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Review Article

An In-Depth Review of Flavonoid Profile in Cotton (*Gossypium hirsutum* L.)

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ABSTRACT

Being economically important for natural fiber, seed cotton and protein, cotton demand is increasing rapidly. With the ever-growing population, there is an ultimate need to increase the cotton production to meet this demand of man and livestock. Different Flavonoids, which are compounds that have antioxidant properties, serve an essential role in sustaining plant function and health. Flavonoids operate largely as photo protectors and phytoalexins, influencing the phytohormone auxin transport that affects the plant structure. Cotton production is also linked to the flavonoids as they play a great role in plant protection and vigor. Flavonoids play a critical role in response to abiotic stress. Leaf reddening in cotton and fungal infection resistance is attributed the flavonoids. Flavonoids also take part in the development of fiber and its color, maintenance of plant health and it's defensive mechanism. With an increasing interest in the biological functions of flavonoids as well as advancements in isolation and classification techniques over the last two decades, the numerous flavonoids known in the cotton plant have risen dramatically. The capacity to regulate flavonoid expression in plants offers a chance to change defense mechanisms and growth. Genetic engineering techniques offer different methods that improves certain characteristics of cotton to further boost its output. This study aims to summarize existing findings on the prevalence and dispersal of flavonoids in cotton as well as to examine the historical research on flavonoids in cotton as well as potential paths for future research on this plant species. This review enlists the flavonoid profile studied by many scientists in the past and their distribution in cotton plant which consist of 52 flavonoids divided into 7 groups.

Keywords: *Cotton, Flavonoids, Genetic engineering, Phytoalexins.*

INTRODUCTION

Gossypium hirsutum L. belongs to Malvaceae is economically important for natural plant fiber, cultivated in over 80 countries (Ahmad & Hasanuzzaman, 2020). 87% of the cotton-growing region of the globe exist in the developing countries.

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Other than fiber, the seed of cotton provides an additional revenue and protein source for animal and human diet (Ahmad & Hasanuzzaman, 2020; & Kouakou et al., 2007). Approximately 97 percent of the total world cotton output comes from *G. hirsutum*, while the rest of it comes from *G. herbaceum*, *G. barbadense*, *G. arboreum* and *G. barbadense (*Ahmad & Hasanuzzaman, 2020). Since the 1950s the total area of cotton is 30 to 36 million hectares. Global output of cotton has grown 400 percent from 6.6 Mt in 1950-51 to 26.8 Mt in 2012-13 (Ahmad & Hasanuzzaman, 2020).

Flavonoids have the utmost significant importance as secondary plant metabolites. When used in vacuoles as waste products, flavonoids perform a significant role in different organs helping in health perseverance and operation of plants (Mata, 2007). Flavonoids operate largely as photo protectors and phytoalexins and influence the phytohormone auxin transport which affects the plant structure (Peer & Murphy, 2007). They display a spectrum of biological actions including antioxidants and antifungals (Aoki et al., 2000). In chemotaxonomy, flavonoid profiles were also utilized to determine phylogenetic connections among species of plants (Almaraz-Abarca et al., 2006).

Early flavonoid studies in Gossypium hirsutum focused on floral flavonoids. Development and innovations to maximize the output of cotton include studies on the involvement of flavonoids in the protection of plants and the production of fiber (Tan et al., 2013). More recently, the attention has moved to flavonoids, which are compounds that have antioxidant properties. They are responsible for particular biological actions. Flavonoids play a functional role in response to plant stress and they are also one of the casual factors of leaf reddening (Nix et al., 2017). Flavonoids include chemicals, found in dried flowers (recognized as Flos gossypii) that have been utilized in TCM (traditional Chinese medicine) (Wu et al., 2008) and they also take part in the development of fiber and its colour (Tan et al., 2013; & Feng et al., 2013).

This study aims to summarize existing findings on the occurrence and distribution of flavonoids in cotton as well as to examine the historical research on flavonoids in cotton along with the potential routes for future research on this plant species. An earlier analysis of the flavonoids in the Malvaceae family discovered 23 flavonoids in the species of *Gossypium hirsutum* (Ismailov et al., 1994). With a growing interest in the biological functions of flavonoids, as well as advancements in isolation and classification techniques over the last two decades, the numerous flavonoids known in the cotton plant have risen dramatically. This review enlists the flavonoid profile studied by many scientists in the past and their distribution in cotton plant which consist of 52 flavonoids divided into 7 groups.

Flavonoid General Structure and Biosynthesis:

When it comes to flavonoids, the most prevalent structure is a 2-phenylbenzopyranone, where the three-carbon linkage among the phenyl groups is mostly cyclized with O_2 (Corradini et al., 2011). (Figure 1). The degree of oxidation and unsaturation in a three-carbon segment separates the main flavonoid classes based on a flavone skeleton C6-C3-C6 (Figure 1).

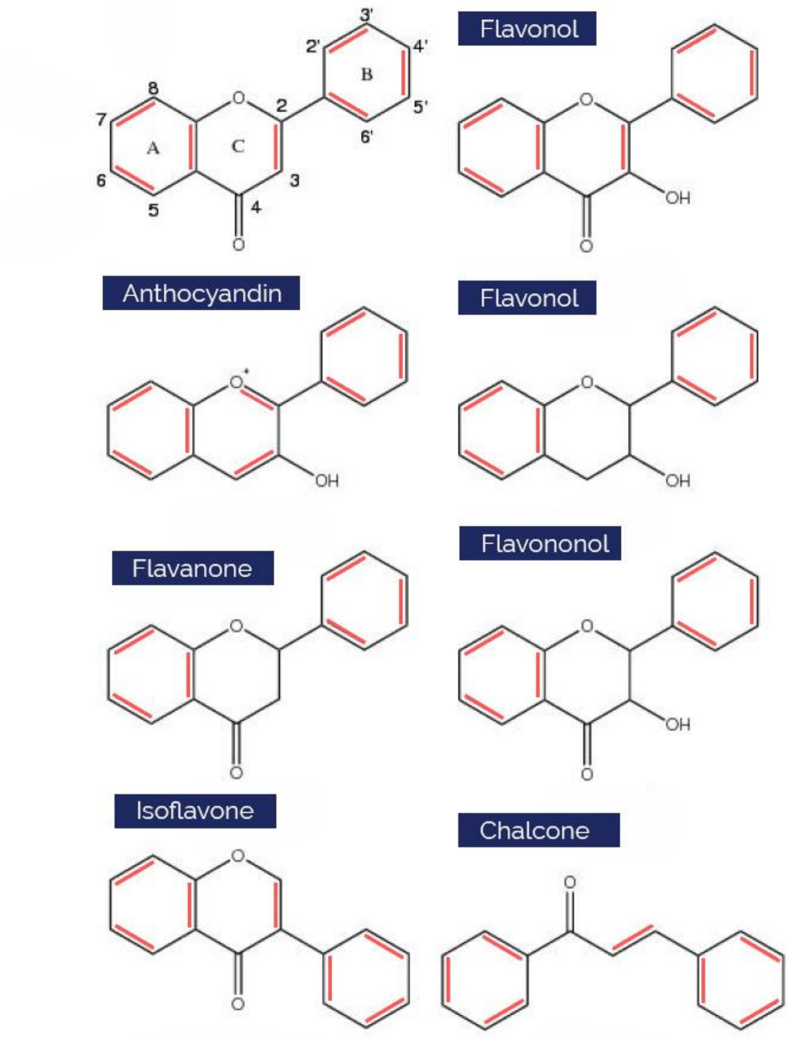


Figure 1: Simplified numbering and structure of flavonoid compounds depending on the flavone framework from the top left and the simplistic structure of flavonoid categories

Flavonoids consist of flavanols, isoflavones, anthocyanidins, flavones, flavanones, chalcone, flavanols, and aurones which have various types with their derivatives in different classes. A high number of Glycosidic conjugates exist in plant tissues (Harborne, 2013). The combination makes it possible to preserve flavonoids in the cell vacuole which makes the flavonoid lower responsive that leads to much more water solubility ultimately minimizing the cytoplasmic injury and enhancing polarity (Corradini et al., 2011).

Flavonoid biosynthesis occurs in the endoplasmic reticulum by the phenylpropanoid metabolic route in plants (Brunetti et al., 2013; Taylor & Grotewold, 2005). In successive enzymic reactions involving chalcone synthesis, chalcone essential for flavonoid biosynthesis is produced from malonyl-CoA and 4-coumaroyl-CoA. Further enzyme changes are needed along with the metabolic pathway to create the other types of flavonoids with the chalcone's linked ring closure that form the characteristic 3-ringed flavonoid structure. With a complete overview of the flavonoid-forming enzymes and genes in the biosynthetic route identification in different plant species, genetic alternation of the biosynthetic pathway has been utilized to achieve desired features such as increasing plant-defense synthesis of flavonoids and floral colour (Davies & Schwinn, 2006).

Manipulation of flavonoid expression can impact the development and growth of plants directly as well as indirectly by modifying the transport of auxins (Brown et al., 2001). Flavonoids are also an inhibitors of auxin transport, especially flavonols and isoflavones. These influence the apical dominance, plant height, root development, and inflorescence count (Brown et al., 2001; & Peer et al., 2004). The capacity to regulate flavonoid expression in plants offers a chance to change defense mechanisms and growth. These techniques offer novel methods that improves certain characteristics of cotton to further boost its output.

Different studies on the function of flavonoids in diverse plants has centered on the defense activities and it's interactions with other species such as pathogens, herbivores and other microbes which are helpful against abiotic stress. Previous research of cotton *G. hirsutum* was mostly concerned with the floral flavonoids, including efforts to find pigments (Hedin et al., 1967) and to establish the phylogenetic connections within *Gossypium* (Parks, 1965a; & Parks, 1965b). The recent study focused on the biological activity of flavonoids, a function of flavonoids in the development of cotton, and tolerance to biotic and abiotic stresses have been done (Nix et al., 2017; & Edwards et al., 2008). Research in this area pursue to discover potential ways to increase fiber output and decrease lepidopteran and wildlife disease losses.

Flavonoids Play a Protective role:

Cotton uses flavonoids as part of an herbicide defense mechanism to boost the synthesis of poisonous flavonoids that hinder lepidopteran larval development (Hanny, 1980). Phenolic chemicals have a vital function in protecting cotton plants against herbivores (Chan et al., 1978). Proanthocyanidins (condensed tannins) and flavonoids have been reported to hinder the development of the larval tobacco budworm (Chan et al., 1978; & Shaver & Lukefahr, 1969). Chrysanthemine (cyanidine 3-glucoside) is an anthocyanin that is a feeding inhibitive to *Helicoverpa Zea* and has reduced its larval development by half over the course of 5 days feeding (Harborne, 2001). The level of chrysanthemine was found to be adversely associated with the larval sizes in tobacco budworm larvae with an assimilation of 0.07 percent of food at an effective median dosage (ED50) (Hedin et al., 1983). Quercetin-3-glucoside (Isoquercitrin) was toxic to 1-day old larvae and 0.06% of the larval diet was equally effective in reducing larval development of 5 days old larvae (Hedin et al., 1988). The larval toxicity in G. hirsutum and *G. arboreum* by flavonoids was investigated. The toxicity in tobacco budworms larvae at *G. arboreum* was shown to be greater with Gossypetin 8-glucoside and Gossypetin 8-rhamnosid than any other flavonoid tested with an ED50 level of 0.007 percent and 0.024 percent respectively (Hedin et al., 1992). It should be noted that although *G. hirsutum* was not explicitly identified by these scientists, it was previously reported (Parks et al., 1975; & Hanny, 1980).

The entire phenol concentration (containing flavonoid) in cotton escalates in reaction to herbivory by the moth Oriental leafworm, *Spodoptera litura*. High-performance liquid chromatography (HPLC) analysis indicated that the flavan-3-ol catechin with gallic acids, caffeic acids and phenolic acids had significant elevations, indicating their function in plant defense. Assays have shown different amounts of anti-feed action of these compounds in *S. litura* with low levels of catechin activity. However, considerable increases in the detoxification of enzymes have been reported in the *S. litura* gut fed on cotton leaf treated with increased catechin levels. This further demonstrates its function in plant defensive mechanisms (Usha Rani & Pratyusha, 2013).

Flavonoids help in fungal infection resistance. The increased resistance to *Rhizoctonia solani* infection, found in older cotton plants, has been caused by an enhancement of polyphenols, especially catechins (Hunter, 1974). Higher catechin and gallocatechin concentrations were due to tolerance against fungal plant pathogens *Verticillium dahlia* in wilt-resistant varieties of *G. hirsutum* (Mace et al., 1978). Moreover, greater catechin and gallocatechin concentrations, as well as isoquercitrin observed in early cotton leaves (one to three apex nodes) help in reducing the mycelial development (Howell et al., 1976).

Reddening of Leaf:

Reddening of the leaves and coloration of the cotton may be attributed to an abiotic stress physiological response such as accumulation of soil sodium ions (Edreva et al., 2002). Reddening of leaf happens due to significant enhancement in red pigments and a fast decrease in chlorophyll concentration resulting in yield losses between 30-60 percent (Pagare & Durge, 2010). Investigations of the polyphenol compound of cotton leaves reveal a soar in anthocyanin pigment with leaf reddening, but other flavonoids and derivatives of cinnamic acid have not been modified appreciably. This elevation in anthocyanin pigments was attributed to the increase in cyanide glycosides as a result of the transformation of malvidin glycoside from green leaves to cyanide glycosides from the reddening of the leaves (Nix et al., 2017). This changes to cyanidine glycosides from malvidine to (O-dihydroxy substitution in the B-ring) (Figure 2) Enhance anti-radical and anti-oxidant activity (Badar et al., 2020), Increased capacity to defend against oxidative damage (Nix et al., 2017).

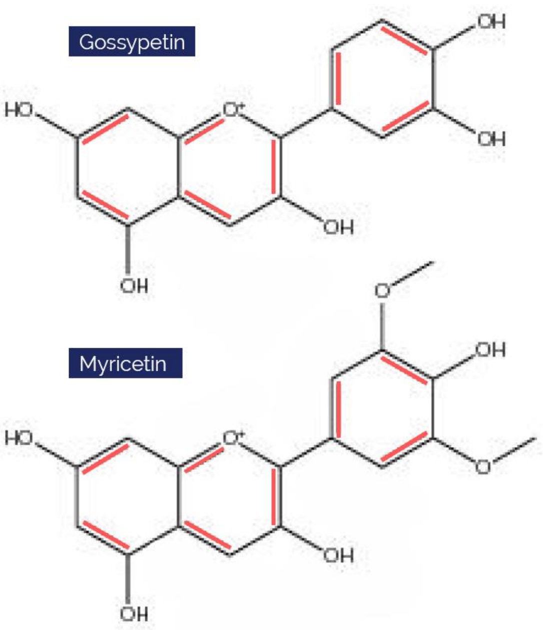


Figure 2: Cyanidin and malvidin, anthocyanidins of cotton

Additional study has shown the protective role of cyanidine glycosides in cotton. G. hirsutum was found to generate sesquiterpenoid phytoalexins 2, 7-dihydroxycadalene and lacinilene C in relation to an infection caused by the pathogen *Xanthomonas campestris* (Edwards et al., 2008). These phytoalexins, however, show light-dependent toxicity to the host plant cells. Cotton creates a dark red flush on the infection site, and its strength is associated with the resistance to bacteria in the isogenic lines. Red pigments generated by anthocyanins in infected areas protect healthy tissues towards the infectious ROS and light-activated phytoalexins (Kangatharalingam et al., 2002). Additional study has also demonstrated the importance of epidermal pigments in defending healthy cells against plant proprietary light-activated phytoalexins, red cells showing 3–4 times more photoactivating wavelengths of light absorption. An analysis showed that isoquertin (quercetin-3-glucoside), red anthocyanine, chrysanthemine (cyanidine-3-glucoside) and yellow flavonol are the main chemicals responsible for increasing absorption capacity (Edwards et al., 2008).

The reddening of the leaf was also assumed to be a reaction to a strong defensive insect herbivory; however this was not experimentally confirmed (Manetas, 2006). Given the function played by cyanidine 3-glucoside in the protection against the species of Helicoverpa and the role of leaf reddening in the treatment of abiotic stress, the assumption that this defense of herbivory can exist in cotton is not unreasonable.

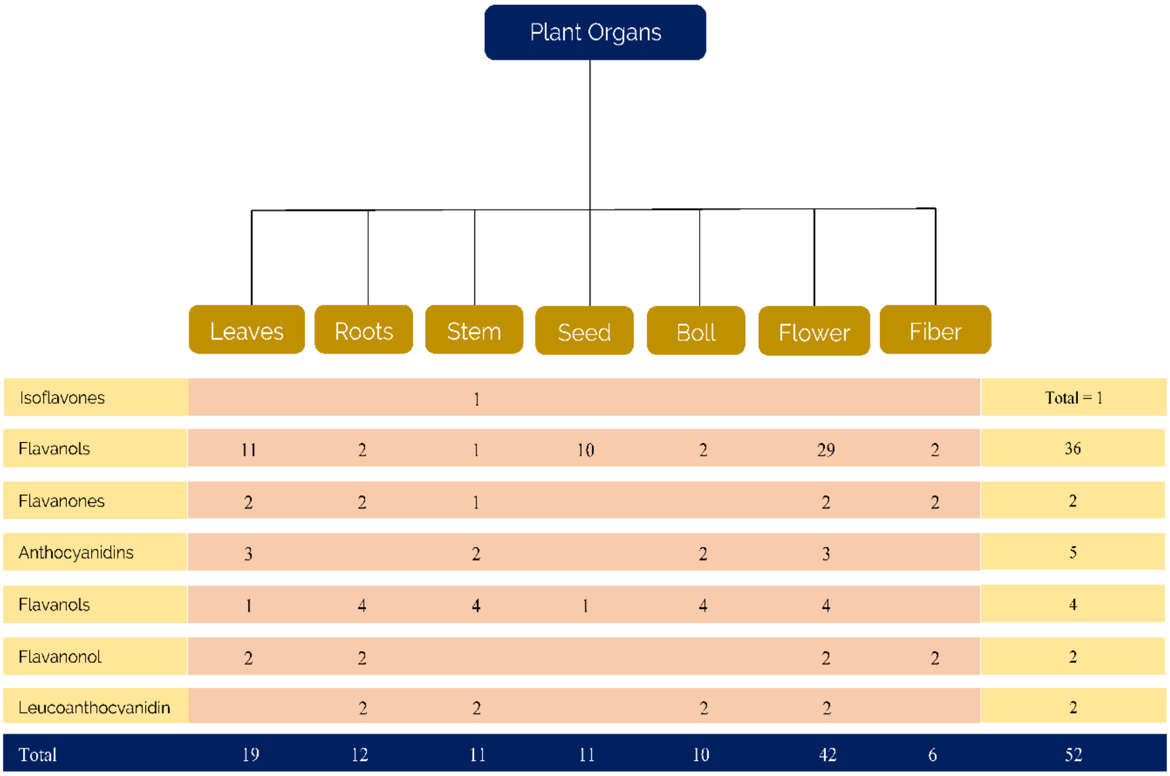
Significance of Flavonoids in the Production of Cotton:

In the quality and colour of cotton fiber, flavonoids have an important and significant role. Naturally, G. hirsutum has brown and green fiber. The accumulation of flavonoids and changes gene expression in brown cotton fibers is considerably higher than white fiber of cotton and the biosynthetic flavonoid pathway is significantly greater (Feng et al., 2013). The quality of the generated fiber is also affected by flavonoid metabolism, especially during the elongation phases (both micronaire and fiber length). The formation of fibers is adversely linked to flavanone naringenin, with fewer fibers forming with increased naringenin levels. Changing the naringenin metabolism gene to lower its expression for fiber levels may give a new strategy to enhance the growth of cotton fiber (Tan et al., 2013).

Gossypium hirsutum flavonoids and their distribution:

Flavonoids are present across a range of plant parts in *Gossypium hirsutum*, from bolls to roots, with leaves to flowers in the highest diversity. (Table 1).

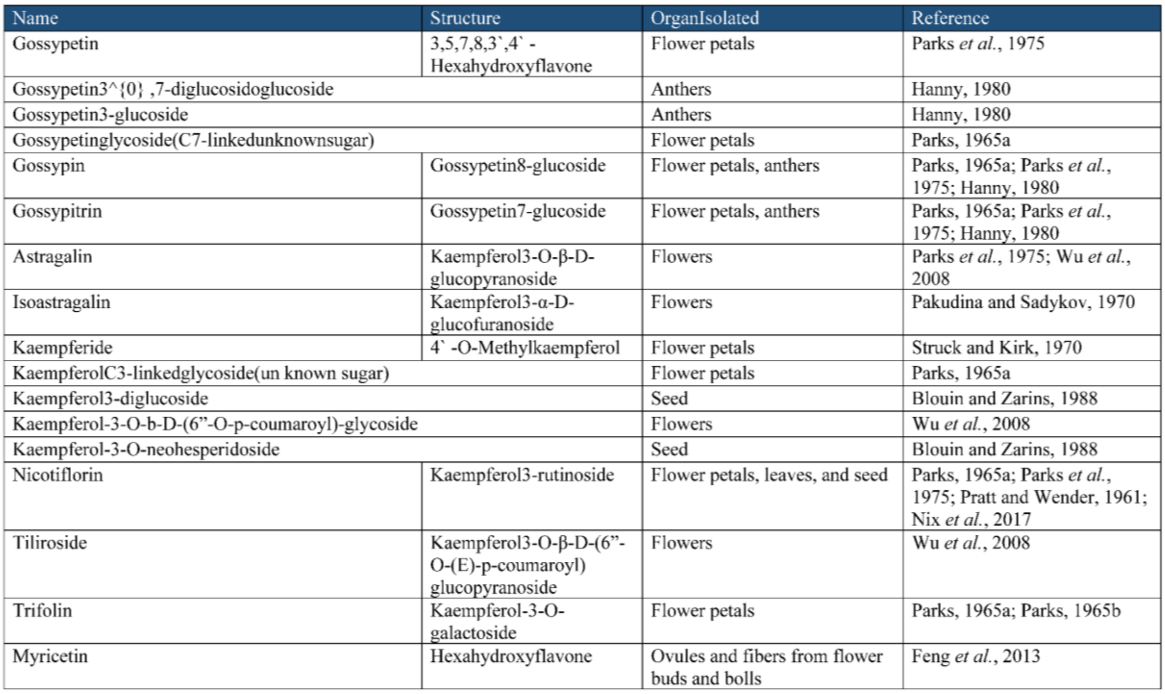
Table 1: Distribution across the *Gossypium hirsutum* of flavonoid groups and numbers of plant organ representatives

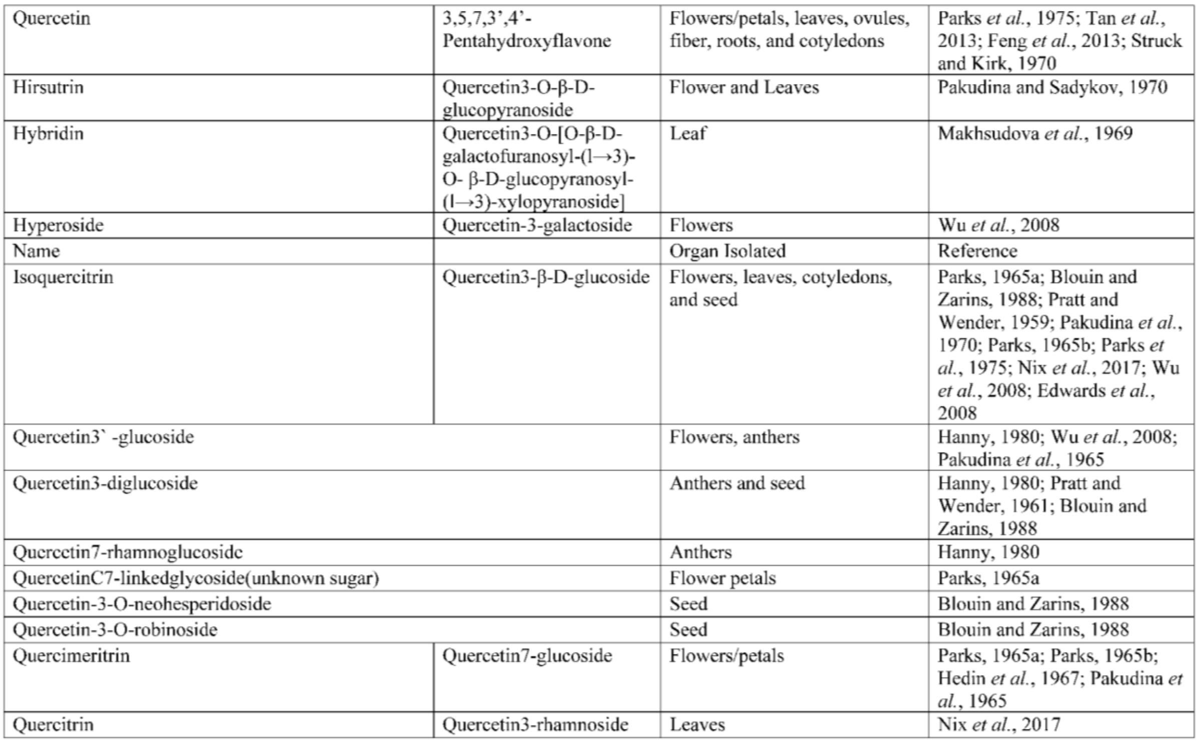


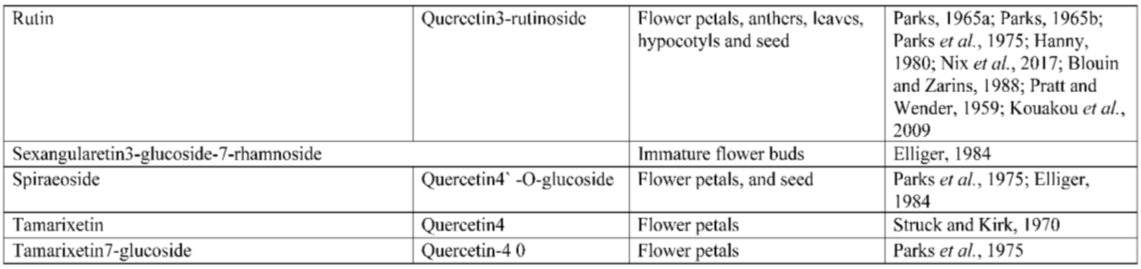
	Leaves	Roots	Stem	Seed	Boll	Flower	Fiber	
Isoflavones			1					Total = 1
Flavanols	11	2	1	10	2	29	2	36
Flavanones	2	2	1			2	2	2
Anthocyanidins	3		2		2	3		5
Flavanols	1	4	4	1	4	4		4
Flavanonol	2	2				2	2	2
Leucoanthocvanidin		2	2		2	2		2
Total	19	12	11	11	10	42	6	52

52 flavonoids, including newly 36 flavonols identified (Table 2) and 5 anthocyanidins (Table 3). 4 flavanols (catechins/flavan-3-oles), 2 flavanonols, 2 leucoanthocyanidins, 2 flavanones, and a 1 isoflovone are the other known flavonoids (Table 4).

Table 2: Distribution of flavonols in Cotton (*Gossypium hirsutum* L.)

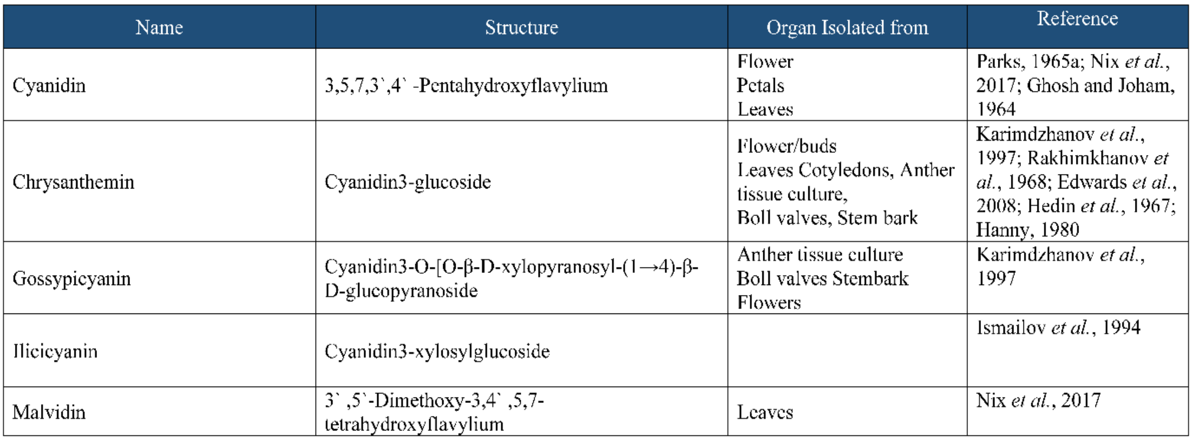






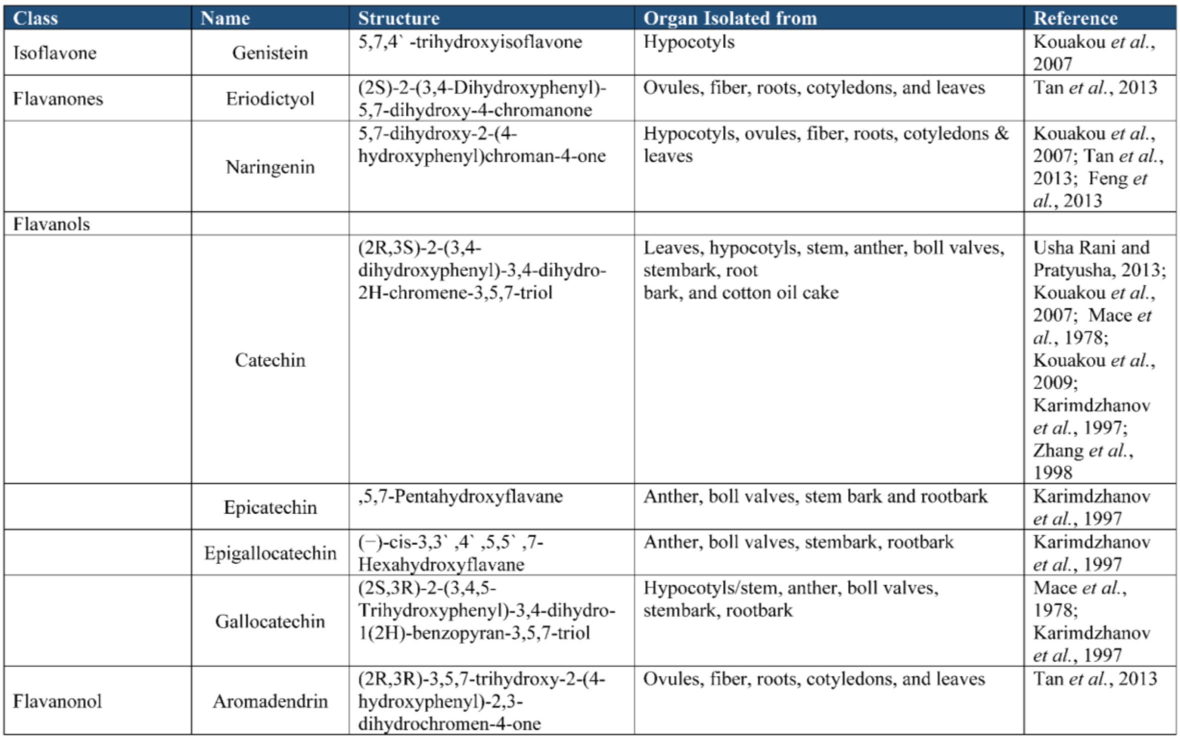
Name	Structure	OrganIsolated	Reference
Gossypetin	3,5,7,8,3`,4` -Hexahydroxyflavone	Flower petals	Parks *et al.*, 1975
Gossypetin3^{0} ,7-diglucosidoglucoside		Anthers	Hanny, 1980
Gossypetin3-glucoside		Anthers	Hanny, 1980
Gossypetinglycoside(C7-linkedunknownsugar)		Flower petals	Parks, 1965a
Gossypin	Gossypetin8-glucoside	Flower petals, anthers	Parks, 1965a; Parks *et al.*, 1975; Hanny, 1980
Gossypitrin	Gossypetin7-glucoside	Flower petals, anthers	Parks, 1965a; Parks *et al.*, 1975; Hanny, 1980
Astragalin	Kaempferol3-O-β-D-glucopyranoside	Flowers	Parks *et al.*, 1975; Wu *et al.*, 2008
Isoastragalin	Kaempferol3-α-D-glucofuranoside	Flowers	Pakudina and Sadykov, 1970
Kaempferide	4` -O-Methylkaempferol	Flower petals	Struck and Kirk, 1970
KaempferolC3-linkedglycoside(un known sugar)		Flower petals	Parks, 1965a
Kaempferol3-diglucoside		Seed	Blouin and Zarins, 1988
Kaempferol-3-O-b-D-(6”-O-p-coumaroyl)-glycoside		Flowers	Wu *et al.*, 2008
Kaempferol-3-O-neohesperidoside		Seed	Blouin and Zarins, 1988
Nicotiflorin	Kaempferol3-rutinoside	Flower petals, leaves, and seed	Parks, 1965a; Parks *et al.*, 1975; Pratt and Wender, 1961; Nix *et al.*, 2017
Tiliroside	Kaempferol3-O-β-D-(6”-O-(E)-p-coumaroyl) glucopyranoside	Flowers	Wu *et al.*, 2008
Trifolin	Kaempferol-3-O-galactoside	Flower petals	Parks, 1965a; Parks, 1965b
Myricetin	Hexahydroxyflavone	Ovules and fibers from flower buds and bolls	Feng *et al.*, 2013
Quercetin	3,5,7,3’,4’-Pentahydroxyflavone	Flowers/petals, leaves, ovules, fiber, roots, and cotyledons	Parks *et al.*, 1975; Tan *et al.*, 2013; Feng *et al.*, 2013; Struck and Kirk, 1970
Hirsutrin	Quercetin3-O-β-D-glucopyranoside	Flower and Leaves	Pakudina and Sadykov, 1970
Hybridin	Quercetin3-O-[O-β-D-galactofuranosyl-(l→3)-O- β-D-glucopyranosyl-(l→3)-xylopyranoside]	Leaf	Makhsudova *et al.*, 1969
Hyperoside	Quercetin-3-galactoside	Flowers	Wu *et al.*, 2008
Name		Organ Isolated	Reference
Isoquercitrin	Quercetin3-β-D-glucoside	Flowers, leaves, cotyledons, and seed	Parks, 1965a; Blouin and Zarins, 1988; Pratt and Wender, 1959; Pakudina *et al.*, 1970; Parks, 1965b; Parks *et al.*, 1975; Nix *et al.*, 2017; Wu *et al.*, 2008; Edwards *et al.*, 2008
Quercetin3` -glucoside		Flowers, anthers	Hanny, 1980; Wu *et al.*, 2008; Pakudina *et al.*, 1965
Quercetin3-diglucoside		Anthers and seed	Hanny, 1980; Pratt and Wender, 1961; Blouin and Zarins, 1988
Quercetin7-rhamnoglucoside		Anthers	Hanny, 1980
QuercetinC7-linkedglycoside(unknown sugar)		Flower petals	Parks, 1965a
Quercetin-3-O-neohesperidoside		Seed	Blouin and Zarins, 1988
Quercetin-3-O-robinoside		Seed	Blouin and Zarins, 1988
Quercimeritrin	Quercetin7-glucoside	Flowers/petals	Parks, 1965a; Parks, 1965b; Hedin *et al.*, 1967; Pakudina *et al.*, 1965
Quercitrin	Quercetin3-rhamnoside	Leaves	Nix *et al.*, 2017
Rutin	Quercetin3-rutinoside	Flower petals, anthers, leaves, hypocotyls and seed	Parks, 1965a; Parks, 1965b; Parks *et al.*, 1975; Hanny, 1980; Nix *et al.*, 2017; Blouin and Zarins, 1988; Pratt and Wender, 1959; Kouakou *et al.*, 2009
Sexangularetin3-glucoside-7-rhamnoside		Immature flower buds	Elliger, 1984
Spiraeoside	Quercetin4` -O-glucoside	Flower petals, and seed	Parks *et al.*, 1975; Elliger, 1984
Tamarixetin	Quercetin4	Flower petals	Struck and Kirk, 1970
Tamarixetin7-glucoside	Quercetin-4 0	Flower petals	Parks *et al.*, 1975

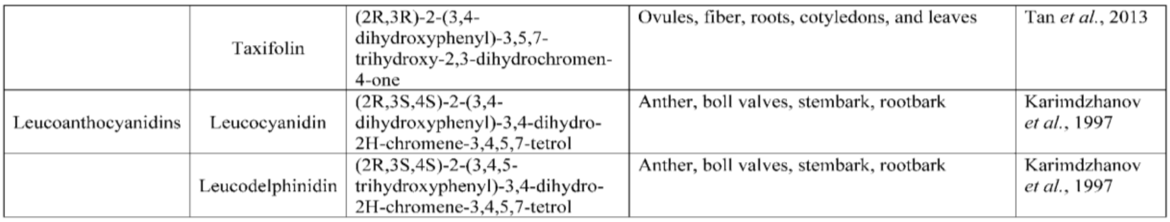
Table 3: Distribution of anthocyanidins and anthocyaninsin in Cotton



Name	Structure	Organ Isolated from	Reference
Cyanidin	3,5,7,3`,4` -Pentahydroxyflavylium	Flower Petals Leaves	Parks, 1965a; Nix *et al.*, 2017; Ghosh and Joham, 1964
Chrysanthemin	Cyanidin3-glucoside	Flower/buds Leaves Cotyledons, Anther tissue culture, Boll valves, Stem bark	Karimdzhanov *et al.*, 1997; Rakhimkhanov *et al.*, 1968; Edwards *et al.*, 2008; Hedin *et al.*, 1967; Hanny, 1980
Gossypicyanin	Cyanidin3-O-[O-β-D-xylopyranosyl-(1→4)-β-D-glucopyranoside	Anther tissue culture Boll valves Stembark Flowers	Karimdzhanov *et al.*, 1997
Ilicicyanin	Cyanidin3-xylosylglucoside		Ismailov *et al.*, 1994
Malvidin	3` ,5`-Dimethoxy-3,4` ,5,7-tetrahydroxyflavylium	Leaves	Nix *et al.*, 2017

Table 4: Other flavonoids found in Cotton (*Gossypium hirsutum* L.)





Class	Name	Structure	Organ Isolated from	Reference
Isoflavone	Genistein	5,7,4` -trihydroxyisoflavone	Hypocotyls	Kouakou *et al.*, 2007
Flavanones	Eriodictyol	(2S)-2-(3,4-Dihydroxyphenyl)-5,7-dihydroxy-4-chromanone	Ovules, fiber, roots, cotyledons, and leaves	Tan *et al.*, 2013
	Naringenin	5,7-dihydroxy-2-(4-hydroxyphenyl)chroman-4-one	Hypocotyls, ovules, fiber, roots, cotyledons & leaves	Kouakou *et al.*, 2007; Tan *et al.*, 2013; Feng *et al.*, 2013
Flavanols				
	Catechin	(2R,3S)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-2H-chromene-3,5,7-triol	Leaves, hypocotyls, stem, anther, boll valves, stembark, root bark, and cotton oil cake	Usha Rani and Pratyusha, 2013; Kouakou *et al.*, 2007; Mace *et al.*, 1978; Kouakou *et al.*, 2009; Karimdzhanov *et al.*, 1997; Zhang *et al.*, 1998
	Epicatechin	,5,7-Pentahydroxyflavane	Anther, boll valves, stem bark and rootbark	Karimdzhanov *et al.*, 1997
	Epigallocatechin	(−)-cis-3,3` ,4` ,5,5` ,7-Hexahydroxyflavane	Anther, boll valves, stembark, rootbark	Karimdzhanov *et al.*, 1997
	Gallocatechin	(2S,3R)-2-(3,4,5-Trihydroxyphenyl)-3,4-dihydro-1(2H)-benzopyran-3,5,7-triol	Hypocotyls/stem, anther, boll valves, stembark, rootbark	Mace *et al.*, 1978; Karimdzhanov *et al.*, 1997
Flavanonol	Aromadendrin	(2R,3R)-3,5,7-trihydroxy-2-(4-hydroxyphenyl)-2,3-dihydrochromen-4-one	Ovules, fiber, roots, cotyledons, and leaves	Tan *et al.*, 2013
	Taxifolin	(2R,3R)-2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-2,3-dihydrochromen-4-one	Ovules, fiber, roots, cotyledons, and leaves	Tan *et al.*, 2013
Leucoanthocyanidins	Leucocyanidin	(2R,3S,4S)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-2H-chromene-3,4,5,7-tetrol	Anther, boll valves, stembark, rootbark	Karimdzhanov *et al.*, 1997
	Leucodelphinidin	(2R,3S,4S)-2-(3,4,5-trihydroxyphenyl)-3,4-dihydro-2H-chromene-3,4,5,7-tetrol	Anther, boll valves, stembark, rootbark	Karimdzhanov *et al.*, 1997

There have been no records of G. hirsutum chalcones, aurons and flavones. G. hirsutum flowers have highest count of flavonoids as they contain highest number (42) of the total (52) flavonoids found. Flavonols are the most common family of flavonoids containing gossypetin, kaempferol, myricetin, quercetin and their conjugates. (Figure 3).

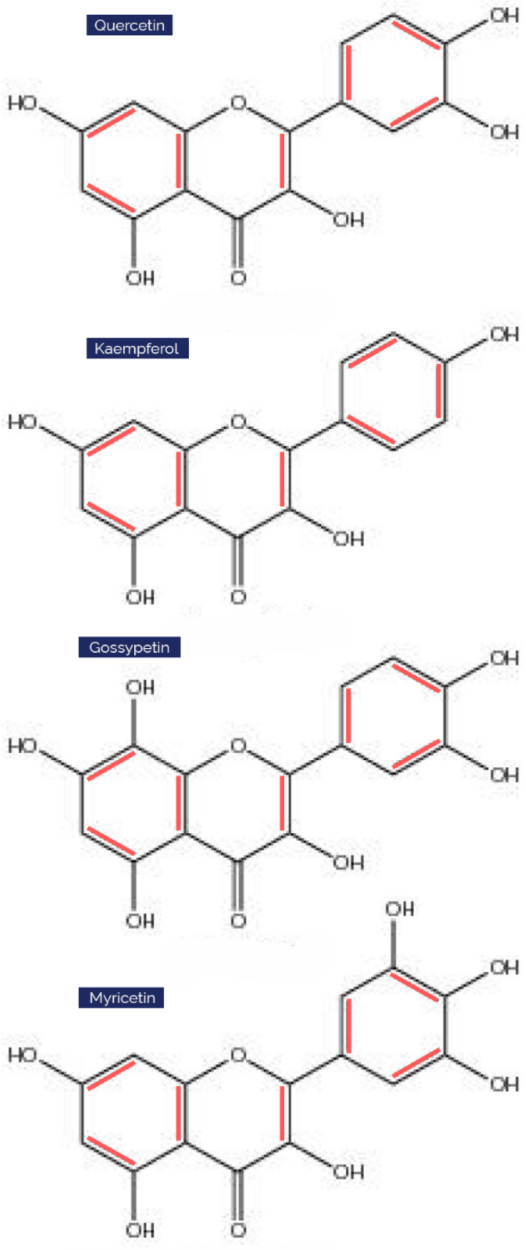


Figure 3: Flavonol aglycones found in cotton

G. hirsutum leaves contain 19 flavonoids comprises of 5 different groups. In comparison, less flavonoids (6–12) are identified in the stem, seed, roots, boll, and cotton fiber (Table 1).

Future Research:

Although several cotton flavonoids have been discovered previously, limited information on their use processes and information related to their interactions and activities especially with regard to pathogen interactions in plant and pollination pathway is known. This review highlights prospective possibilities that support the necessity for additional study on cotton flavonoids, in particular in the management of insects.

Genetically transformed Bt cotton contributes to increase yield and reduces the use of insecticides (Ahmad & Hasanuzzaman, 2020). There is also a constant danger that pest species will evolve tolerance against these genetically altered species. (Baker et al., 2008). For example, under laboratory conditions, Bt resistant mutants of *Helicoverpa armigera* were produced (Akhurst et al., 2003). Several genes from field populations conferring resistance to poisons have been discovered (Mahon et al., 2007). Further research on the determination of the linkage of flavonoids expression of these targeted flavonoids for lowering larva, regulating feeding manner and increasing toxicity towards insecticides, could provide a remarkable tool for the cotton textile industry to move one step ahead of rapidly developing pests. Flavonoids might be used to enhance tolerance management techniques by decreasing the efficiency of lepidopteran pests for Bt cotton cultivation systems. Selected flavonoids suppress larval development, however additional research is needed to identify particular ones for each cotton lepidopteran pest. Flavonoids limit the growth of Helicoverpa zea, a polyphagous crop pest The impact of 42 flavonoids administered to H. zea in an artificially increased diet showed 20 that decreased larval development by half. All except one of these inhibitory substances had a structural commonality: each displays adjacent (ortho) substitutions for phenolic hydroxyl groups. In fact, seven of these chemicals are present in cotton (taxifolin, quercetin, eriodictyol, rutin, quercitrin, myricetin and catechin) (Elliger et al., 1980). Moreover, numerous flavonoids previously addressed with different lepidopteran (chrysanthemin, gossypin and isoquercitrin) show larval suppression of growth and toxicity, also had these structural characteristics. Limiting larval capability by decreasing larval development improves the chance of beneficial insect predation or parasitism that ultimately also decrease adult size. Yet again, improving the fitness of Bt moths sensitive to refuge e.g. vitexin might increase resistance strategies even more.

For certain lepidopterans, flavonoids have a role in oviposition. Flavonoids discourage the recognition required for direct interaction with plant material. Luteolin, for example, 7-malonyl glucoside and rutin are stimulants for monarch butterflies, Danaus plexipuss and black swallowtail for Papilo polyxenes. Papilo xuthus is driven to oviposition by the presence of routin (quercetin 3-rutinoside) on citrus trees, however, quercetin 3-(2-β-D xylopyranosylrutinoside) is discouraged from oviposition on the non-host plant Orixa japonica. Thus, the switch from oviposition to deterrence in this lepidopteran takes place by simply adding sugar xylose to the flavonoid component (Nishida et al., 1990). The identification of the flavonoids that encourage oviposition of lepidopteran pesticides in cotton-cropping systems could hinder eggs from laying on cotton while boosting egg laying on refugees.

The selection of cotton cultivars with high levels of protective flavonoids including Bt genes or enhancing the expression to greater levels of plant defensive flavonoids may give a new tool to enhance the plant defense mechanism. Similarly, the identification of flavonoids associated in oviposition for cotton lepidopteran pests might potentially contribute to the selection of Bt cultivars having less appeal to such pests. Moreover, knowledge of flavonoids can promote the survivability of Bt sensitive moths and can boost shelter attractions which can be exploited to expand sensitive populations that will further delay the development of resistance.

Flavonoids can provide the potential for identifying the natural host plant of cotton invertebrates, such as Helicoverpa species, as a new biomarker. Refuge cultures limit the incidence of resistance to Helicoverpa. Past techniques for the identification of native host plants are relatively straightforward and rely on the capacity to discriminate groups of plants from C_3 to C_4 by utilizing stabilized carbon isotopes. Pigeonpea is the preferred refuge because more helicoverpas are produced and consequently less space needs to be cultivated than other refuge crops. More studies have been done on the utilization of a stable nitrogen isotope to discriminate among C3 plants that have been created for the legume e.g pigeonpea or non-legume e.g cotton (Baker & Tann, 2013). Stable isotope analysis combined with the identification of secondary metabolites e.g gossypol, cotton-developed moths and non-cotton C_3-plants were successfully described

(Brévault et al., 2012; & Orth et al., 2007). These techniques don't have the precision to recognized the host crop for these highly mobile pesticides. Flavonoid profiles have been previously demonstrated to be used to discriminate against phylogenetic connections and to distinguish species within genera (Almaraz-Abarca et al., 2006). Lepidopterans have also been demonstrated to isolate flavonoids from the host plant throughout their growth (Burghardt et al., 2001).

Gene expression research for cotton flavonoid production have not been explored here in-depth. However, these studies are able to provide a new way to improve the production of cotton, given the part played by numerous flavonoids in preserving plant health and processes for plant development and protection. In addition, research into the identification of flavonoids in cotton with regionally associated cropping patterns might prove that flavonoids are capable of acting as new biomarkers for native host cotton lepidopteran pests.

CONCLUSIONS

Flavonoids play an important role in the protection and defense of cotton plant which ultimately enhances the vigor of plant leading to the higher yield and higher tolerance in plant. Cotton uses flavonoids as part of an herbicide defense mechanism to boost the synthesis of poisonous flavonoids that hinder lepidopteran larval development. As of now, 52 *Gossypium hirsutum* flavonoids are studied and identified but the underlaying information and research about the existence of flavonoids in this important economic crop on their usage for plant defense is still lagging. More research in this field can give novel and sustainable technologies in order to complement existing cotton production enhancement techniques.

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