k p k p " u , d w n w p f w 4 w 2 " 2 2 2 2 d c | " ± k h v k " w | w p n w w p f c m k " F P C c f c e , m n c t " i g p " r t q o q v ¾ t " d ¾ n i g n g t k p k p " ¾ p g c f c e , m n c t , " f , , p f c m k " i g p q o w p " f k g t " d ¾ i g t ± g m n F P C g ' d k n ' k { t g 0 t " " F c n c p " d w " d ¾ n i g n g t g " o g v k n F P O V 5 c " x g " F P O V 5 d " q n o c m " Æ | g t g " 5 " k | q h q t o f c \* F P O V + " g p | k o k p k p " c m v k x k v g u k " k n g " i g t ± g m n g o k v q v k m " j Æ e t g " d ¾ n Æ p o g ü k j " Æ a t g a g t g f c o " g f g p k ü m q r { c n c t m g p . " F P O V 5 c " x g " 5 d " k u g " f g " p q x q " o g x g " f k 0 . " 4 2 3 8 + 0

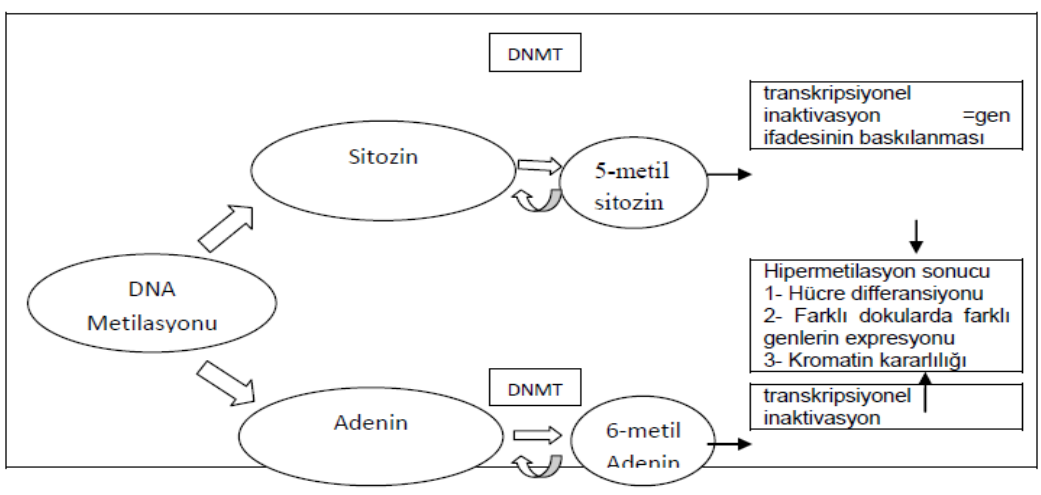
DNA metilasyonu. " j k u v q p " o q f k h k o l m a y a n p r o t e i n l e r l e , " x g " m q o d k p c u { q p " j c n k p f g " m t q o c v k p " { c r , " x g " g t k o g v k n c u { q p w " i g p " g m u r t g u { q p w p w . " v t c p u r q | q m c n , v , o " ¾ | g n n k m n g t k p k " f Æ | g p n g o g { g " { c t f , o e

p u c p " m c p u g t n g t k p f g . " d c p n c o c n " l g n k t i g p o (invazyon), metastazlar ve kemoterapi direnci dahil q n o c m " Æ o p l a s t i k g "

ig n k o g p k p " ± g k v n k " c c o c n c t , p f c " m e v m , " u  
 5 2 2 ø f g p " h c | n c " k g p ± " g x k v n l g p k p A u p i g e n e t i k g o t a r k u g t n g t  
 f g k v k k " k (K a g w a l k v e G u p A t 2 0 1 2 ) o A v A t "

F P C " o g v k n c u { q p w . " k m k " o g m c p k | o c " { q n w { n  
 D k t k p e k " q n c t c m . " v t c p u m t k r u k { q p " h c m v ¾ t A " k  
 d c n c p o c " { g t n g t k . " v t c p u m t k r u k { q p " h c m v ¾ t A '  
 i g p " c m v k x k v g u k p k " f q t w f c p " g v m k n g t 0 " m k p e  
 o g v k n " E r I " d c n c { , e , " r t q v g k p n g t " k ± k p " d c n  
 histon d g c u g v k n c | n c t " f c j k n " d c u m , n c { , e , " m t q o c  
 h c m v ¾ t n g t n g " k n k m k n k f k t " \* E j k p " x g " f k 0 . " 4 2

I g p g n " q n c t c m . " i g p n g t k p " r t q o q v g t " d ¾ n i g  
 i g p g n n k m n g " v t c p u m t k r u k { q p " c m v i d i r x A k s i n e , q p w " x g  
 metilasyon gen susturmadan sorumlu gen promoterlerinde olabilir. DNA CpG  
 c f c n c t , p , p " j k r g t o g v k n c u { q p w " j A e t g " f ¾ p i A u  
 x g " c r q r v q | f c " ± q m " ¾ p g o n k " q n c p " i g p n g t k " u w  
 ¾ p g o n d ö y d a k \* t " g t m k 0 n " " 4 D 0 w 9 " + p g f g p n g . " u r g u k h k m " k p j k  
 c m v k x k v g u k p k p " f A | g p n g p o g u k . " v g t c r ¾ v k m " j g t  
 c ± , u , p f c p " w o w v " x g t k e k f k t " \* E > ¶ f l " x g " f k 0 . " 4



g m k DNA Metilasyonu x g " g v m k n g t k " \* [ q m w . " 4 2 3 5 + 0

J A e t g { k " m c p u g t f g p " m q t w { c p . " u k p { c n " k n g  
 j A e t g " f ¾ p i A u A p f g " x g " m q p v t q q f i n A " i ¾ A g k g k ¾ q A  
 u w r t g u ¾ g p n g t k p " r t q o q v g t " d ¾ n i g f g m k " j k r g

susturulmaktaf , t 0 " D w " u w u v w t w n o c " k n g " m c p u g t " j Ñ e t  
c t v o c m v c f , t 0 " D w " u w u v w t w n o c " c p e c m " i g p n g t f  
i g t ± g m n g 0 ö g Ñ n c v n g , f k o c n c t " u r q t p g w e 3/4 t p " f i c g ' p v n Ñ g o t 3/4 t p " " u d w  
o w v c u { q p " i 3/4 t Ñ m Ñ t g m Ñ g j p k r " g f t k o g g v t k " n c n g q p " k n g " u v  
o g v k n c u { q p " f w t w o n c t , p f c m k " f g k k m n k m n g t " j  
g v m k n g t k p k p " d g n k t n g p o g u k p f g " d g n k t v g ± " q n c  
\* M c t c ± q d c p . " 4 2 3 8 + 0

DNMT ve TET enzimleri o g v k n n g p o k " F P C " u g x k { g u k p k  
g v m k n k " d k t " g m k n f g " t q n " c n o c m v c f , t n c t 0 " F  
u w u v w t w n o c u , p , " u c n c { c t c m " d g n k t n k " r t q v g k  
u w u m w p " i g p n g t k " c m v k h n g g p k g k 0 " x D w " f q g m k n f u g  
k h c f g u k " x Ñ e w v " v e t c h , p f c p " c m v k h " q n c t c m " m q p  
q n c p " i g p q o . " F P C " f k | k u k " Ñ | g t k p f g " f g k k m n  
i g t k " f 3/4 p Ñ Ñ o n Ñ " f k p c o k m " d k t ' 0 { c ' 4 2 ' 3 Ñ e | 0 c p o c m v

P q t o c n " h k | { q n q l k m " m q w n n c t " c n v , p f c " F P  
o g v k n c u { q p w " k ± k p " 3/4 p g o n k j f Ñ e t t < g " u d r 3/4 m u Ñ p h o k g m u " k d " n u  
o g v k n c u { q p w p " u Ñ t f Ñ t Ñ n o g u k p f g p " u q t w o n w " k m g  
i 3/4 t g x " u n u n l a b e t a b e r D P O V ø n g t k p " c , t b e l i r l i g g a n l e r i t g u { q p  
etkileyen anormal metilasyon modelleri, d k t ± q m " m c n l a n t t ' c v e Ñ k t n g g t t . k  
m q n q t g m v c n . " r t q u v c v . " o g o g . " g p f e q p a n g r e a s t k { c n .  
kanserleriyle k n k m k n g \* p C f n k f t c k y n u o c k t k v " k x t g " f k 0 . " 4 2 3 7 +

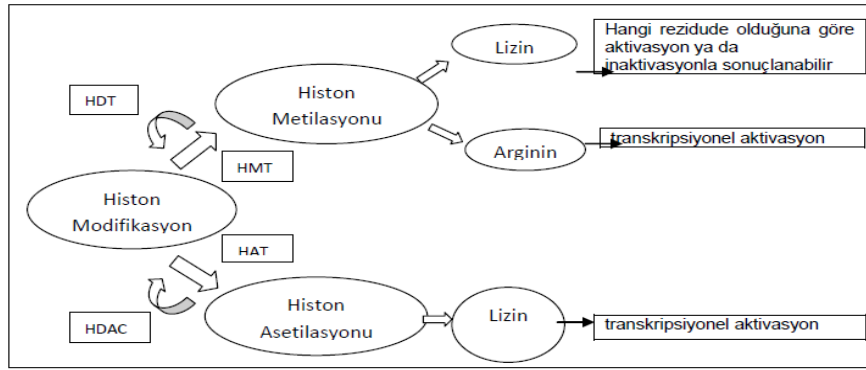
p u c p " i g p q o w p f c m k " r t q v g k p " m q f n c { c p " i g p  
f 3/4 p g o n g t k p f g " c m v k h " k m g p . " f k g t " f 3/4 p g o n g t k  
h q p m u k { q p g n " f g k n f k t 0 " D k t " i g p k p " c m v k h " q n  
transkripsiyon f c m v 3/4 t n g t k p k p " d c n c p o c u , " i g t g m o g m  
v t c p u m t k r u k { q p g n " u g x k { g f g " f Ñ | g p n g p o g u k . " n  
o q f k h k m c u { q p n c t , " k n g " u c n c p o c m v c f , t " \* M Ñ ± Ñ

J k u v q p n c t . " g r k i g p g v k m v g " d c g e m f a d e s i d e k t " m k n k  
m t q o c v k p " { c r , u , " m d ' p t v q t n q n " Ñ p d j g k ' r d " k q k D N A k w " m d k d  
o g v k n c u { q p " o g m m p k | o c u M e p p i n g e h g ' t j f Ñ e t t 0 g n g t k p f g m  
f c x t c p , , " j c m m , p f c m k " d k n i k o k | " F P C " a o g v k n c



c | f , t 0 " Dk | " d k n k { q t w | " m k " d c | , " j k u v q p " o q f k h  
c f c " j k r g t o g v k n c u { q p " k n g " d c n c p v , n , " q n c t c  
veya yok olur (Esteller, 2006).

J k u v q p " o q f k h k m c u { q p n c t , . " p l a ã n h i s t o n q | q o "   
m w { t w m n c t , p c " \* c o k p q " v g t o k p c n " w ± n c t , + " c u g v  
i g t ± g m n g \* o g m k g f " k k 0 ± 0 k v g p " i ã p ã o ã | g " m e f c t  
c u g v k n c u { q p w " k n g " k n i k n k " c t c v , t o c n c t " u c { g  
f g c u g v k n " v t c p u h g t c | " \* J F C E + " g p | k o n g t k p k p "  
c n f , , " m e p , v n c p o , v , t " \* M ã ± ã m q n w . " 4 2 3 6 + 0



g m k d k 4 0 q p " o q f k h k m c u { q p n c t , " x g " g v m k n g t k "

HAT enzimi, asetil koenzim-C 0 " j k u v q p g k p k p k " f g k v k t f k  
g p | k o " q n w r " i ã p ã o ã | g " m e f c t " k p u c p n c t f c " g p  
v c p , o n c p o , v , t 0 " G p " c | " 4 7 " ã { g " k ± g t g p " J C V  
c k n g { g " q t i c p k | g " q n o w v w t 0 " H e h i s t o n o l m ' a y l n C V " c k n  
j g f g h n g t " v t c p u m t k r u k { q p " c m v k x c u { q p w . " i g p  
k n g t n g o g u k " i k d k " ± g k v n k " u ã t g ± n g t f g " { g t " c n  
d c n c p o c | " q p f c p " | k { c f g " ± g m k t f g m k d g u g n p h c {  
o w n v k r t q v g k p " m q o r n g m u n g t k " { q n w { n c " F P C " k n g

F P O V " x g " J F C E " k p j k d k v ¾ t n g t k p k p " d k t " c t c  
p g f g p " q n o c m v c f , t 0 " G r k i g p g v k m " f g k k m n k m n  
m k k g g n " ¾ g f c x k n g t k p " m w n n c p , o , p , " u c n c o c m v

c m v k x g u k p g " { q n " c ± c p " g r k i g p g v k m " k n c ± n c t . " u c j k r v k t 0 " D w " k n c ± n c t . " d c , o u , | " q n c t e m " { c " birlikv g " m w n n c p , n c d k n k t 0 " F P O V " x g " J F C E " k p j k d k v i g n g p g m u g n " v g t c r k p k p " d k t n g v k t k n o g u k { n g " g

J F C E " k p j k d k v  $\frac{3}{4}$  t n g t k . " h c t m n , " d k { q n q l k m " kanser, spinal o w u m Ñ n g t " c v t q h k . " C n | j g k o g t " j c u v c n , k p h n c o c u { q p . " c u v , o . " t q o c v k | o c " x g " r c t c | k i t w r , n p " t v , g p f c x k n g t k \* p M Ñ g ± " Ñ 3 n p g " n r w n c " p 4 f 2 c 3 f 6 , + t 0

F P C " o g v k n c u { q p w " ± q m " mifiktasyon olarak kabul " g r k i edilirken, histon modih k m c u { j q p u w c q t p , " . o " q f k h k { g " g f k e k " g p | k d k t " f g p i g " k n g " m q t w p w t m g p k i " bu p d k u s p e s i f i k g p " f c o q f k h k m c u { q p n c t \* , M g g m m { g ' t ' x ' g ' g f { k " 0 m . c " n 4 2 3 2 +

## 2.5 V g | k p " C o c e ,

Hidroksisinnamik asitlerden, kafeik asit, ferulik asit, m- ve p-kumarik asitler antioksidan, anti-fibroz, antiviral, anti-v  $\tilde{A}$  o  $\frac{3}{4}$  t " -xomb'otik pktivkeler gibk "  $\pm$  g k v n k d k { q n q l k m " c m v k x k v g n g t " u c j k r " q n f w m n c t , " o i  $\frac{3}{4}$  t o  $\tilde{A}$  v  $\tilde{A}$  t " \* g D w " x c g p " n f c k o f 0 c " 4 n 2 k 3 v 5 g + t 0 c v  $\tilde{A}$  t f g " h g p q n k n i k n k " o g x e w v "  $\pm$  c n , o c n c t " x c t m g p . " g r k i g metilasyonu  $\tilde{A}$  | g t k p g " g v m k u k p k " c  $\pm$  , m n c { c p "  $\pm$  c n , o c " {

Antikarsinojenik etkileri ortaya konulan bu fenolik asitlerin epigenetik r c t c o g v t g n g t f g p " q n c p " F P C " o g v k n c u { q p w p c " n k v g t c v  $\tilde{A}$  t f g "  $\pm$  k x n g " " c f | k f , U t d " 4 \* 2 R 6 c 2 n e w 0 u { | c e r | , c n o , " q n c p d g u k p n g t f g " d w n w p c p " h k v q m k o { c u c n n c t , p " g r k i i  $\frac{3}{4}$  u v g t o k " q n w r " d w " c n c p f c m k " c t c v , t o c n c t " k

D w " c o c  $\pm$  n c " d w " v g | "  $\pm$  c n , o c u , p f c " k p u c p n c c n f , m n c t , " x g " v , d d k " d k v m k n g t k p " { c r , u , p f c " olan kafeik asit, o-m w o c t k m " c u k v . " h g t w n k m " c u k v  $\emptyset$  k p " k p u epigenev k m " f g k k DNA metilasyonuna olan etkilerinin belirlenmesi c o c  $\pm$  n c  $\emptyset$  " o C { p , t bu fenolik maddelerin DNA asetilasyonu ve DNA f g c u g v k n c u { q p w "  $\tilde{A}$  | d g v t " k p f n g "  $\emptyset$  r e ' k ' h g v ' m k n g t { k " f n g }

### 3. [ " P V G O

#### 3.1 Materyal

##### 3.1.1 ¥ c n , o c f c " M w n n e p , n e p " M k o { c u c n n e t " x g

C i c t q | " \* U k i o c . " C ; 7 5 ; + . " G v k f { w o " d t q o Ã t  
F P C " n c f f g t " \* H g t o g p v c u . " U O 2 5 3 3 + . " U q f { w o " M n  
Asit (Sigma-Aldrich, C0625), Ferulik Asit (Sigma-Aldrich, Y0001013), o-Kumarik  
Asit (Sigma-Aldrich, H2,280-9), Dulbecco Modifiye Eagle Medyum (DMEM,  
U k i o c . " F 7 9 ; 8 + . " H g v c n " u , , t " u g t w o w " \* H D U . "   
Trypsin-EDTA (Gibco, 25200), cDNA Sentez Kiti (Abm, G236), Kilogreen qPZR  
Kiti (Abm, mastermix-MU + . " k p p w R T G R " T P C " | q n c - K S { q p " M k v  
2040010), BCA Protein Test kiti (Biovision, K813-2500), Mitochondria/Cytosol  
Fractionation Kiti (Biovision, K256-25), Methltransferase Activity Assay Kiti  
(Colorimetric) (Biovision, K986-100).

##### 3.1.2 ¥ c n , o c f c " M w n n e p , n e p " E k j c | n e t

Laminar flow kabini, K p x g t v g f " o k m t q u m q 80. deri E Q 4 " k p  
f q p f w t w e w . " C i c t q | " l g n " g n g m v t q h q t g | k " c r c t c  
R | t " e k j c | , . " I g t ± g U n q " | w c v l o c c p n v , O t o m a t i k B i o t e l e T a k e 3 c | , . "   
o k m t q " T P C 1 F P C " ¾ n ± Ã o " e k j c | , . " G v Ã x . " L g n " i ¾ t  
Vorteks, Otomatik mikropipet, O c p { g v k m e F n g c k t { , q p v k , | t g M i k r o d a l g æ k j c | , .  
h , t , p . " J c u u c u " v g t c | k 0

##### 3.1.3 ¥ c n , o c f c " M w n n e p , n e p " R t k o g t n g t

¥ c n , o c o , | f c " J g r I 4 " j Ã e t g " j c v v , p f c " F P  
i ¾ t g x " c n c p " F P O V 3 . " F P O V 5 C . " F P O V 5 D . " V G V 3 . "

J C V " i g p n g t k " u g ± k n g t g m " w { i w p " f k | k n g t " d g n k  
d n c u v n c o c u , -D' NPCEUDVK" 1 x R g t t k k o , " g m t , c d , c { p n , c " c f t ç e t w n w w " v  
¥ c n , o c f c " m w n n c p o c m " c o c e q n ( a d " l d k w t " o r c t u k , o p g c t " " 3 f  
skalada sentezlettirilerek -4 2 Å E ø f g " u c m n c p o , v , t 0 " M w n n c p ,  
x g t k n o k v k t 0

Her deneyin sonunda, kontrol aktivitesi yenidg p " ¾ n ± Å n o Å " x g " d c  
m q p v t q n " c m v k x k v g u k " k n g " m e t , n c v , t , n o , v  
u Å t g m n k " m q p v t q n " g f k n o k v k t 0

**Tablo 1:** U g ± k q m d k p " i g p n g t " k ± k p " v c p , o n c p c p " r t k o g

Gen	n g t k " R G e n i B r i m e r (5x 3')
<b>DNMT1</b> (DNA metil transferaz 1)	AGGCGGCTCAAAGATTTGGAA
	GCAGAAATTCGTGCAAGAGATTC
<b>DNMT3A</b> (DNA metiltransferaz 3 alfa)	CCGATGCTGGGGACAAGAAT
	CCCGTCATCCACCAAGACAC
<b>DNMT3B</b> (DNA metiltransferaz 3 beta)	AGGGAAGACTCGATCCTCGTC
	GTGTGTAGCTTAGCAGACTGG
<b>TET1</b> (tet metilozin dioksijenaz 1)	CATCAGTCAAGACTTTAAGCCCT
	CGGGTGGTTTAGGTTCTGTTT
<b>GAPDH</b> (gliseraldehit-3-fosfat dehidrojenaz)	GGAGCGAGATCCCTCCAAAAT
	GGCTGTTGTCATACTTCTCATGG
<b>HDAC1</b> (histon deasetilaz 1)	TGGAAATCTATCGCCCTCAC
	TCTCTGCATCTGCTTGCTGT
<b>HDAC3</b> (histon deasetilaz 3)	GCAAGGCTTCACCAAGAGTCT
	AGATGCGCCTGTGTAACGC
<b>HAT</b> (histon asetiltransferaz)	TACAGCGGAAGATCCATCCAA
	CTGTTGTGCCTCTATCGCCA

## 3.2 Metod

### 3.2.1 J Ñ e t g " M Ñ n v Ñ t Ñ " ¥ c n , o c n e t ,

¥ c n , o c o , | f e c k " k g p t u " c m p c " p m c g t t c k " 4 j + Ñ ' e m v g n " n j c c p v , v n , o " ,  
HEPG2 j Ñ e t g " j c v v , " j Ñ e t g " m Ñ n v Ñ t Ñ " n c d q t 2 c v w x c t  
x g " ' ; 7 " p g o " k ± g t g e g m " J Ñ e t g k g n n f g g t " k k p p " m i Ñ g d n g k " g k f o k k n " o x  
' 3 2 " H g v c n " U , , t " U g t w o w " \* H D U + " m w n n c p , n c t c  
' 3 " r g p k u k n k p " k ± g t g p " F O G O " \* F w b e s i g y e r i e q ) u " O q  
u c n c p o , v , t 0 " J Ñ e t g n g t k - 5 " { Ñ p f w g h o k t w p r c ð d c l m  
i g t ± g m n g v k t k n o k v k t 0 " J Ñ e t g p k p " k Ñ e r i k { c e , p o  
r g v t k n g t f g " Ñ t g v k n - g p " j Ñ e w g m w t c c " t x ' a d t r a p n e g a p { o c k " : Ñ  
R c u c l n c o c " k n g o k p g " i g ± k n f k k p f g " ¾ p e g n k n  
w | c m n c v , t , n , t 0 " F c j c " u q p t c " j Ñ e t g n g t " R D U " \*  
D g u k { g t k p f g p " w | c m n c v , t , n c p " j Ñ e t g t k " r g  
k n c x g " g f k n o k v k t 0 " U c p v t k h Ñ l " { c t f , o , { n c " ±  
m q p w n c t c m " { g p k " d k t " r g v t k { g " c m v e t , n o , v , t  
u c n c p o , v , t 0 " J Ñ e t g n g t k p " u c { , n o c u , " k ± k p  
n c o , p { f , o " u c g t ± g m n g v k t k n o k v k t 0

#### 3.2.1.1 Kafeik Asit, Ferulik Asit ve o-Kumarik Asit

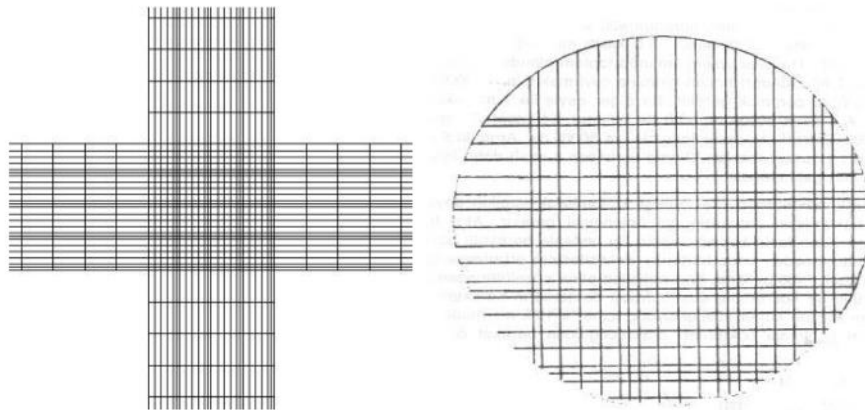
Mq p u c p v t c u { q p n e t , p , p " J c | , t n c p o c u ,

O q n g m Ñ n g t " c , t n , m n c t , " d k n k p g p " v q | " j c r  
m w o c t k m " c u k v " d g n k t n k " j c e k o n g t f g " f m M o g v k n u  
m q p u c p v t c u { q p f c " c p c " u v q m n c t " j c | , t n c p o , v  
¾ p e g u k p f g " v c | g " d g u k { g t k { n g " u g { t g n v o g " k  
j c | , t n c p o , v , t 0 " M q p v t q n " i t w d w p c " d g u k { g t k  
w { i w n c p M U Q o p w p 0 " u q p " m q p o k g v o g o k q p k w t " 0 " 2 0 7

### 3.2.2 J Ñ e t g " E c p n , n , , p , p " U e r v e p o c u ,

#### 3.2.2.1 V t k r e p " O c x k " D q { c o c " V g u v k " k n g " J Ñ e t g

J Ñ e t g " e c p n , n , , p , p " d g n k t n g p o g u k " c o c e ,  
D w " d q { c " p g i c v k h " { Ñ m j g Ñ e u t c g j n k g r t " k ø K t e " c ø q { ð f { , c t " "  
q n o c f , , p , " d g n k t n g o g o k | k " u c n c o , v , t 0 " V t  
o g o d t c p , " | c t c t " i ¾ t o g o k " x g " e c p n , " d k t " j Ñ e  
e c p u , | " j Ñ e t g n g t " d q { c { , " c d u k " t q g ð t g d m " t i g ¾ t " Ñ p k  
V j q o c " n c o , p c " { Ñ m n g p g p " j Ñ e t g n g t g " v t k r e p " o c  
u c { , o " k n g o k " i g t ± g m n g v k t k n k t " \* g m k n " 5 0 3 +

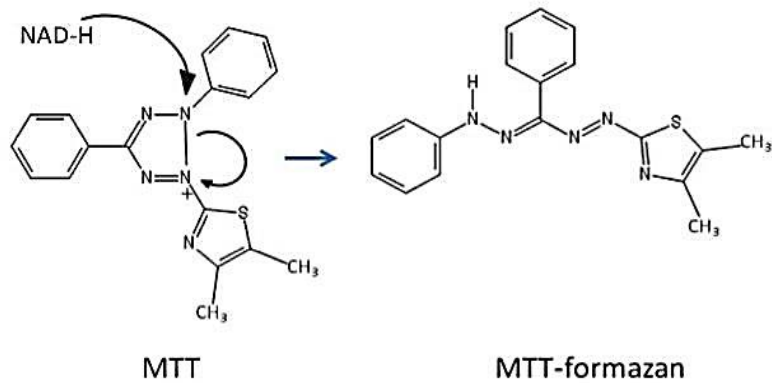


g m k ñ H b 5 a 0 3 < , p f c m k " m e t g n g t k p " i g p g n " x g " u , p , t r  
V q r n c o " j Ñ e t g " u c { , u , " ? " V q o c " n c o , p f c " u c { , n c

#### 3.2.2.2 J Ñ e t g " E c p (M T F v e y a K N s t a h V i y d e)

E c p n , " j Ñ e t g n g t " ± g k v n k " d q { c o c " (m ¾ p v g o n  
u Ñ t g u k p k " c | c n v o c m " x g " p w o w p g { k " c t v , t c e c m "  
k ± k p " d w " { ¾ p v g o " i g n k v k t k n o k v k t 0 " O w n v k y  
q m w { w e w n c t , + " { Ñ m u g m " f g t g e g f g " j c u u c u k { g v n  
p g f g p n Ñ è e g ð m c { j , u , p , p " d k t " ¾ n ± Ñ u Ñ " q n c t c m " d

ctc v , t , no , v , t 0 " U c f g e g " e c p n , " j Å e t g n g t " x  
 \* G N K U C " q m w { w e w + " ¾ n ± Å n g p (4,5-dimethyltiazol-2-il)-2,5-difenil tetrazolyum d t q o Å t + " f c { c n , " j , | n , " d k v k t m Q " n D w k  
 { ¾ p v g o " ± q m " { ¾ p n Å " x g " m c p v k v c v k h v k t " \* O q u o c p  
 ¥ c n , o c f c " h g p q n k m " c u k v n g t k p " J G R I 4 " j Å e t  
 f w t w o w p c " i ¾ t g " k m k " h c t m n , " o v g c v { q k v p " " \* g M M M " o x k g { v c k  
 v g u v k " O q u o c p p " \* 3 ; : 5 + " { ¾ p J G R k 4 ð ð ð ¼ c g k i g t ± p  
 j Å e t g " j c v v , . " F O G O " 2 d x g g u " k 5 ' 9 { " g à t E k ø " f ð ð ð m k 7 " " p E g Q o n k  
 ± q c n v , ¥ q o , c n j v Å t c ¾ (4,5-dimethyltiazol-2-l)-2,5-difeniltetrazolyum  
 d t q o Å t " \* O V V + " v k g f e i k v a k i t , " f e v l i k i a s i t n e o - f u c a r i k a s i t f i n H E P G 2  
 j Å e t g n g u k p g v q m e p m " m q p u c p v t c u { ; q 8 p ø n n c , t m " " r d n g e n n k t  
 (2x10<sup>3</sup>/kuyucuk+ " g m k n g t g d ð 4 6 ð p c ð ð ; k p m Å n o , v , t 0 " C t  
 f q | n c t " k n g " o w c o g n g " g f k n g t g m " 4 6 " u c c v " d q { v  
 u q p t c " j Å e t g n g t g " O V V " ± ¾ | g n v k u k " w { i w n c p c t c  
 u q p w p f c " ± ¾ | Å p o Å " q n c p " , h " q { t Å | c g | { c k p p " g m t d k k u t v k c m o n g g  
 i g t ± g m n g U v Å k t t g k " n o d p w f 0 " u , x , " m , u , o " w | c m n c  
 F O U Q " g m n g p g t g m " ± c n m c n c { , e , f c " f Å Å m " f g x k t  
 m t k u v c n n g t k p k p " ± ¾ | Å p o g u k " k ± s p e k t r o f o t m e f r i k m k m c " k  
 ¾ n ± Å o " { ¾ p v g o k { n g n " c m ç 6 " 2 q " m p w d " w G N K U C " f n g p g t w n g t w k  
 j g u c r n c D w " , d v , n 0 ö f c " j k ± " h g p q n k m " o c f f g " k n g  
 i t w d w " x g " h g p q n k m " c u k v n g t " k n g " o w c o g n g " g  
 dozlardan k " h g p q n k m " c u k v n g t k p " j Å e t g " e c p n , n , , p



g m k H ð 5 0 4 < c p f c " O V V " k p f k t i g o g u k " \* \ g t d k p c v k



### 3.2.3 V q v c n " T P C " | q n c u { q p w

F q m w " { c " f c " j u ã ç r t ã u n ( g ç p k v p " " m v k n r k ç p , n c t c m " r c  
{ c t f , o , { n c " T P C ø p , p " g m u v t ç m v ç u " ç k ç k ç 1987 g u k " k n  
{ , n , p f c " E j q o e | { p u m k " x g " U c e e j k " v c t c h , p f c p  
1987).

Y ã m u g m " q t c p f c " x g t k o " x g " m c n k v g f g " T P C " ã t  
T P g c u { " f ¾ p f ã t o g " m q n q p n c k g " k n g k v d ' k t k g " v k  
i g n k v k t o k n g t f k t 0 " D w " { ¾ p v g o " m w n n c p , n c t c  
vitro translasyon ve ters transkripu k { q p " f g p g { n g t k " u , t c u , p f c " c  
sonra { ã m u g m " m c n k v g n k " e F P v ç m i k m o l i z i d e m e y l e r i n d e n c D N A , " q n w  
r t q d { n c r t o , c " m " k ± k p " T P ç ü n ö l a r a k k u l l a n g ö g v n g f ç , t " \* Y w  
2002).

Fenolik asitlerin sitotoksik m " g v m k u k " u c r ç f ç p f g t m v ç t p k " u ç i ç r t k e  
kafeik asit, ferulik asit ve o-kumarik asit petrilere ekilo k " q n c p " j ã e t g n g t  
(1x10<sup>6</sup>+ " u v g t k n " q n c t c m " g m n g p g t g m " 4 6 " u c c v "  
w | c m n c v , t , n o , v , t 0 " v M g p n g ç k ' h g h ç t w ç m ' g h g ç ç f ç  
m w n n c p , n o , v , t 0 " V q r n c p c p " j ã e t g n g t f g p " C p c  
ã t g v k e k " h k t o c p , p " ¾ p g t f k k " r t q v q m q n " f q t v  
k ± g t k u k p f g " d w n w p c p " N k | k | " i ã t n ( ç ç p x w g " " n ç w , n m c c o p c ,  
h k t o c p , p " r t q u g f ã t ã " w { i w n c p o , v , t 0 " N k | k | "  
k n g o k p f g p " i g ± k t k n o k v k t 0 " Q t v c { c " ± , m c p " r g  
m g | " v g m t c t n c p o , v , t 0 " U ç r e p ç u ç k l e n e r e k ç o ç m " 2 ç ç n ç ç ç f ç ç " r  
u c m n c p o , v , t 0 "

J ã e t g " r g n g v k p g " 6 2 2 " n " n k | k | " \* T N + " u q n ã  
f c m k m c " k p m ã d g " g f k n k t g m " c n , e , " v ã r e ç i l e n " k ± k p g  
¾ t p g m " 3 3 2 2 2 " i ø f g " 4 " f c m k m c " u c p v t k h ã l " g f k n  
T P C " d w n w p f w w " k ± k p " u ã | ã p v ã " d , t c m , n o , v , t  
{ g t n g v k t k n o k " ã | g t k p g " 6 2 2 " n " ' 9 2 ø n k m " g  
santrik h ã l " g f k n o k v k t 0 " U r k p " h k n v t g " T " { g p k " d k t  
u q n ã u { q p w " J U " g m n g p o k v k t " x g " 3 3 2 2 2 " i ø f g " 3  
u , x , " d q c n v , n c t c m " 9 2 2 " n " { , m c o c " u q n ã u { q  
u c p v t k k n h o ã k l " v g k f t 0 " C t f , p f c p " c n , e , " v ã r v g m k " u , x

i ø f g " 5 " f c m k m c " u c p v t k h Ñ l " g f k n o k v k t 0 " U q p " q  
v c o " q t v c u , p c " 8 2 " n " T P C c | " k ± g t o g { g p " u w " g m  
u q p " Ñ p a Ñ BNA -: 2 " à E ø f g " u c m n c p o , v , t 0

### 3.2.3.1 T P C ø p , p " U r g m v t q h q v q o g v t k m " C p c n k | k

| q n g " g f k n g p " T P C " ¾ t p g m n g t k p k p " m q p u c  
T P C 1 F P C " ¾ n ± Ñ o " c r c t c v , " m w n n c p , n c t c m " D k q v  
f c p u k v g " \* Q F + " k n g " ¾ n ± Ñ n m > Ñ . 7 ) . v 4 Ñ t 2 " " \* p Q F " F 4 P 8 C 2 ø p p o , " p l " "  
p o " r t q v g k p k p " c d u q t d c p u " x g t f k k " f c n i c " d q { v

### 3.2.3.2 V q v c n " T P C ø p , p " C i c t q | " L g n " G n g m v t q h q

E n g m v t q h q t g | k " k n m " q n c t c m " u x g ± n k " d k n k c  
Ñ | g t k p g " ± c n , , t m g p " ð w ð g w k p w t g 0 " 3 D 6 " : ø f g , " P q d  
i ¾ t Ñ n o Ñ v Ñ t 0

C i c t q | . " f g p k | " { q u w p w p f c p " g m u v t c m v g " g f  
d k t " f q t w u c Ñ n " w ð n w k { o i g w t n f c k o t c 0 " k ± k p . " { c n p , | e c "  
k j v k { c ± " x c t f , t " x g " r e k m z o B u t e k e n e , a g a r o z j e l l e r i n c v c n k |  
j c | , t n c p o c u , " d c u k v " x g 2 ) ! j , | n , f , t " \* D c t t k n " x g

| q n g " g f k n g p " T P C ø n c t , p " i ¾ t Ñ p v Ñ n g p g d k n  
{ Ñ t Ñ v Ñ n o Ñ v Ñ t 0 " ' 3 ø n A s e t i k " a s i t - E D T A q ( T A E ) I t a m p o h u k n g " V  
j c | , t n c p o , v , t 0 " J c | , t n c p c p " l g n " o k m t q f c n .  
c i c t q | w p " ± ¾ | Ñ p o g u k " u c n c p o , v , t 0 " ¥ ¾ | Ñ p o  
k n g o k p f g p " i g ± k t k n g t g m " Ñ | g t k p g " a f o r e 7 " Ò N "  
v c d n c u , p c " f ¾ m Ñ n g p " l g n " m c v , n c , p e c { c " m e f  
g n g m v t q h q t g | " v c p m , p c " { g t n g v k t ó k g ø K - ø k ' t { 0 c " "  
f q t w " { Ñ t Ñ { g d k n o g u d k + " " k m w k v p d " w g a ð n i v t q t h w d " t { g g t k i p g  
m c { p c , n p c c p " o d , c v , t 0 " G n g m v t q h q t g | " v c p m , " 3 z " V  
Ñ u v Ñ " m c r c v , n o , v , t 0 " 7 " Ò n " T P C " ¾ t p g k . " 4 "  
j q o q l g p k | g " g f k n g t g m " o k m t q r k r g v " { c t f , o , {  
M w { w e w m n c t c " o c g m g t ' ò k g n v ¾ t p g m , { Ñ m d n q " 4 ø f g " c

**Tablo 2:** Mw { we w m n c t c " { Å m n g p g p " T P C " ¾ t p g m n g t k " x g " o

**T P C " k ± k p =**

**O c t m g t " k ± k p = " " " " "**

5 n " T P C " ¾	<b>Toplamda 8 kuyucuklara { Å m n g p o</b>
2 n " d q { loading dye)	
1 n " g p l g m	

6 n " m d " F P marker	<b>Kuyucuklara 5 n " { Å m n g p o</b>
2 n boya (6xloading dye)	
2 n " g p l g m	

GÅ± " m c { p c , p c " d c n c p c p " g n g m v t q h q t g | " ; 2 d q { w p e c " { Å t Å v Å n o Å v Å t 0 l g [ n Å t Å v Å t 0 l g v t k p m g o k w o i ¾ t Å p v Å n g p g t g m " F P T " N p i j y D k u " R { q K g o f g e h q v q t c h n c p f , t , n o , v , t 0

### 3.2.4 cDNA Sentezi

e F P C " u g p v g | k " k ± k o " G c u { " U e t k r v " R n w u " e F x g " V g t u " V t c p u m t k r v c | " g p | k o k " \* T V + " m w n n c p ¾ p g t f k k " r t q v q m q n g f q k t k n o k u w p f o " e F P C g m g p v x g " { c r , n , g , x " g V c k d n n R k " T 5 " k { v c o " o E V n " Å | g t g " u - g p v g | n 4 2 Å E ø f g " u c m n c p o , v , t 0



Dw" dc ncofc " R\ Tøpkp " ±g-Transkriptaz Polimeraz p " dkt  
 Zincir Reaksiyonu (RT-R\ T+= " j Ñet gngtfgp " k|qng " gfk n  
 tgv t q x kt Ñung t f g p " k|qng " g f k n g p " T g x g t u " v t c  
 FPC " \* e FPC+ " u g p v g | k p k " i g dksprsyomu ganalizkriñio g u k " u  
 { cr , n c d k n f k u d u " j d k t n , { ¾ g v' gjocfuk t-PZR' Tlaq DNA g m " | c o  
 r q n k o g t c | , p " 7 ø " p Ñmng c | " c m v k x k v g u k " u c { g u  
 f c n n c p o c " p q m v c u , p f c " m g u k n o g u k p g " f c { c p , t 0  
 h n q t g u c p " k f f g v k p k p " d c u m , n c p o c u , " \* u ¾ p Ñ o Ñ +

R\ Tøfg " { g t " c n c p " d k n g g p n g t = " c o r n k h k { g  
 k ± g t g p " m e n , r " F P C . " c o r n k h k { g " g f k n g e g m " m e n  
 u g ± k n o k " { c m n c , m " 4 2 " d c | n , m " u g p v g v k m " m , u c  
 primerler, termostabil karakterli Taq DNA polimeraz, enzimidir. Mg+2 iyonu da

k n g o f g " m q h c m v ¾ t " q n c t c m " ¾ p g o n k f k t 0 "

R\ T " k n g o k p f g " j g f g h " FPC"ø pf,¾pp"i Ñ"q cctncvu,,  
 i g t ± g m n g k t 0 " J g t " f ¾ p i Ñ " h c t m n , " u , e c m n , m n c t

F g p c v Ñ t c u { RqÇ". ± kmhcn", t k pFe k t k p k p " c ± , n o c u ,  
 j c n k p g " i g n k t 0 " C p p g c n k p i " \* d k t n g o g + " v g m " |  
 c f , o , f -8 t2 "ÅEg" c 7 2 u , p f c " i g t ± g m n g k t 0 "

Extension (uzama) DNA polimeraz enziminin maksimum aktiviteye sahip

q n f w w f" g9"4 iÅE t" ± g m n g k t 0 " V g m " u c t o c n " j g f g h " F  
 | k p e k t " d c n c t " x g " V c s " r q n k o g t c | " q t v c o f c m k "

V g m " k r n k m n k " F P C " ± k h v " -k 2 h k i¾p ki " Ñ h q t n c t " c i n  
 c f , o , p " v g m t c t , { n c e'Pehivanç, 2003)g f g t 0 " \* Q m w v w e w " x



g m k ~~StepOne Real-Time PZR Systemi~~ \* R c o w m m c n g " © p k x g t u k v g u k " D k { q n c  
 D k { q m k o { c " N e d q t c v w x c t , +

I g t ± g m " | c o c p n , " R \ T " ± c n , o c n c t , " C D O " M k  
 m w n n c p , n c t c m " Ñ t g v k e k i k g ö c g t p g ñ p g t f k t k ñ v k  
 e F P C " o k m v c t n c t , . " { c r , <sup>2</sup>o n c " d u q , t e c c v n w x , c m n , c o t , , | . f " c g  
 g f k n o k v k t 0 " I g t ± g m " | c o c p n , " R \ T " u q p w e w p f c  
 x 4 0 5 " r t q i t c o , " m w n n c p , n c t c m " n j c g p u " c I r C h R e F p J o ø , g " " i x 3 4  
 p q t o c n k | g \* g g f n k k o n " k 5 g 0 t k " t i g p " k ± k p " c { t , " c { t , " c  
 u v c p f c t v " m e n k d t c u { q p " g t k u k " q n w v w t w n o w  
 C o r n k h k m c u { q p " u q p w e w p f c " g n f g " g f k n a d e p " E v " \* v  
 i g p k p " w { i w n c o c n c t " u q p w e w p f c " o T P C " f Ñ | g  
 d g n k t n g p o k v k t 0

### 3.2.6 R t q v g k p " F Ñ | g { k p f g " G m u r t g u { q p " U g x k { g

#### 3.2.6.1 T R C " V e o r q p w " k n g " R t q v g k p " | q n c u { q p

T c f { q " k o o Ñ p q r t g u k r k v c u { q p " v c { k p k " \* T K R C  
 k k ± p " m w n n c p , n c p " d k t " n k | k u " v e o r q p w f w t 0 " T K R C

q n c t c m " r t q v g k p n g t " c t c u , p f c m k " t a n g p o n u n u h c { , h " j c | , t n c p ø , v g , " " x V g c t d k n n q o " k 6 v k t 0

**Tablo 4:** T K R C " v c o r q p w p w p " j c | , t n c p , , "

RIPA Tamponu
3 7 2 " o O " U q f { w o " M n q t
%1 NP-40 ya da Triton X-100
%0,5 Sodyum Deoksikolat
' 2 . 3 " U F U " * U q f { w o " F
50 mM Tris pH:8.0

J c | , t n c p c p " v c o r q p " k ± k p " ' 3 2 ø n w , m h v e p f { m q t w p o w v w t 0 " n g o " i g t ± g m n g o g f g p " ¾ p e g " v c o r q p w { n c " v q r n c p c p " j Ñ e t g n g t " 5 2 " f c m k m c " d 3 2 2 2 " t r o ø f g " 3 7 " f c m k m c " d q { w p e c " u c p v t k h Ñ l u Ñ r g t m c w e p v { g p k " d k t - 4 g à E ø f g t h c h n a p p c t v m t 0

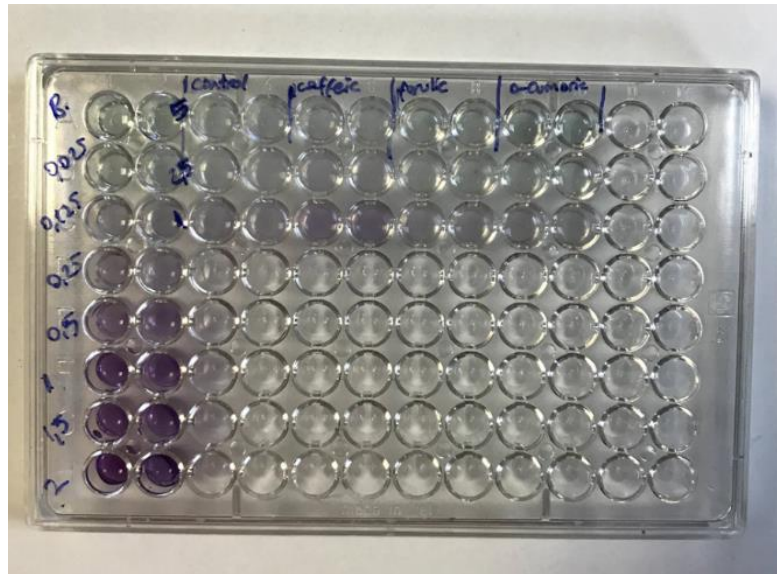
### 3.2.6.2 D k m k p m q p k p k m " C u k v " \* D E C + " [ ¾ p v g o k " k n

R c w n " M 0 " U o k v j ø k p " i g n k v k t f k k " d w " { ¾ p reaku k { q p " d k Ñ t g v " 2 t g e q p k g t p k w f ' w t 0 ' q E w C u <sup>1+</sup> , p c " d c k { q p w p c " k p f k t i n g k k t p g t 0 ' k u m k p d w k ' k p g k t i g D E C " t g p m n k " d k t " m q o r n g m u " q n w v w t w t n c t " x g " d w ' q t c p v , n , f , t 0 " Q n w c p " d w " t g p m " m q o r n g m u k " 7 \* U o k v j " 1985). " f k 0 . "

7 8 4 " p o ø f g " c d u q t d c p u " x g t g p " m q { w " o q t " t g p r t q v g k p k p " c o k p q " c u k v " m q o r q | k u { q p w p f c p " c | h c | n c " d k n g k m " { q m v w t 0 " C p e c m " D E C " t g c m v k h k " metod k n g " c o k p q " c u k v n g t . " f g v g t l c p n c t . " n k r k o g v q f w p c " i ¾ t g " f c j c " k { k " v q n g t g " g f k n k t 0 " p d w " { ¾ p v g o f g " i k t k k o " g v m k u k " i ¾ u v g t k t 0 " D k q x Ñ t g l v k t e d c ' p , p " d g n k t w n v k w u k w ' p v f c c n " k i o g c t v ± n g c m t n " g f q v k t t k n c

**DUC " U v c p f c t v n e t , p , p " J e | , t n e p o c u , =**

De-k { q p k | g " u w " m w n n c p c t c m " DUC " BCA test p f c t f , p  
 m k v k p k p " v c n k o c v n e t , " f q t w n v w M k p f d k " ± DUC ü kUp  
 d w n w p c p " r t q v g k p " u v c p f c t v n e t , " u , , t " u g t w o  
 mg/ml; 0,5 mg/ml; 0,25 mg/ml; 0,125 mg/ml; 0,025 mg/ml konsantrasyonlarda  
 m w n n c , p t , n g m k 0 n " U 5 g 0 ( t + g n v k n o k " u v c p f c t v " ± ¾ | g n v k  
 j c h v c { c " m e f c t " m w n n c p , n e d k n o g m v g f k t 0



g m k ü ğ 5 0 0 ¼ j Æ e t g " j c v v , p f c " D E C " { ¾ p v g o k " k n g " r

**D E C " T g c m v k h k ø p k p " J e | , t n e p o c u , =**

D E C " ± c n , o ğ ğ | t g t e m v d d h h p k ± k p . " T g c m v k h " C ø  
 q t c p , p f c " m e t , v , t , n o , v , t 0 " Q n o c u , " i g t g m g p  
 m e t , v , t , n , t 0 " J g t " p w o w p g " k ± k p " 4 2 2 " Ü n " D  
 u v c p f c t v n e t , " x g " ¾ t p g m n o g k t n g v " c g m i e g " o D E C " k t ± g k c p m v  
 j c | , t n (Tablo 5). v , t



**Tablo 5:** DE C " U q n Ã u { q p w "

DE C " U q n Ã u { q p w "	
<b>BCA Reaktif A</b>	500 ml
<b>BCA Reaktif B</b>	25 ml
<b>BSA Standart (2 mg/ml)</b>	5 x 1 ml

**Ok mt q r n c m c " R t q u g f Ã t Ã = "**

Ok mt q r n c m c p , p j " g m w { D w U e C w m u n v c c t p , f p c c t v n c t , " x g " r 4 7 " Û n " g m n g p o k v k t 0 " U v c p f c t v " x g " p w o w p g " m w g m n g { g t g m . " 5 2 " u c p k { g " d q { w p e c " k { k e g " m c t , f c m k m c " k p m Ã d g " g f k n o k r u k t 0 " q p m Ã d i c , u c q m f , c p ' p d , t c m , n o , v , t 0 " Ok mt q r n c m c " q m w { w e w u w p f c " 7 8

**3.2.6.3 F P C " O g v k n c u { q p w p f c " I ¾ t g x " C n c p " F P O Belirlenmesi**

**3.2.6.3.1 P Ã m n g g t " r t q v g k p n g t k p " u c h n c v , t , n o c**

Fenolik asitler EC<sub>50</sub> f q | n c t , p f c " 4 6 J' g u r d c 4 v " j d Ã c e { w p m e g c t w { i w n c p o , v , t " x g " d w " | c o c p " u q o p r a v t p l a c a n j Ã e t g j Ã e t g n g t f f r a s i y o n B i o v i s i o n M i t o c h o n d r i a / C y t o s o l F r a c t i o n a t i o n K i t m w n n c p , n c t c m " p Ã m n g e t " h t c m u k { q p n c a c p , k p " q n g ¾ p g t f k k " v c n k o c v n c t " f q t w n v w u w p f c " i g t ± g m n + 6 à E ø f g " 7 2 2 i ø f g " 5 " f c m k m c " d q { w p e c " u c p v t k h q n w c p " r g n g v " ¾ p e g f g p " u q w v w n o w " R D U ø f g " k r F V V . " 3 2 " Û n " R O U H " x g " 3 " Û n " r t q v g c | " k p j k d k v m w n n c p , n o , v , t 0 " F c j c " u u q p t w c v " w q m w c " p D ' w r h g h r g g v " C 3 7 " u c p k { g " d q { w p e c " x q t v g m u n g p o k v k t 0 " C t f , p m c t , , k c " ¾ g p g m " k ± k p " 3 3 " Û n " D w h h g t " D " g m n g p f c m k m c " d w | f c " d g m n g v k n o k v k t 0 " D w | f c " d g m x q t v g m u n g p o k f g " k 3 0 2 2 2 i ø f g " 7 " f c m k m c " d q { w p e v c d c m c " d c m c " d k , t t " 0 g " r Q g t p v f c q " t v h c c d " c c m c , f p c o " , { g v p k " d k t d k t " ¾ t p g g " 3 2 2 " Û n " D w h h g t " E " g m n g p o k v k t 0 " 3

Ùn " r t q v g c | " k p j k d k v ¾t Æ " g m n g p o k v k t 0 " J g t " g m n g p f k m v g p " u q p t c " 3 20 "" fCt m k m p d " c p + 5 t 3 2 g E n o u n g g i p 7 o f k f c m k m c " u c p v t k h Æ l " k n g o k " i g t ± g m n g v k t k n o k c n , p - x 2 è à n E o m f n g " p w , v , t 0 " t | r t n g v g k k m g p k p " Æ o n h m g c d g n k t n g p o k v k t 0

**5 0 4 0 8 0 5 0 4 " F P O V " C m v k x k v g " [ ¾ p v g o k "**

q n g " g f k n g p r " t q p v Æ n k m p n g g t t "" D N A v n m e t i t r a n s f e r a z t c m " c m v k x k v g n g t k p k p " p c u , n " f g k v k k " D k q x k u k \* E q n q t k o g v t k e + " m w n n c p , n c t c m " d g n k t n g p o k v k

D w " m c r u c o f c " ¾ p e g n k m n g " ¾ t p g m n g t " j c | , m w n n c p , n o , v , t 0 " M q p v t q n " k ± k p " { c n p , | e c " d w l r q | k v k x g " e q p v t q n " k n g " 6 6 " Ù n " O V " C u u c { " D w h h g 15, 25, 35 ve 45 Ù n " 4 2 2 " Ù O " U C J " u v c p f c t v n c t , p , " u , t 1 m w { w e w m " q n c e c m " g m k n f g " c { c t n c p o , v , t 0 " J q n c e c m " g m k n f g " O V " V g u v " V c o r q p " k n g " Æ | g t k p g

**Tablo 6:** T g c m u k { q p " m e t , , o , "

	" t p g m " t g c m u k { q p " m e t , , o , "
<b>MT test tamponu</b>	5 9 " Ù n
<b>Enzim mix I</b>	4 " Ù n
<b>Enzim mix II</b>	4 " Ù n
<b>Enzim mix III</b>	8 " Ù n
<b>U C O " m q h c m v ¾ t</b>	3 " Ù n
<b>OxiRed™ probe</b>	2 Ù n

R q | k v k h " m q p v t q n . " v g u v " ¾ t p g m n g t k . " u v c p Ù n " ¾ t p g m " t g c m u k { q ( T a b l o 6 ) t " J c , | o , t " n g p e p p " ¾ k p v g k n t n g c | " 6 7 " f c m k m c " d q { w p e c " j g t " 5 2 " u c p k { g f g " d k t { c r , n c p m k f v g k p p g " { ö c p w e n k p g " i ¾ t g " d g n k t n g p o k m w n n c p , n c t c m " o g v k n v t c p u h F P O V " k p j k d k v k Æ x k bilinen 5-aza-2'-f g q z { e { v k f f k e p + g " r \* q 7 k " v k | h c " m q p v t q n " q n c t c

### 3.2.6.4 SDS-PAGE Elektroforezi

G n g m v t q h q t g | " c p { q p k m " x c t n , , p f c " f g v g t  
 poliakrilamid jellerde, r q n k r g r v k v " | k p e k t n g t k p k p " c { t , n o  
 d k t " c t c ± " q n f w w " m e p , v n c p o , v , t " \* U j c r k t q " x

G n g m v t q h q t g | " k n g d l g " n k n k " g t h k p f i n g " i c g n t k g m  
 R q n k c m t k n c o k v " l g n " g n g m v t q h q t g | k " \* R C L G + " k  
 x c t n , , p f c " N e g o o n k " \* 3 ; 9 2 + " v e t c h , p f c p " v c  
 u k u v g o k p f g " ' : . 7 ø n k m , " t c o { c t c ' , l c g n , k f . α " g n k " i 3 / 4 t d g n , q m ' , 9  
 j c | , t n c p o , v , t 0 " R q n k c m t k n c o k v " v e d c m e " l g n r  
 R g p s w k p " F w c n " I g n " G n g m v t q h q t g | " \* Q y n " U g r c  
 i g t ± g m n g v k t k n o k v k t 0

**Tablo 7:** C { t , o c " x g " u , m , , t v n t p e c d u g n g t k p k p " j c

L g n " k ± g t l C { t , o c " l ; U , m , v , t (%4)	
Akrilamid/ Bisakrilamid	2,85 ml 750 Û n
Distile su	4,5 ml 2,5 ml
Tris-HCl	2,5 ml
Tamponu	
% 10 SDS	150 Û n 100 Û n
APS	50 Û n 25 Û n
TEMED	65 Û n 5 Û n

E c o " r n c m e n c t " l g n k p " f ¾ m Ñ n g e g k " u v c p f c  
 c { t , o c " l g n k " c t f , p f c p " u , m , v , t o c " l g n k " f ¾ r  
 v e t c m " { g t n g v k t k n o k v k t 0 " Q f c " u , e c m n , , p f  
 f q p o c u , k d g m n g p d l g n " f q p f w m v c p " u q p t c " v e t c m "  
 u q p t c " k n m " m w { w e w c " o q n g m Ñ n " c , t n , , " d k n  
 m w { w e w m n c t c " k u g " D E C " k n g " o k m v e t n e t , " d g n k t r  
 elektroforez tamponu v e t n , , p f c " ¾ t p g m n g t k p " c { t , o c "  
 v q r n c p c d k n o g u k " k ± k p " c m , o " ¾ p e g " 3 2 " o C ø g . " f  
 o C ø g " c { c t n c p e t c m " g n g m v t q h q t g | " k n g o k " i g t ±

G n g m v t q h q t g | " k n g o k " d k v v k m v l a g a p " o d a u q p t c .  
u , e c m n , , p f c " 6 7 " f c m k m c " u Ñ t g - 1 5 0 , 5 0 m e t a n o 4 " E q q o c  
x g " ' 3 4 " c u g v k m " c u k v " k ± g t g p " d t q d m " j ± 3 4 0 " g d q k a k  
hem de sabitn g p o k v k t 0 " C t f , p f c p " l g n " d c n c p o c { c p  
k ± k p " ' 9 ø n k m " c u g v k m " c u k v " k ± g t g p " ' 5 2 ø n w m  
u c m n c p o , v , t 0

### 3.2.6.5 Western Blot Analizi

Y g u v g t p " d n q H n T c T o w b i n , 3 ; 1 0 n m { m g | , p f c " x N g " 3 ; : 3  
Burnette v c p , o n c o , v , k 0 h g G o n k g { m v g t " q h q n k ç h t k n c o k f "  
proteinlerin destek membrana transferi ve membrandaki proteinlerin immunolojik  
o g v q v n c g t t n k c n " o g 3 4 k v v g o P r o t e i n l e r , g n l e m b r a n , { s i t o p l a z m i d e  
p Ñ m m g c g { t p d a b i l m e k t e d i r l e r . D w " p g f g p n g . " h c t m n , " m c p u g t "  
¾ t p g m n g t f g g m u k r " t r g t u q { v q g p k n p c t , " d w " o g \* v C u w Ñ c p " g d g n " k 4 t 2 n 3

G n g m v t q h q t g | " u q p w p f c " e c o " r n c m c n c t , p "  
v c o r q p w " k ± g t k u k o p g f o g d " t c p p k " v t k q u g " n Ñ a n q f x k ± n g p o k  
m w n n c p , n c e e c m " q n c p " p k v t q u g n Ñ n q | " o g o d t c p . "  
u q w m " 3 z " v t c p u h g t " v c o r q p w " k n g " ¾ p e g f g p " f q  
f q t w " u , t c u , { n c " u Ñ p i g t . l " g M j ç v p o k c v p t " q % g n Ñ n h q k r  
Y j c v o c p " % " 3 " h k n v t g " m c , f , " x g " u Ñ p i g t " u c p f x  
x g " c r c t c v " u , m , e c " m c r c v , n o , v , t 0 " J c | , t n c p  
m w v d w p w p " f c " m c v q v v c " q n o c u , p t ç p f u k l m g n t c " v v c g p f n k  
{ g t n g v k t k n o k v k t 0 " V t c p u h g t " k n g o k " 3 Z " v c c  
; 2 " f c m k m c " u Ñ t g u k p e g " i g t ± g m n g v k t k n o k v  
w | c m n c v , t , n o c u , p , " u c n c o c m " k ± k p " o g o d t c p  
deney v Ñ r Ñ " k n g " p c | k m ± g " Ñ | g t k p f g " { w x c t n c p , t "  
v c o r q p n c t , " v g o k | n g p g t g m " c n c p " m w t w n c p o , v ,

V t c p u h g t " u q p w e w p f c " u c p f x k ± " c r c t - c v , p , p  
u r g u k h k m " d c n c p o c n c t , p " g p i g q n Ñ p ç g p k " k n g è  
u , e c m n , , p f c " 3 " u c c v " k p m Ñ d g r a h g r i m e r n a n i k o r a v k t 0 " I  
c n , p - 4 Ñ ø m " g " i g e g " d q { w " d g m n g v k n o k v k t 0 " C t f ,

d q { w p e c " V D U V " k n g " { , m e p o , v , -alkali " fo f f a p t c u , p f  
\* ¾ t p ; anti-kabbit IgG- C N R " m q p l w i c v , + " k n g " d e n , " q n c p  
k p m ã d g " g f k n o k v k t 0 " n g o " u q p w p f c " o g o d t c p  
{ , m e p o , v , t 0 " D w " k n g o " d w | f q n c d , p f c " q t d k v c

I ¾ t ã p v ã n g o g " k ± k p " o g o d t c p . " c p v k m q t " d c  
C u j o c p " \* 3 ; : 8 + " v e t c h , p f c p " v c p , o n c p c p " C n m e r  
M Tris-HCl (pH 8,8), 1 M NaCl, 100 mM MgCl<sub>2</sub>, 100 mM ZnCl<sub>2</sub>, Dietanolamin,  
NBT (P k v t q d n w g v g v t c | q n { w o + . " R O H m ö , 4 k p o , 3 - | k p o g v  
k p f q k n h q u h c v + " k n g " k p m ã d g " g f k n o k v k t 0 " I ¾ t  
c n ã o k p { w o " h q n { q f c " u c m n c p o , v , t 0

Q n w c p " r t q v g k p " d e p v n c t , p , p " f g l p z e r k v q o g v  
{ c | , n , o , " k n g " d g n k t n g p o k v k t 0

### 3.2.6.6 u v c v k m u g n " C p c n k | n g t " " "

G n f g " g f k n g p " u q p w ± n c t = " j g t " d k t " x g t k " k ± k  
g f k n o k v k t 0 " H e t m n , " i t w r n c t " k ± k p f g " x g " c t c  
c p c n k | " g v o g m - t e s t f e k p f U v W g m p f ¾ p h ã " C p q x c " x g " r  
Mann-Y j k v p g { " W " v g u v n g t k " w { i w n c p o , v , t 0

## 4. BULGULAR

### 4.1 Sitotoksisite Analizi

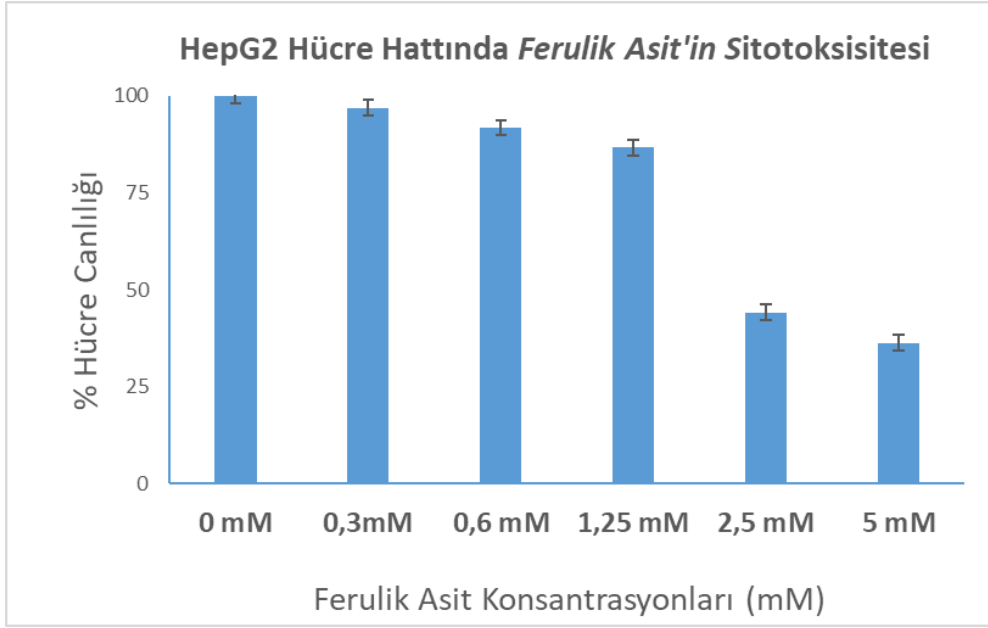
Hg p q n k m " c u k v n g t k p " J g r I 4 " j Ñ e t g n g t k p g " q n c p " u k J Ñ e t g n g t " ; 8 ø n<sup>3</sup>/kumucuk q n c m e c f m " 4 g m k n f g " g m k n o k v kafeik asit, ferulik asit ve o-m w o c t k m " c u k v k j p c " v J v g r " I k 4 " k j p Ñ e g t v g n k (EC<sub>50</sub>+ " d w n w p o w v w t " \* V c d n q " : + 0 " J w g t i " w d k b e h g p f i c elde edilen EC<sub>50</sub> f g g t k = " g v m g p " p o " c f Ñ e g p k p j w v i w p c p e J ' 7 2 b n k m " d k t " g v m k " x g { c " j Ñ e t g " j c v v , p , p " ' 7 2 x g { c " ¾ n Ñ o f Ñ t 0

**Tablo 8:** EC<sub>50</sub> F g g t n g t k

HepG2	
Fenolik Asit	EC <sub>50</sub> F g g t k
Kafeik Asit	1,02 mM
Ferulik Asit	3,1 mM
O-Kumarik Asit	5 Mm

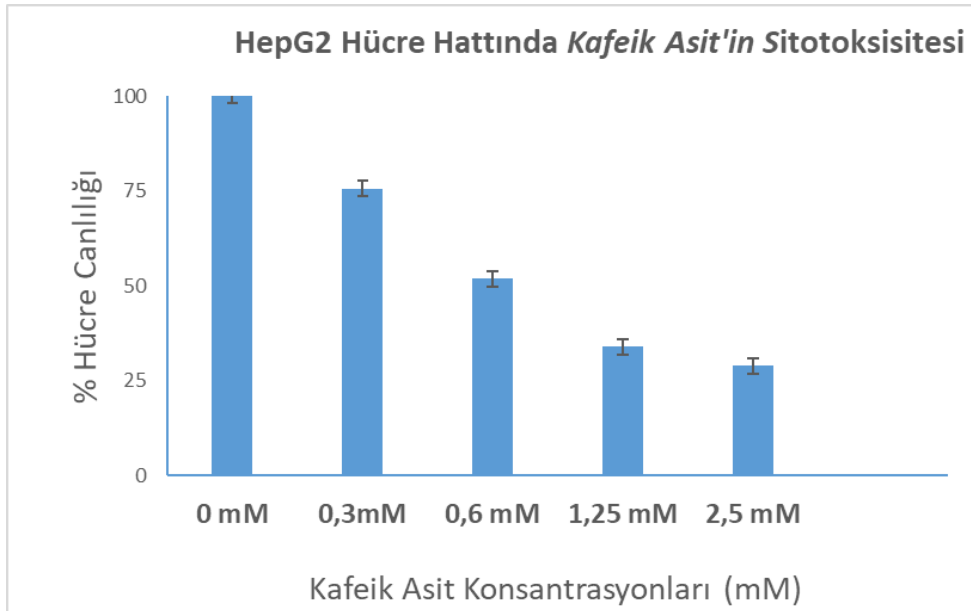
J k ± " h g p q n k m " o c f f g " k n g " o w c o g n g a s i t e v o g f k k n g " o w c o g n g " g v v k k o k | " i t w r n e t , " m e t , n c c u k v n g t k p " j Ñ e t g " e c p n , n , , p c " g v m k u k " u c r v c p

g m k n " 6 0 3 0 3 ø f g " i ¾ t Ñ n f Ñ Ñ " i k d k " { Ñ m u g m " i t w r n e t f c " j Ñ e t g " e c p n k n ; i t " w f Ñ c Ñ m p f f c q m k " " h j g Ñ e q t c p n e t , p c " i ¾ t g " f c j c " f Ñ Ñ m " d w n w p o w v w t 0 " h g t w n k m " c u k v " j Ñ e t g n Ñ o t g k p { " q ' n 7 " 2 c ø u o k , p k y o l a t k c x | g n " c d u w , u c r v c p o , v , t 0



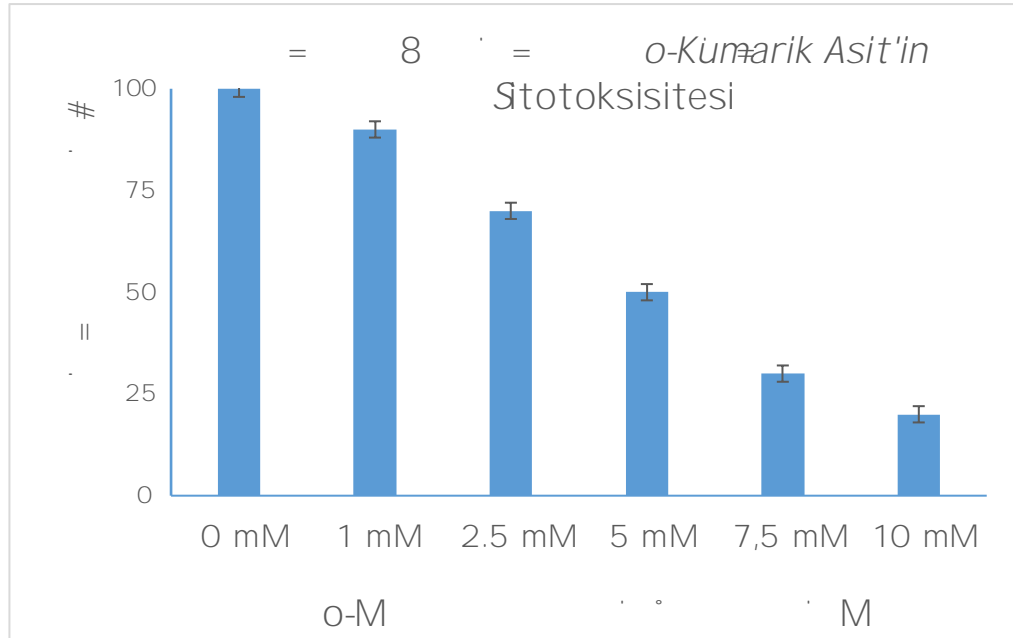
g m k n P 6 0 B 0 B m " m q p u c p v t c u { q p n e t f c m k \* " U M c p h w g + k n n e " t C u k n v k ø " k h p u k v q v q m u k u k v g " f g p g { k p k p . " v t M q r p n v k t n q g n " " 3 4 n g ± Ā g o t Ā n p g Ā p k " " q 3 t 2 v 2 c ' , < " M q p v t q n " i t w d w p f c p " h e t m n , " \* r > 2 0 2 7

Benzg t " g m k n f g " m ø f h g k w " 3 0 2 4 " d t k q ĩ Ā c m " d w e c p n , n , , p , " f q | c " d c n , " q n e t c m " c | c n f , , " u c



g m k n P 6 0 B 0 H m " m q p u c p v t c u { q p n e t f c m k \* " U M c p h w g + k n n e " t C u k n v k ø " k h p u k v q v q m u k u k v g " f g p g { k p k p n ö v t M q r p n v k t n q g n " " 3 4 n g ± Ā g o t Ā n p g Ā p k " " 3 2 2 ' , < " M q p v t q n " i t w d w p f c p " h e t m n , " \* r > 2 0 2 7

VÃ o " d w p n c t c -kumarik' asitim a t k v m v 'q m u k m " g v m k n g t k " q t v c { c " m q p w n 4.1.3). o-Mwto "c t k g n h k c n s o "klozu' 5k mM q la'ak G E j g u c r n c p o , v , t 0



g m k n P 6 0 3 0 5 n " m q p u c -Mwto c u k m p 6 u k f o m p " j Ã e t g v ± a c p n k m k h c t m n , " u k v q v q m u k u k v g " f g p g { k p k M q p w t q m h k g n g g 4 m g t Ã k o " A c n , p o , v , t 0 " , < " M q p v t q n " i t w d w p f c p " h c t m

## 4.2 Western Blot Analizi

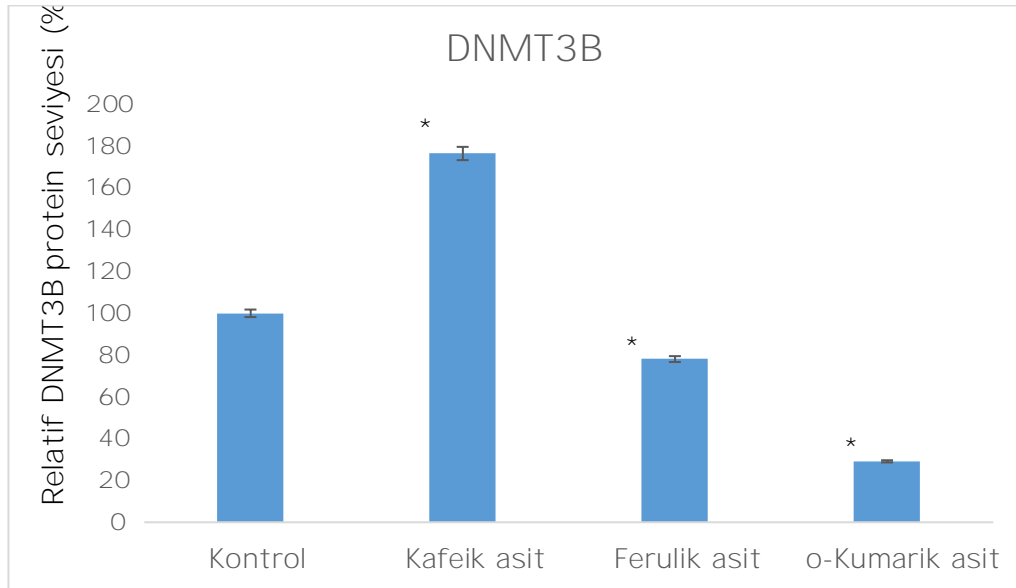
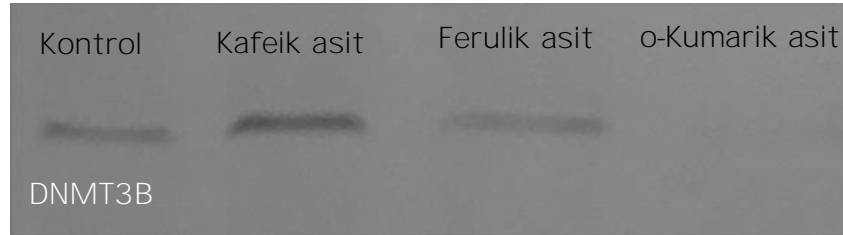
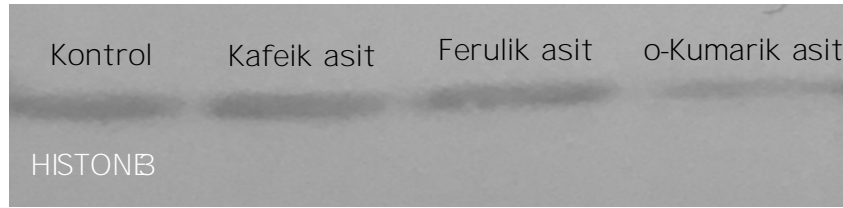
Fenolik asitlerden olan kafeik asit, ferulik asit ve o-kumarik asidin HepG2

j Ã e t g " j c v v , p c " w { i w n c p o c u , " u q p w e w " j Ã e t g f g " J F C E 5 . " J C V 3 " x g " V G V 3 " r t q v g k p " u g x k { g u k p f g m D n q v " c p c n k | k p f g " d w n w p c p " u q p w ± n c t " o T P C " g c p n c o n , ç f i n w r " m a b . D w p c " v d a , m , o , q n c t t c m " d w " r t q o T P C " g m u r t g u { q p " f Ã | g { n g t k p f g m D e l e y s o n u c o n , " f g q n w o w " r t q v g k p " d c p v n c t , p , p " { q w p n w m n c t , Scion Image Software r t q i t c o , " m w n n c p , n c t c m " d g n k t n g p o k

H g p q n k m " c u k v n g t k p " w { i w n c p f , , " J g r I 4 " j Ã u g x k { g u k p f g m k " d c p v n c t , p , p " f g p u k v q o g v t k m " c

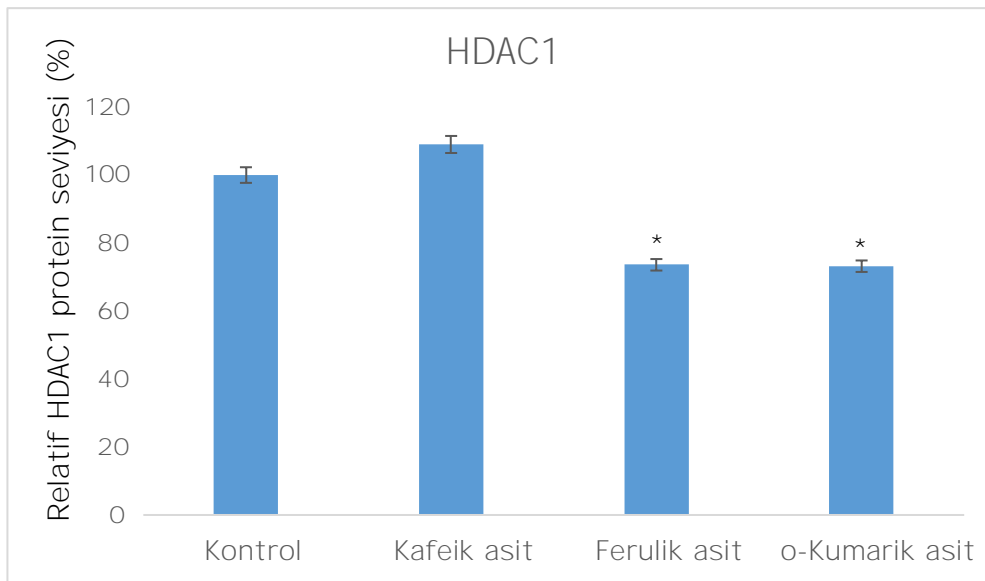
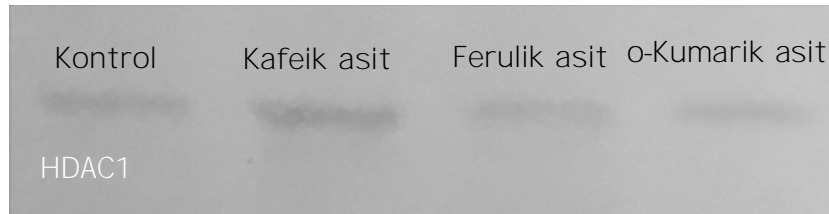
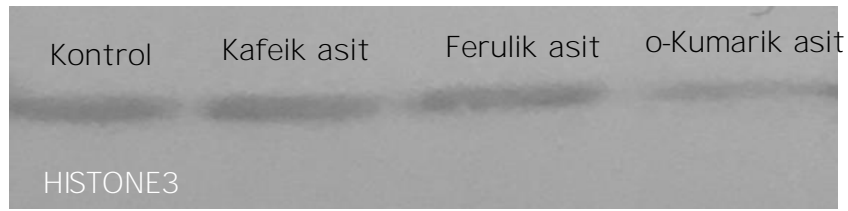


asit, ferulik asit ve o-kumarik c u k v " u%9 8 ğ a%21(9,nc%70,9 c | c n , " o g { f c }  
 i g n o k v k t " \* g m k n " 6 0 4 0 3 + 0



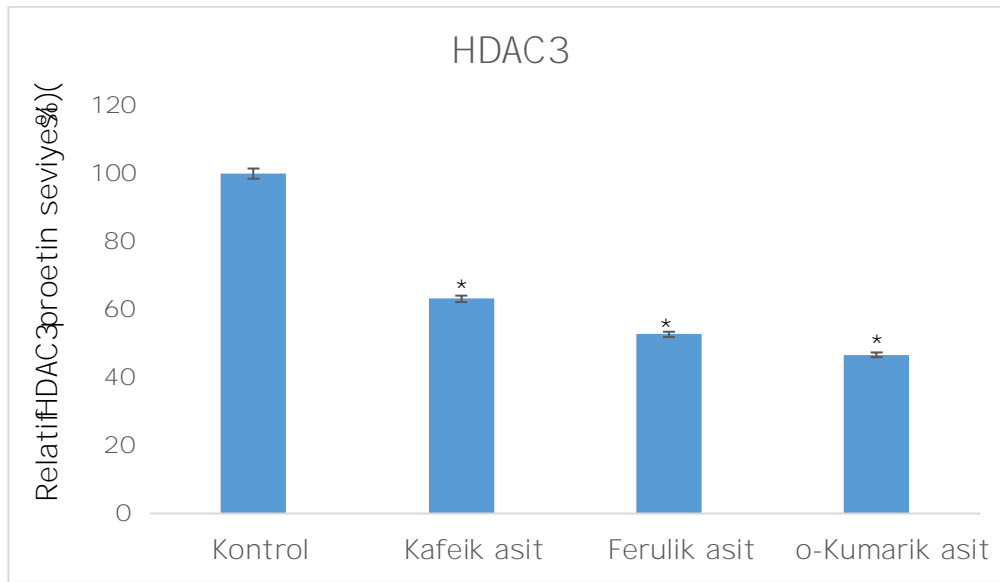
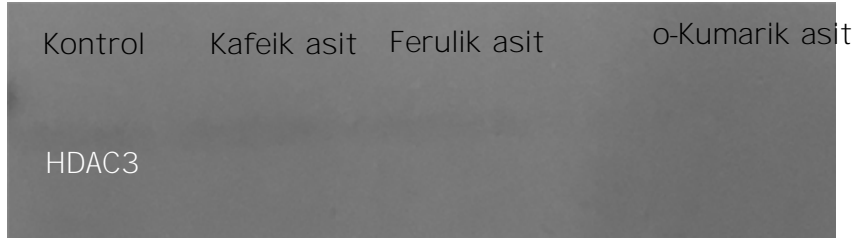
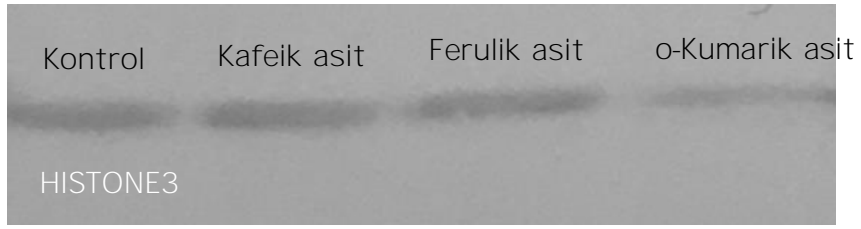
g m k n Kafeik asit, Ferulik asit ve o-Mwo c t k m" c u k v k p " k p u c p " m c t c e k g t  
 j c v v , p f c " F P O V 5 D " r t q v g t p w n g a k { E k t p g p g h s p K g g m k q k 0 c  
 d c p v n c t , p , p " { q w p n w m n c t , itonKetik analizLile belirlgpi α ke ov, k' tm0w"nMqppv,  
 f g g t n g t n k , " p ' . 0 3 , 2 " 2 M q t p v t q n " i ( p < 0 . 0 5 ) . w p f c p " h c t m n ,

Fenolik c u k v n g t k p " w { i w n c p f , , " J g r I 4 " j Ñ e t g "  
 u g x k { g u k p f g m k " d c p v n c t , p , p " f g p u k v q o g v t k m " c  
 asit, ferulik asit ve o-mwo c t k m" c %9 kv t " %26,4 ve " %26,8 { c n | c c " n , " o g { f c }  
 i g n o k v k t " \* g m k n " 6 0



g m k n K a f e i k a s i t F e r u l i k a s i t v e o - K u m a r i k a s i t i n k u l l u m u n d e k i n e t i m e n t e k g t " m e p u g t k " j c v v , p f e " J F C E 3 " r t q v U k p w e g x k { g k k p g p g h 5 p k g g h p u k 0 c n d c p v n e t , p , p " { q w p n w m n e t , " K o c i g L " r t g p i a k e o v , k ' t n 0 w " n M c p p v , f g g t n g t n k , " p ' 0 3 , K o a v t t n " i t w d w p f c p " h e t m n , " \* r > 2 0

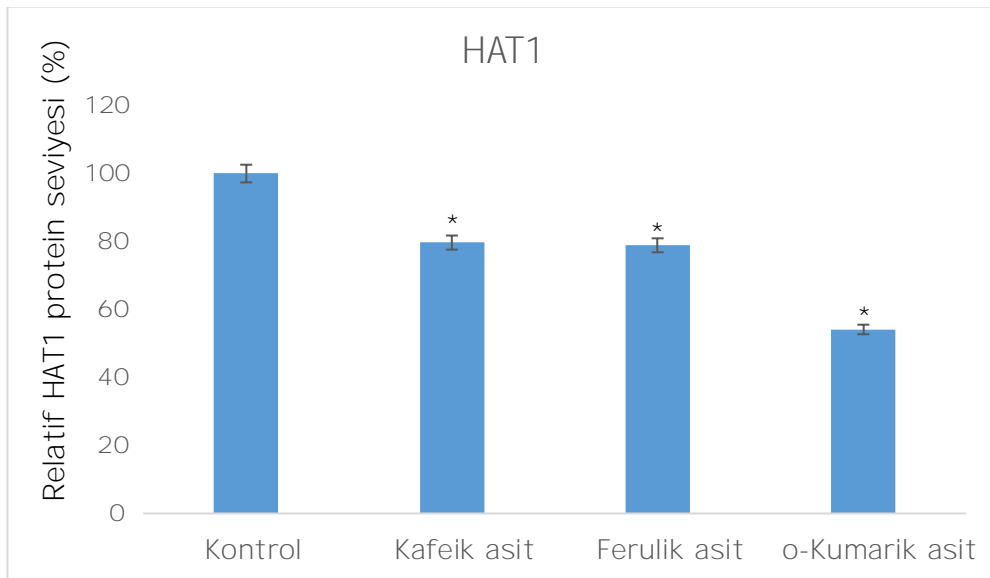
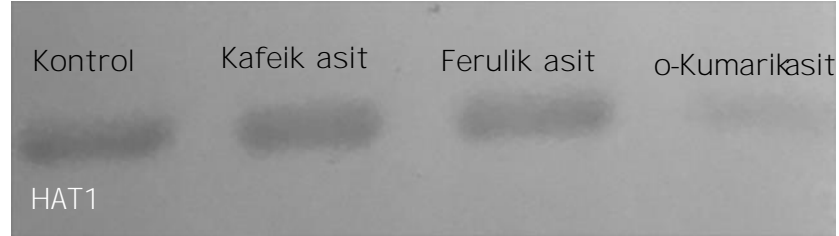
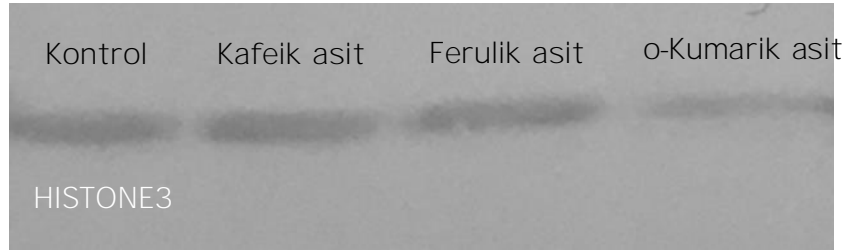
H g p q n k m " c u k v n g t k p " w { i w n c p f , , " J g r I 4 " j u g x k { g u k p f g m k " d c p v n e t , p , p " f g p u k v q o g v t k m " c a s i t , f e r u l i k a s i t v e o - k u m a r i k c u k v " u % 3 6 , 8 c % 4 7 , 3 v e n % 5 3 , 3 c | c n , " o g { f c p i g n o k v k t " \* g m k n " 6 0 4 0 5 + 0



**g n 4.2.3.** Kafeik asit, Ferulik asit ve o-Mwo c t k m " c u k v k p " k p u c p " m c t c e k g t j c v v , p f c " J F C E 5 " r t q v u k p w e g x k { g k k p g p g n 5 p k g g m p u k 0 c n d c p v n c t , p , p " { q w p n w m n c t , " K o i k a n a l i z i l e b e l i t g p i t k e o v , k ' t n 0 w ' n M q p p v , t f g g t n g t n k , " p ' . 0 3 , 2 " 2 M q t p v t q n " i t w d w p f c p " h c t m n , " \* r

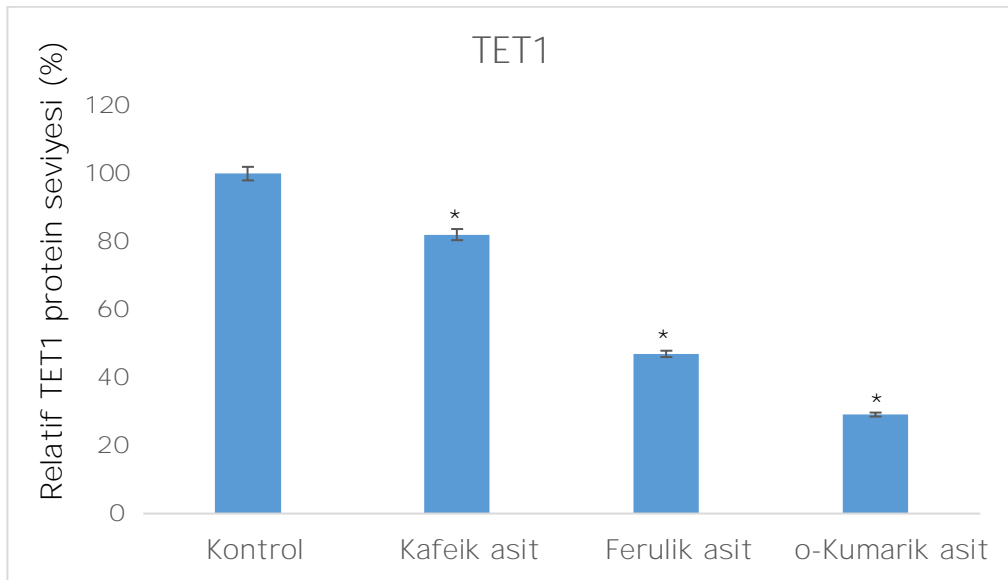
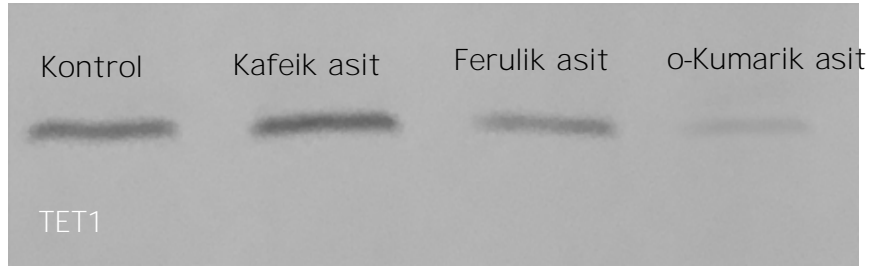
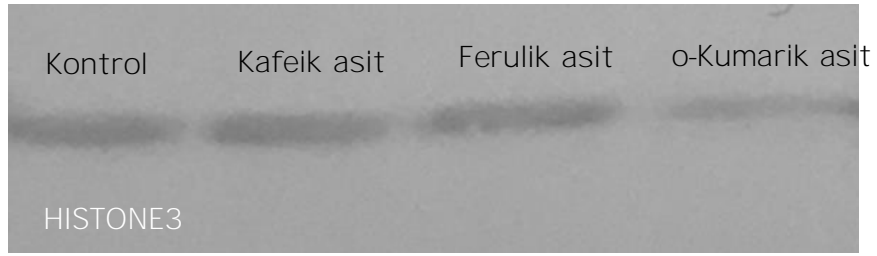
H g p q n k m " c u k v n g r t I k 4 p " j w A e i t w g n " c j p d v v , p r t e n c g " q n w u g x k { g u k p f g m k " d c a n a l i z i s o n u c u p d a p r o t e i n s e v i y e s i n d e k a f e i k v t k m a s i t , f e r u l i k a s i t v e o - m w o c t k m " c u k v k p " k p u c p " m c t c e k g t j c v v , p f c " J F C E 5 " r t q v u k p w e g x k { g k k p g p g n 5 p k g g m p u k 0 c n d c p v n c t , p , p " { q w p n w m n c t , " K o i k a n a l i z i l e b e l i t g p i t k e o v , k ' t n 0 w ' n M q p p v , t f g g t n g t n k , " p ' . 0 3 , 2 " 2 M q t p v t q n " i t w d w p f c p " h c t m n , " \* r

i g n o k v k t " \* g m k n " 6 0 4 0 6 + 0 "



**Şekil 4.10** Kafeik asit, ferulik asit ve o-kumarik asitin kullandığımız hücre kültürüne etkilerinin HAT1 protein seviyesine etkilerinin araştırılması amacıyla yapılan deneylerin sonuçları. Kontrol grubundaki hücrelerin HAT1 protein seviyesi %100 olarak belirlenmiştir. Kafeik asit (%100), ferulik asit (%79) ve o-kumarik asit (%54) kullanılarak hücre kültürüne eklenen hücrelerin HAT1 protein seviyesinde anlamlı düşüşler gözlemlenmiştir. \* p < 0,05.

Hücre kültürüne eklenen hücrelerin HAT1 protein seviyesinde anlamlı düşüşler gözlemlenmiştir. Kafeik asit, ferulik asit ve o-kumarik asit kullanılarak hücre kültürüne eklenen hücrelerin HAT1 protein seviyesinde anlamlı düşüşler gözlemlenmiştir. \* p < 0,05.



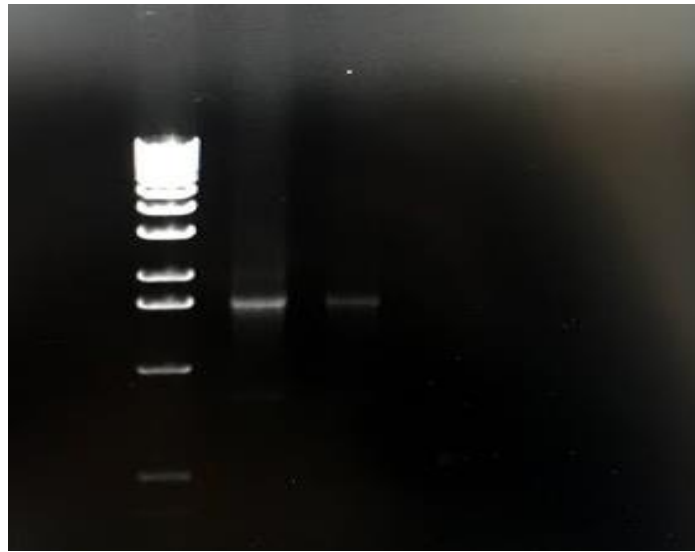
**Şekil 4.10** Kafeik asit, Ferulik asit ve o-Kumarik asit ile tedavi edilen hücrelerin DNMT3A ve DNMT3B proteinlerinin western blot analizinde gösterildiği gibi, Kafeik asit, Ferulik asit ve o-Kumarik asit ile tedavi edilen hücrelerde DNMT3A ve DNMT3B protein seviyeleri kontrol hücrelere göre anlamlı olarak düşmüştür. (\* p < 0,05)

Farklı tedavi gruplarındaki hücrelerin DNMT3A ve DNMT3B proteinlerinin western blot analizinde gösterildiği gibi, Kafeik asit, Ferulik asit ve o-Kumarik asit ile tedavi edilen hücrelerde DNMT3A ve DNMT3B protein seviyeleri kontrol hücrelere göre anlamlı olarak düşmüştür. (\* p < 0,05)

**4.3 mRPC " F | g { k p f g " G m u r t g u { q p n c t , p , p " V  
 \ c o c p n , " R q n k o g t c | " \ k p e k t " T g c m u k { q p w**

**4.3.1 V q v c n " T P C " | q n c u { q p w**

Fenolik asitlerle (kafeik asit, ferulik asit ve o-m w o c t k m " c u k v + " o w c o g  
 q n c p " J g r I 4 " j Å e t g " j c v v , p f c p " v q d e n e d i l e n " T P C " k  
 T P C ø n c t " ' 3 ø n k m " c i c t q | " l g n " k n g " i ¾ t Å p v Å n g p o



**g m k n " M o l 5 0 1 3 0 " 3 < u k v " w { i w n c p c p " J g r I 4 " j Å e t g u k p f g p " g  
 elektroforezi. U q n f c p " u c c " J c v " 3 < " I g p g T: K o n t r o l ( % 1 0 0 " D M S O ); " F P C " O c t  
 Hat 3: Kafeik asit**



g m k n "16 9 t 5 0 n 3 1 0 n 4" < c u k v " w { i w n c p c p " J g r I 4 " j Ñ e t g u k p f g p " elektroforezi. U q n f c p " u c c " J c M p DNA Marker Hat 2: Kontrol (%100 DMSO); Hat 3: Ferulik asit



g m k n "6 0 v 5 0 c 3 t 0 k 5 n < " c u k v " w { i w n c p c p " J g r I 4 " j Ñ e t g u k p f g p " elektroforezi. U q n f c p " u c c " J c v " 3 < " I g p g T w n g t V 0 0 DMSO;" F P C " O c t Hat 3: o-Kumarik asit

### 4.3.2 mRNA Ekspresyon Analizleri

e F P C " u g p v g | k . " Ñ t g v k e k " h k t o c p , p " v c n k o g v k n c u { q p w . " f g c u g v k n g c u { q p w " x g " j k u v q p " m w n n c p c t c m " M k n q I t g g p " 4 Z " s R \ T " O 3 4 p u g y t g f t k " Q k ' z

venkocvncctc " i ¾t g " oTPC " f Ñ| g { k p f g " g m u r t  
J q w u g m g g r k p i " i g p " q n c t c m " I C R F J " m w n n c p , n o  
u g x k { g n g t k " E v " o g v q v w p c " i ¾t g " p q t o c n k | g " g

Eø g v q f w " x g t k o n k n k m " f Ñ| g n v o g u k " q n o c f  
| c o c p n , " R E T " f ¾p i Ñ u Ñ " u , t c u , p f c " j g f g h " F P C ø p  
{ ¾p v g o f k t " \* R h c h h n . " 4 2 2 6 + 0

J g r I 4 " j Ñ e t g " j c v v , p c " h g p q n k m " c u k v n g t  
u g x k { g u k p f g t m " k " k f l g p . k " k f d r c " o g v k n c u { q p " o g m c p  
DNMT1, DNMT3A, DNMT3B, TET1, HAT1, HDAC1 ve HDAC3 genlerinin

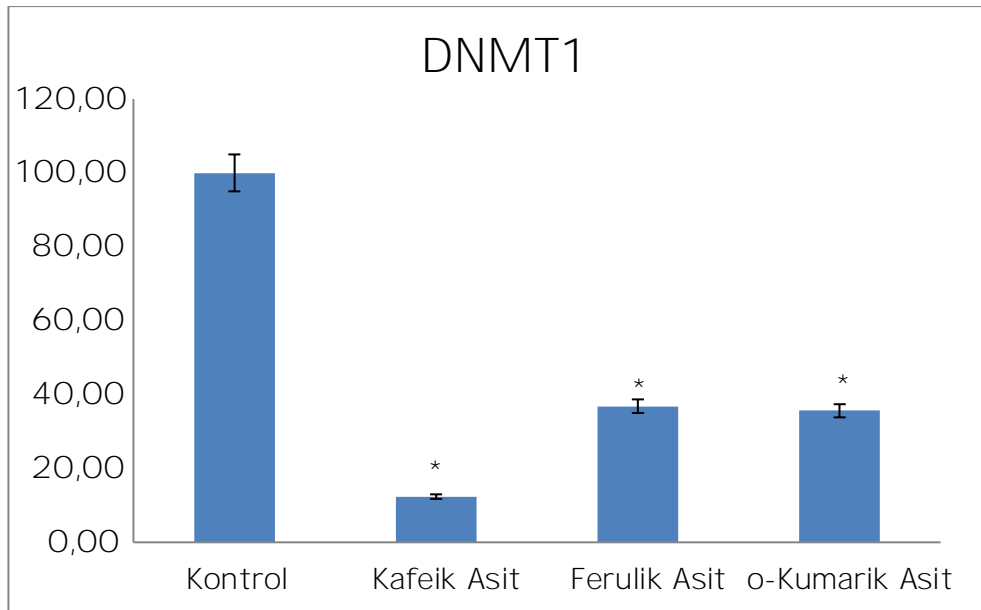
o T P C " u g x k { g n g t k p f g m k " f g Ñ e t g " h j g t v d , g p f k t " h g p k  
EC<sub>50</sub> dozunun uygulano c u , " u q p w e w p f c " F P O V 3 . " F P O V 5 C . "  
HAT1, HDAC1 ve HDAC3 genlerinin o T P C " u g x k { g n g t 69.7%, u , t c u ,  
%99.3, %98.6, %81, %96.4 ve %87.8 c | c n , " i ¾| n g p o k v k t 0 " D g p |

DNMT3A, DNMT3B, TET1, HAT1, HDAC1 ve HDAC3 genlerinin mRNA  
u g x k { g u k p f g " h g t w n k m d a " u c , u t k c % 6 4 , % 4 9 , % 8 4 , % 9 5 ,  
%36.7, %89.4 ve %69.1 c | c n , " u c r v t c " p o g m k u m f r i g a s i t D e f 5 0 | g

f q | w p w p " J g r I 4 " j Ñ e t g n g t k p g " w { i w n c p o c u , "  
F P O V 5 D . " V G V 3 . " J C V 3 . " J F C E 3 " x g " J F C E 3 , " o T P C "  
%48.6, %91.2, %76.1, %36.9, %97.2 ve %80.8 c | c n o c " i ¾| n g o n g p o k v k t 0

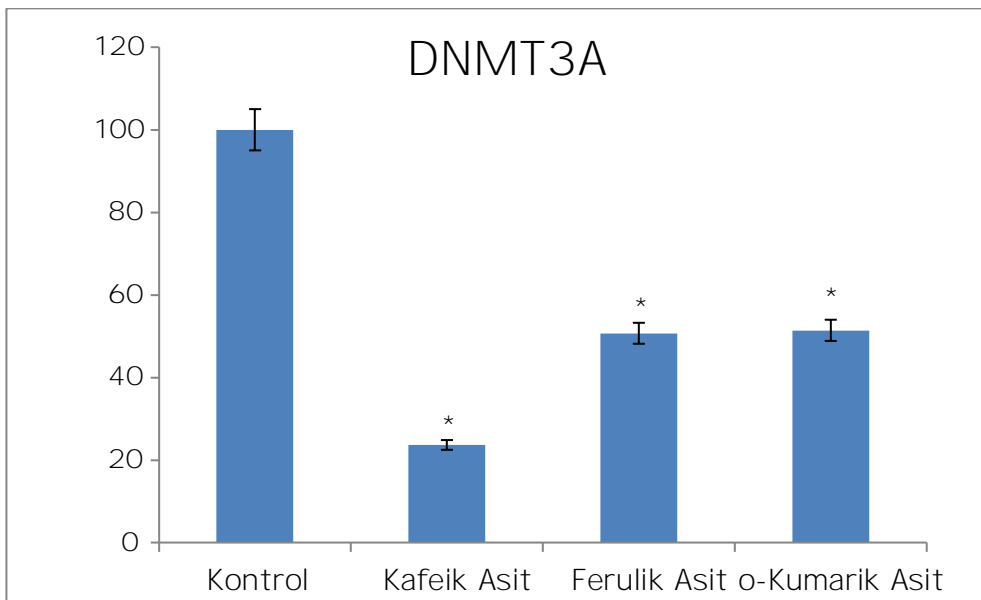
F P C " o g v k n c u { q p w p f c " i ¾t g x " c n c p y ö n F P O V 3 "  
f Ñ| g { k p f g " h g p q n k m " c u k v n g t - f i w g p c " t n k c n h " g d k u m k " v c " u k , y  
%87.6, %64 ve %64.4 c | c n , " o g { f c g p n k " n i " g 6 n 0 o 5 k 0 4 v 0 k 3 t + " 0 \* " "





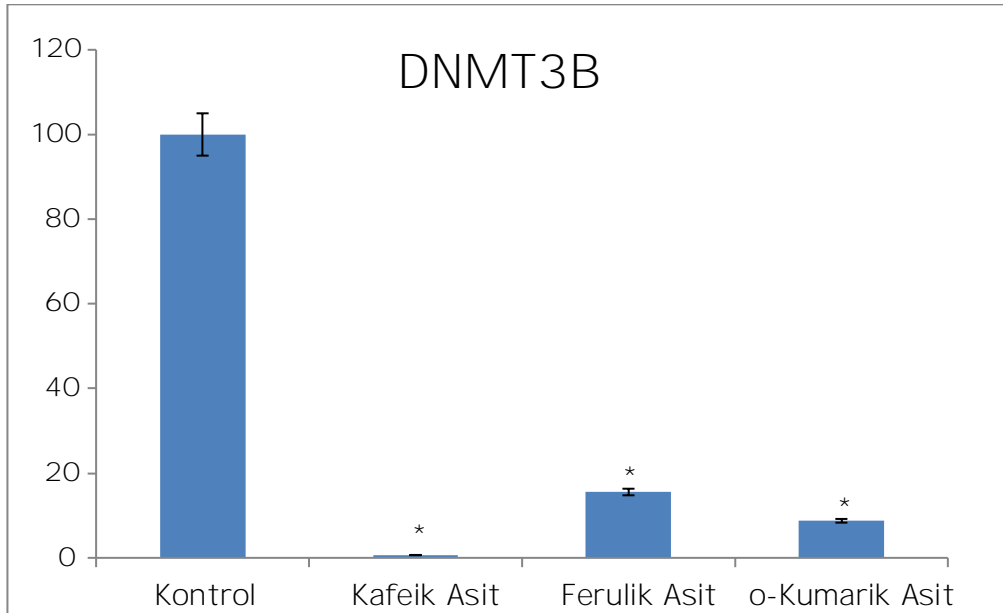
g m k n " K a f e i k a s i t v e o - M w o c t k n k " p e u c k p v " o n k e p t c e k g t " m e p u g t k " j c v v , p f c " F P O V 3 " o T P C " U u q p w k ± n g t k " p l g " R f n k k a g v " p k t 0 c M d p g t f g g t n g t n k , " p ' o 3 , 2 2 v , t 0 " , < " M q p v t q n " i t w d w p f c p " h

DNA o g v k n c u { q p w p f c " i 3 / 4 g e n i m " m R N A e x p r e s y o n u n d e r F P O V 5 C f Ñ | g { k p f g " h g p q n k m " c u k v n g t - i n w o p c " t n k m h " g d u n k ' v c " u k , y ' 9 8 0 6 . " ' 6 ; 0 5 " x g " ' 6 : 0 8 " c | c n , " o g { f c p c " i g n o



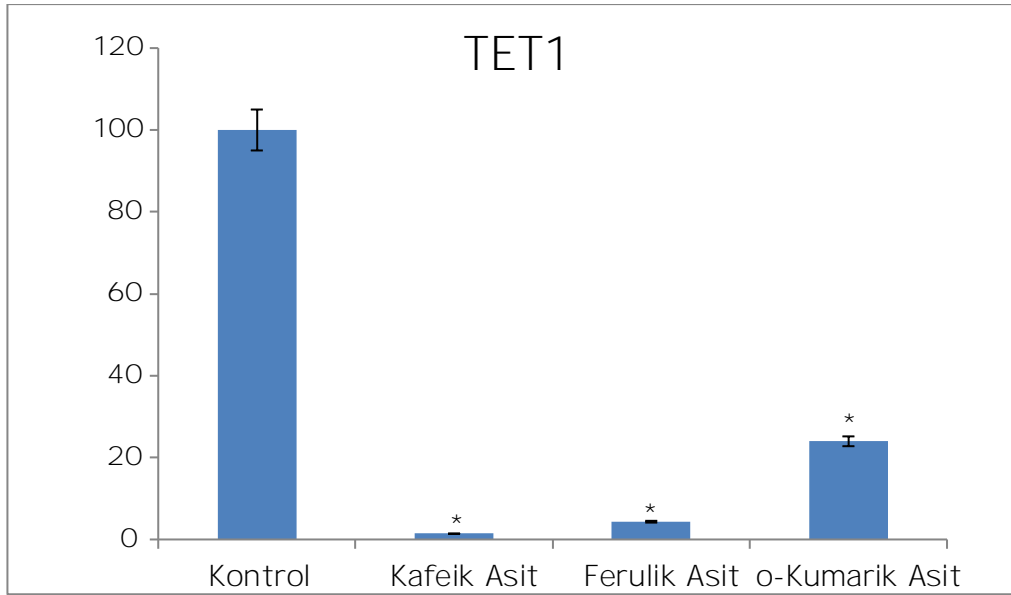
g m k n " K a f e i k a s i t v e o - M w o c t k m " c u k v ø k p " k p u c p " m c t c e k g j c n d a DNMT3A mRNA seviyesine olan etkisi. U q p w ± n c t " I C R F J R k a g " p k t 0 c M d p g f g g t n g t n k , " p ' o 3 , 2 2 v , t 0 " , < " M q p v t q n " i t w d w p f c p " h

DNA ogvkn cu { qpwpfc " i 3/4genin mRNA ekspresyonu FPOV5 D f ã | g { kpfg " hgpqn kasit, ferulik kasit ve o-ri wpc " t ncmh " g d k u n k v " u , %99.3, %84.5 x g " ' ; 3 0 4 " c | c n , " o g { f c p c " i g n o k v k t " \*



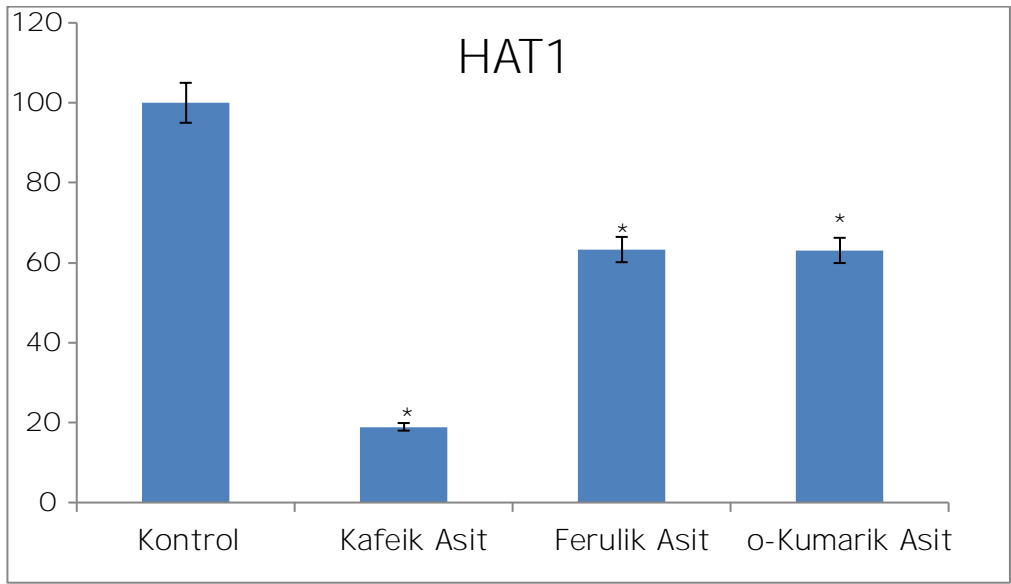
g m k n " 6 0 5 0 4 0 k a f e i k a s i t v e o - M w o c t k m " c u k v ø k p " k p u c p " m c t c e k g j c v v , p f c " F P O V 5 D " o T P C U q g w k n g u k p C R h ç p n g v m t o c n k | g f g g % 3 2 2 " k c " n , p o , v , t 0 " , < " M q p v t q n " i t w d w p f c p

DNA ogvkn cu { qpwpfc " i 3/4genin mRNA ekspresyonu FPOV5 D f ã | g { kpfg " hgpqn kasit, ferulik kasit ve o-ri wpc " t ncmh " g d k u n k v " u , %99.3, %84.5 x g " ' ; 3 0 4 " c | c n , " o g { f c p c " i g n o k v k t " \* g m k n " 6 0 5 0 4 0



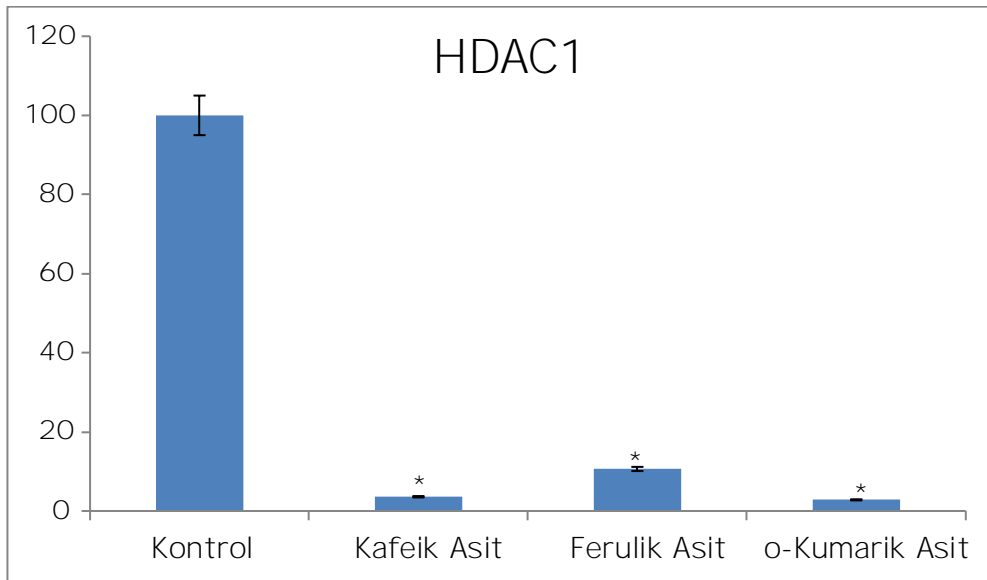
g m k n " K a f e i k a s i t v e o - M w o c t k m " c u k v ø k p " k p u c p " m e t c e k g j c v v , p f c " V G V 3 " o T P C " U u q p x w k ± ( n g u t k " p l g C " R q F n d k " o g v " n p k u t 1 0 0 " M q p g t f g g t n g t n k , " p ' o 3 , 2 2 v , t 0 " , < " M q p v t q n " i t w d w p f c p " h

DNA o g v k n c u { q p w p f c " i g a n i n x m " R N A e k s p r e s y o n C V 3 f Ñ | g { k p f g " h g p q n k m " c u k v n g t - i n w o p c " t n k m h " g d k u m k ' v c " u k , y % 8 1 . 1 , % 3 6 . 7 v e % 3 6 . 9 c | c n g , { f " c o p c " i g n o k 5 ) . v k t " \* g m k n " 6 0 5



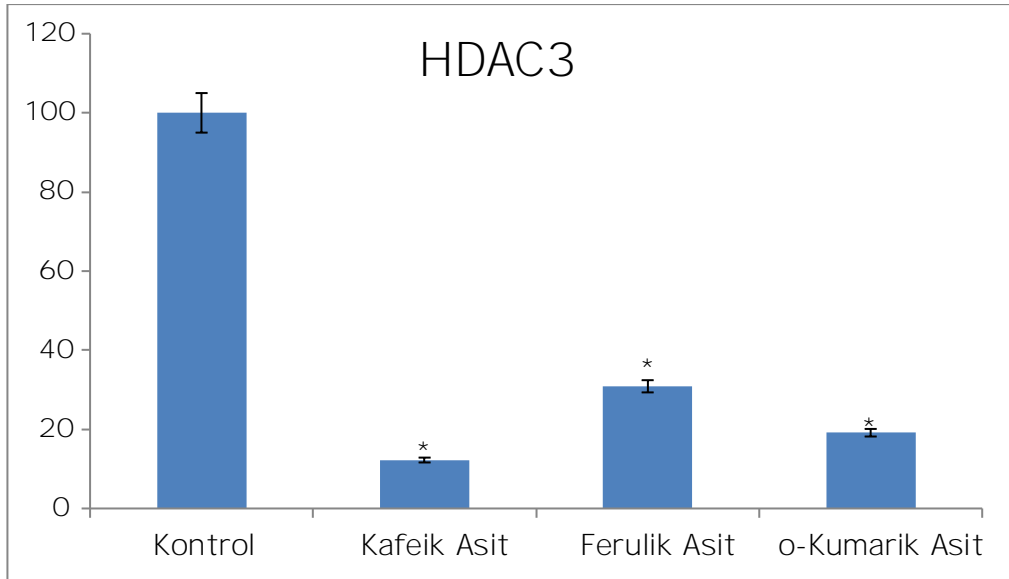
g m k n " K a f e i k a s i t v e o - M w o c t k m " c u k v ø k p " k p u c p " m e t c e k g j c v v , p f c " J C V 3 " o T P C " U u q p x w k ± ( n g u t k " p l g C " R q F n d k " o g v " n p k u t 1 0 0 " M q p g t f g g t n g t n k , " p ' o 3 , 2 2 M q p t " q n " i t w d w p f c p " h c t m n , " \* r

DNA o g v k n c u { q p w p f c " i 3/4 genigim mRNA ekspresybnF CE 3  
 f ã | g { k p f g " h g p q n k m" c u k v n g t-fn w p c" t nkcm" g dk unk' vc" u uk, v  
 ' ; 8 0 6 . " " ' : ; 0 6 " x g " ' ; 9 0 4 " c | c n , " u c r v c p o , v ,



g m k n " 6 0 5 0 4 0 8 k a s i t v e o - M w o c t k m " c u k v ø k p " k p u c p " m c t c e k g  
 j c v v , p f c " J F C E 3 " o T P C U q p w k h g u k p g R f i k p u g v m k u 0 0 M d p g t  
 f g g t n g t n k , " p ' o 3 , 2 2 v , t 0 " , < " M q p v t q n " i t w d w p f c p " h

DNA o g v k n c u { q p w p f c " i 3/4 genigim mRNA ekspresybnF CE 5  
 f ã | g { k p f g " h g p q n k m" c u k v n g t-fn w p c" t nkcm" g dk unk' vc" u uk, v  
 ' : 9 0 : . " " ' 8 ; 0 3 " x g " ' : 2 0 : " c | c n , " u c r v c p o , v ,



g m k n "Kafelik Asit, Ferulik Asit ve o-Kumarik Asit" c u k v ø k p " k p u c p " m c t c e k g j c v v , p f c " J F C E 5 " o T P C " U u g w k h g u k p C R F i k h g v m k u B C M d p g t f g g t n g t n k , p ' o 3 , 2 2 v , t 0 " , < " M q p v t q n " i t w d w p f c p " h

Elde edilen veriler sonucunda fenolik asitlerin DNA metilasyonu o g m c p k | o c u , " k n g " k n i k n k " i g p n g t k p " g m u r t g u t j Ñ e t g n g t k p " ¾ n o g u k p g " p g h g p ' v q a u , d p a ' g x g m ' d o w g j Ñ e t g n g t k p g ' ¾ n o g u k p g " p g h g p ' v q a u , d p a ' g x g m ' d o w g

#### 4.4 DNMT Enzim Aktivitesinin Belirlenmesi

4 6 " u c c v n k m " w { i w n c o c " u q p w e w p f c " J g r I 4 " j g p | k o " c m v k x k v g u k " f g g t n g p f k t k n f k k p f g " d Ñ m , { c u n c p f , , p f c " i ¾ | n a g a m h g p g p ö h ç t h w k w p o w k u v P q | k v k h " m q p v t q n " n k | c v , p f , c k d p v m v d k k " k v g | " ç v , 5 p f " c 0,407 pmol/min/mg protein, m c h g k m " c u k v " n k | c v , p f c " d w " f g ferulk m " c u k v " 0,248 pmol/min/mg ve o-kumarik asit n k | c v , p f c " 2 . pmol/min/mg proteindir.



















































