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STUDIES OF OMEGA-3 FATTY ACID SEMICARBAZIDE DERIVATIVE OF NATURAL SEED OIL

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ABSTRACT

Only two fatty acids are known to be essential for human -alpha-linolenic acid (an omega-3 fatty acid) and linoleic acid (an omega-6 fatty acid). Natural seed is *Cucurbita mixta* (Pumpkin) contain 42.71 % oil. *Cucurbita mixta* (pumpkin) seed oil supply calcium, iron, vitamin A, oil (25 -55%, rich in unsaturated oleic and linoleic acids). The proximate analysis of *Cucurbita mixta* (Pumpkin) seed oil shows 04.70 % moisture & 05.35 % ash. It has congeding point 10.70^0C. It is commonly used in folk medicine. *Cucurbita mixta* (pumpkin) seed oil has been implicated in providing many health benefits. Semicarbazones are potent intermediates for the synthesis of pharmaceutical and bioactive materials and thus, they are used extensively in the field of medicinal chemistry Omega-3 –fatty acid semicarbazide of *Cucurbita mixta* (Pumpkin) oil was synthesized. The absorption spectra, infrared spectra and X-ray diffraction of essential fatty acid semicarbazide was studied. The antibacterial activity of essential fatty acid semicarbazide was studied.

INTRODUCTION

Essential fatty acids were discovered in 1923. Essential fatty acids are the polyunsaturated fatty acids. Essential fatty acids, or EFAs, are fatty acids that humans and other animals must ingest because the body requires them for good health but cannot synthesize them. (Groff, 1995). Fatty acids can be broadly divided into saturated, monounsaturated and polyunsaturated. The polyunsaturated fatty acids (PUFAs) have the most functional significance and are divided into two main types: the n6 and the n3. The distinction between n3 and n6 relates to the position of the first double bond in the carbon chain. The more double bonds, the more unsaturated the fatty acid. Only two fatty acids are known to be essential for human -alpha-linolenic acid (an omega-3 fatty acid) and linoleic acid (an omega-6 fatty acid). (Demain, ?). There are two sub class of long chain polyunsaturated fatty acids (PUFAs), Omega -3 fatty acids - α-Linolenic acid or ALA (18:3n-3), eicosapentaenoic acid or EPA (20:5n-3), docosahexaenoic acid or DHA (22:6n-3), Omega-6 fatty acids:- gamma-linolenic acid or GLA (18:3n-6), Linoleic Acid (LA) or LA (18:2n-6), dihomo-gamma-linolenic acid or DGLA (20:3n-6). Omega-3 fatty acids have been the subject of volumes of international research. Omega-3 fatty acids are essential for brain growth and development. They play an important role throughout life, as critical modulators of neuronal function and regulation of oxidative stress mechanisms, in brain health and diseases. Omega-3 fatty acids may be of value in the treatment of various medical conditions (Demain et.al 2000). while beneficial effects ofomega-3 fatty acids have been linked to Alzheimer's diseases (Richardson, 2002). Attention deficit hyperactivity disorder (Vancassel, Durand, Barthelemy, *et al*. 2002). sautism (Assies, Lieverse, Vreken, *et al*, 2000), schizophrenia (Peet, 2005), hostility (Hamazaki, 2001), anxiety (Mamalakis, 1998), and bipolar disorder (Stoll, 1999). In animal research, an omega-3 deficiency results in as much as a 46-percent increase in serotonin receptor (5HT2) density in the frontal cortex (Delion, 1966). An omega-3 deficiency has also been shown to decrease glucose uptake of brain cells by 30 percent and decrease cytochrome oxidase activity by up to 40 percent (Ximenes, da Silva, Lavialle, Gendrot, *et al*, 2002). Omega-3 deficiency can also alter the delivery of amino acids and sucrose across the blood-brain barrier (Ziylan, Bernard, LeFauconnier, *et al*, 1992). Omega-3 fatty acids are well documented inhibitors of proinflammatory cytokines, particularly TNF-α and IL-1 β (James, 1997). Symptoms of omega 3 fatty acids deficiency include fatigue, poor memory, dry skin, heart problems, mood swings or depression and poor circulation (Mirajkar, 2011). They are not synthesized by the body but only available through the diet (Bell, 1997).

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Neuronal cell membrane structure and metabolism is dependent on blood levels of these fatty acids (Yehuda, S, 2002). The two omega 3 fatty acids are Eicosapentaenoic acid (EPA) and Docosahaxaenoic acid (DHA). It has important function in central nervous system. The health effects of omega 3 fatty acids are come from EPA and DHA.DHA is a major structural component of neuronal membranes and changing the fatty acids composition of neuronal membrane leads to functional changes in the activity of receptors and other proteins embedded in the membrane phospholipids. EPA has important physiological function that affects neuronal activity (Peet, 2005). Evidence that fatty acid metabolism is abnormal in schizophrenia (MacLean, 2005). DHA is also important for normal cognitive development, may function in the brain to protect against ischemic damage (Gibney, 2009). Omega 3 fatty acids may provide an important and novel approach to the development of antipsychotics in the future (Amminger, 2002). Omega-3 fatty acids, may be of therapeutic benefit in acute injury to the brain (Wu, 2008; Lang-Lazdunski, 2003; Wu, 2004; Ying, 2011).

Omega-3 fatty acids have long been known to play a restorative role in several pathways implicated in traumatic insult to the brain (Wu, 2004; Mills, 2011; Hadley, 2011; Prins, 2011; Musto, 2011). An additional proposed reason for why omega-3 PUFAs are so essential to and enriched in the brain is their unique transformation into neuroprotective metabolites, which are critical in the defense against oxidative stress, tissue inflammation, and maintenance of synaptic integrity (Niemoller, 2009; Maroon, 2006; Birch, 2007). Omega-3 is an anti-inflammatory (Castaneda 2005). Essential fatty acid play a crucial role in brain function, as well as normal growth and development (Mirajkar, 2013; Bell, 1997). Omega 3 fatty acids are highly concentrated in the brain and appears to be important for cognitive (brain memory and performance) and behavioral function. Symptoms of omega 3 fatty acids deficiency include fatigue, poor memory, dry skin, heart problems, mood swings or depression and poor circulation (Yehuda, 2002). They are not synthesized by the body but only available through the diet (Peet, 2002). Neuronal cell membrane structure and metabolism is dependent on blood levels of these fatty acids (Stroke, 2005). The two omega 3 fatty acids are Eicosapentaenoic acid (EPA) and Docosahaxaenoic acid (DHA).

It has important function in central nervous system. The health effects of omega 3 fatty acids are come from EPA and DHA.DHA is a major structural component of neuronal membranes and changing the fatty acids composition of neuronal membrane leads to functional changes in the activity of receptors and other proteins embedded in the membrane phospholipids. Arachidonic acid and docosahexaenoic acid (DHA) are the most abundant fatty acids in the brain. Arachidonic acid, dihomogamma-linolenic acid and eicosapentaenoic acid (EPA) are also important as cell-signalling and enzyme-regulating molecules and as precursors of eicosanoids (prostaglandins, thromboxanes and leukotrienes) (Dimmock, 1999). Omega 3 fatty acids may provide an important and novel approach to the development of antipsychotics in the future (Dogan, 1999). In organic chemistry, semicarbazone is a derivative of semicarbazide which contains an additional ketone functional group. Dimmock *et al*., reported an extensive series of semicarbazone (Hulya, 1993). Semicarbazides are the raw material of semicarbazones, have been known to have biological activity against many of the most common species of bacteria (Cotti, 1940; Vogel, 1964; Prasad 1989). Semicarbazones constitute one of the most important class of oxygen and nitrogen donar ligands (Prasad, Jindal, 1990; Prasad, 1990; Sulekha, 1984; Chandra, 1977; Dimmock, 1993). Semicarbazone, themselves are of much interest due to a wide spectrum of antibacterial activities (Pandeya, 1989). Recently some workers had reviewed the bioactivity of semicarbazones and they have exhibited anticonvulsant (Pandeya, 2000), antitubercular (Sriram, 2004), analgesic and anti-inflammatory activity (Singh, 2010), antimicrobial (Lever, 1995), pesticide (Anderson, 2000), herbicide (Copping, 1983) and hypnotic (Pandeya, 1999), Semicarbazone, themselves are of much interest due to a wide spectrum of antibacterial activities (Pandeya, 1983).

MATERIALS AND METHODS

Collection of Materials

The dried *Cucurbita mixta* (Pumpkin) seeds were obtained from local market. They are dried in room, clean and stored in a sealed vessel wrapped with polyethylene bag at 4^0C.

Extraction of oil

After cleaning and removal of the sand and foreign material , the dried *Cucurbita mixta* (Pumpkin) seeds were ground to a fine powder using a grinde. The oil was extracted with n-hexane (1:4 w/v) by continous extraction in a soxhlet apparatus for 12 hours. The solvent was evaporated at 40^0C in rotavapour. The extracted oil was stored in sealed and dark bottles. Their physic-chemical analysis was done by standard BIS methods. All the other chemicals used in the study were of laboratory grade and were used without any modification.

Preparation of Mixed Fatty Acids from oil

Mixed fatty acids from *Cucurbita mixta* (Pumpkin) seed oil were obtained by saponification method in which 100 gm oil was taken in 250 ml round bottom flask and 30 % alcoholic NaOH was added. The content were refluxed for 4 hrs. on stirring water bath. At the end of the reaction, the excess alcohol was distilled off and soap was dissolved in hot water. Then fatty acids were liberated by acidifying the soap solution

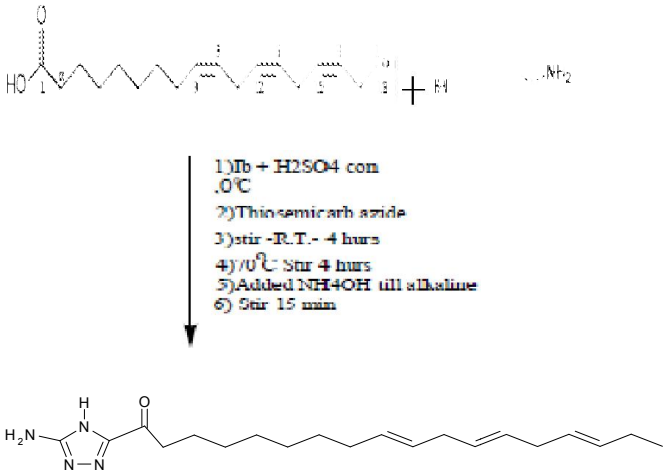
with 1:1 H_2SO_4 (added till development of red colour in methyl red), washed and dried over anhydrous sodium sulphate.

Separation of Fatty Acid

Fatty acids are separated by TLC on silica gel plates with hexane / diethyl ether (85/ 15, v/v) as eluent. It detected after primuline spray under UV light. Spot corresponding to the respective fatty acid present. Standard solution of omega-3-6--fatty acid was prepared (Commercial compound) spot on TLC obtained by fatty acid compared with the spot of standard. Omega-3-6-fatty acid from mixed fatty acid is separated by micro-column filled with silica gel (3cm) suspended in hexane (fatty acids being dissolved in the same solvent). Normal fatty acids are eluted by 4 ml of hexane / diethyl ether (93/7, v/v) & hydroxyl fatty acids by 4 ml of hexane / diethyl ether (50/50, v/v) the separated fatty acid omega-3-6-fatty acid used for the preparation of derivative of semicarbazide.

Preparation of Essential Fatty Acid Semicarbazide (EFASC)

Essential fatty acid (omega-3-6-fatty acid, 1 gm) were dissolved in 4 ml of methanol and 1:1 H_2SO_4, to this solution thiosemicarbazide (4gm) in methanol was added with constant stirring at room temperature about 4 hrs and then reflux at 4 hrs added NH_4OH till alkaline stir about 15 min and kept it overnight. Crystals was filtered, dried and recrystallized.



Essential fatty acid semicarbazide derivative (EFASC)

Absorption Spectra of EFASC

The absorption spectra of essential fatty acid semicarbazide (EFASC) was recorded against a blank solution shown in Fig. 1 The absorption spectra was recorded in the wavelength range 320-520 nm.EFASC shows the absorption maximum at 350 nm shows absorption 1.824.

Infrared Spectra of EFASC

The infrared spectra of essential fatty acid semicarbazide (EFASC) was taken in the range of 4000 cm^{-1} to 750 cm^{-1} on perkin Elmer 221 IR spectrophotometer using KBR pellet techniques . The characteristic bands observed are as in Table 1. Fig. 2. Shows IR spectra of EFASC.

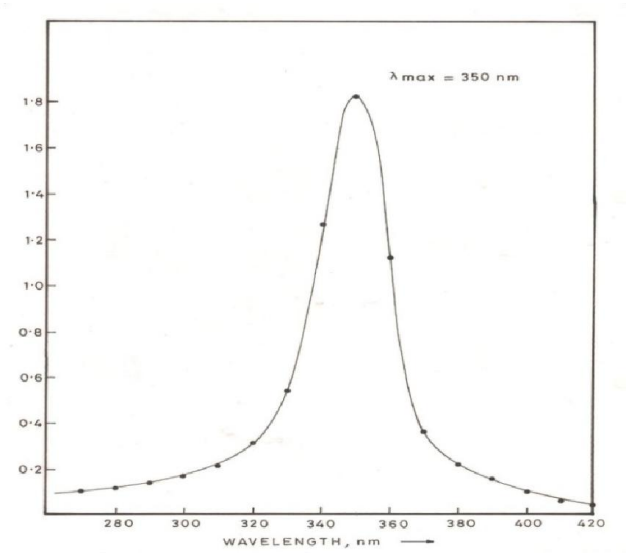


Figure 1. Absorption Spectra of Essential Fatty acid Semicarbazide (EFASC) of *Cucurbita mixta* (Pumpkin) seed oil

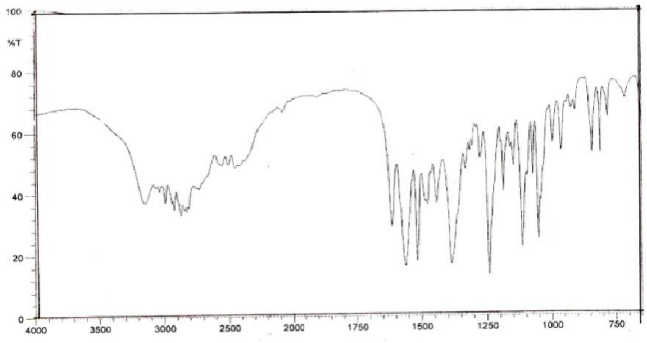


Figure 2. Infrared Spectra of Essential Fatty acid Semicarbazide (EFASC) of *Cucurbita mixta* (Pumpkin) seed oil

Table 1. Infrared Spectra of Essential Fatty acid Semicarbazide (EFASC) of *Cucurbita mixta* (Pumpkin) seed oil

Sr.No.	Frequency Wave number	Expected Elements
1)	750	Ring with four adjacent free H atom
2)	800	Trisubstituted alkanes
3)	960	Disubstituted alkenes ($R_1CH=CHR_2$)
4)	1050	Sulfonic acid
5)	1120	Secondary alcohol
6)	1175	Methyl esters (R-$COOCH_3$)
7)	1250	Alkanes
8)	1380	Alkane –CH_3
9)	1520	C=C & C=N Stretch
10)	1550	Tertiary nitro compound
11)	1620	Amide H bond, combination NH det.
12)	2500	Charged amines (C=NH)
13)	2600	Deuterated amines
14)	2850	-CHO
15)	2900	Alkanes (-CH-)
16)	2960	Alkanes (-CH_3)
17)	3150	Sec. amides bonded NH

X-RD Spectra of EFASC

X-RD spectra of essential fatty acid semicarbazide (EFASC) was taken on PW 3710 diffractometer using CuK_2 radiation (Y= 1.54060). The X-RD diffraction of EFASC recorded at angle 2θ from 18.5013 to 38.538. The data of X-ray diffraction of EFASC were presented in Table 2. and X-RD spectrum in Fig.3. for the determination of a, b & c Hesse-lipson procedure is used.

Table 2. X-RD Spectra of Essential Fatty acid Semicarbazide (EFASC) of *Cucurbita mixta* (Pumpkin) seed oil

Sr.No.	2θ	hkl	Sin^2 θ Observed	Sin^2 θ Calculated	d(A^0) Observed	d(A^0) Calculated
1	18.501	110	0.0374	0.0332	4.7957	4.3742
2	20.131	110	0.0395	0.0315	4.41097	4.2030
3	21.653	111	0.0454	0.0399	4.10423	4.0056
4	24.563	111	0.0492	0.04010	4.62432	4.0992
5	25.461	210	0.04997	0.04635	3.49846	3.1035
6	27.481	210	0.05013	0.04989	3.24572	3.02861
7	28.190	210	0.05368	0.05030	3.16563	2.99685
8	28.950	210	0.05798	0.05012	3.08425	2.9605
9	29.701	211	0.05997	0.06168	3.00802	2.8349
10	30.486	211	0/06324	0.06883	2.93226	2.7356
11	32.096	211	0.06439	0.06905	2.78875	2.6089
12	33.399	300	0.06835	0.07089	2.68291	2.43540
13	34.759	300	0.06994	0.07212	2.58093	2.3238
14	35.193	300	0.07039	0.07368	2.55016	2.01048
15	35.476	310	0.07336	0.08154	2.53044	1.9939
16	36.309	310	0.07989	0.08538	2.47427	1.3748
17	36.862	310	0.08134	0.08923	2.43839	1.2050
18	38.538	310	0.08564	0.08998	2.33613	1.0601

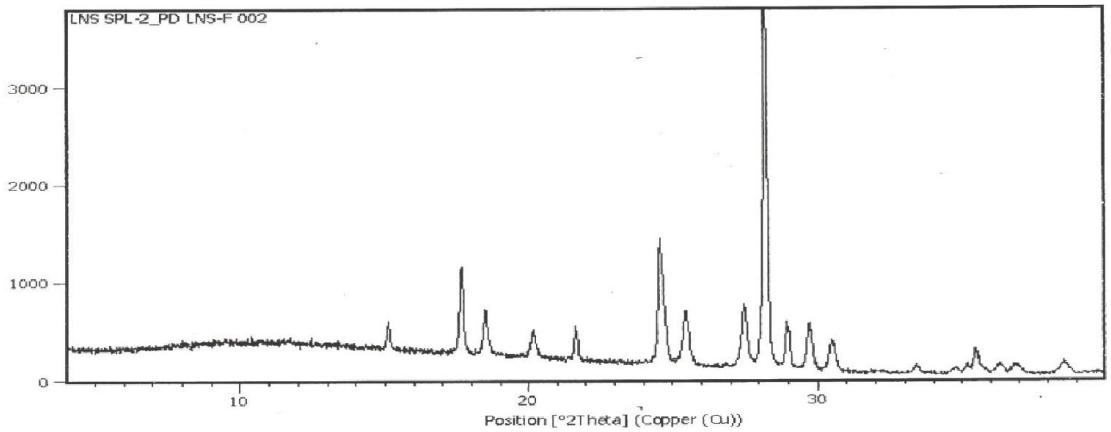


Figure 3. X-RD Spectra of Essential Fatty acid Semicarbazide (EFASC) of *Cucurbita mixta* (Pumpkin) seed oil

Antibacterial Activity of EFASC

Antibacterial Activity of essential fatty acid semicarbazide (EFASC) of *Cucurbita mixta* (Pumpkin) seed oil was analyzed. Table 3. Well diffusion method was used for in vitro antibacterial testing Nutrient agar plates, nutrient agar slant and nutrient broth were prepared and kept for sterility testing at 37^0C for 24 hrs. Next day pure culture of E.coli, Staphylococcus aureus and Aspergellus niger were inoculated on nutrient agar slant to obtain 24 hrs. Fresh culture of microorganisms. & kept in broth for 6 hrs. Crftriaxone was used as s standard Using stock solution 40µ / well antibacterial assay was carried out by agar well diffusion method. After 6 hrs each plate is examined Table 3, Fig 4.

Table 3. Antibacterial Activity of Essential Fatty acid Semicarbazide (EFASC) of *Cucurbita mixta* (Pumpkin) seed oil

Sr.No.	Bacteria	Reference Substance	Inhibition Zone (EFASC) 40 µ / well
1	E.coli	40 + 2.0	12 + 00
2	S.aureus	43 + 1.0	20 + 0.5
3	A.niger	19 + 2.0	14 + 0.5

RESULTS AND DISCUSSION

Cucurbita mixta (Pumpkin) seed is reddish colour & its oil is yellow in colour with pleasant nutty taste, paint like odour. Its acid value & peroxide number is 1.05 mg KOH/g of oil, 0.98 Meg/Kg . Iodine value is 163.5 g/100 g of oil it indicate a high composition of poly unsaturated fatty acid ia an assest in nutrition as high content of saturated fatty acid is implicated in cardiovascular diseases. It contain fatty acid that helps to maintain healthy blood vessels. Experimentally it found that *Cucurbita mixta* (Pumpkin) seed oil is used a medicinal important. Absorption spectra of essential fatty acid semicarbazide (EFASC) of *Cucurbita mixta* (Pumpkin) seed oil shows maximum absorption 3.182 at 370 nm. Infrered spectra of EFASC shows that at 750 cm^{-1} ring with four adjacent free H atom, at 800 cm^{-1} trisubstituted alkanes, at 960 cm^{-1} disubstituted alkenes ($R_1CH=CHR_2$) at1050 cm^{-1} sulfonic acid, at 1120 cm^{-1}secondary alcohol, at 1175 cm^{-1} methyl esters ($R\text{-}COOCH_3$), at 1250 cm^{-1} alkanes, at 1380 cm^{-1} alkane $–CH_3$, at 1520 cm^{-1} C=C & C=N Stretch, at 1550 cm^{-1}, tertiary nitro compound, at1620 cm^{-1} amide H bond, combination NH det.at 2500 cm^{-1} charged amines (C=NH), at 2600 cm^{-1} deuterated amines, at 2850 cm^{-1} –CHO, at 2900 cm^{-1} alkanes (CH-), at 2960 cm^{-1} alkanes ($-CH_3$), at 3150 cm^{-1} sec. amides bonded NH. X-RD spectra of essential fatty acid semicarbazide (EFASC) of *Cucurbita mixta* (Pumpkin) seed oil indicate a= 7.0432, b= 9.3548 & c= 8.1325 using Hesse-Lipson procedure shows that the structure is orthorhombic. The antibacterial activity was evaluated by diffusion method. It shows thatantibacterial activity at varied level in E.coli, S. aureus & A.niger. The bacteria S.aureus was found to be more active in inhibition zone than E coli & A.niger. The result calculated that EFASC of *Cucurbita mixta* (Pumpkin) oil posses good antibacterial activity.

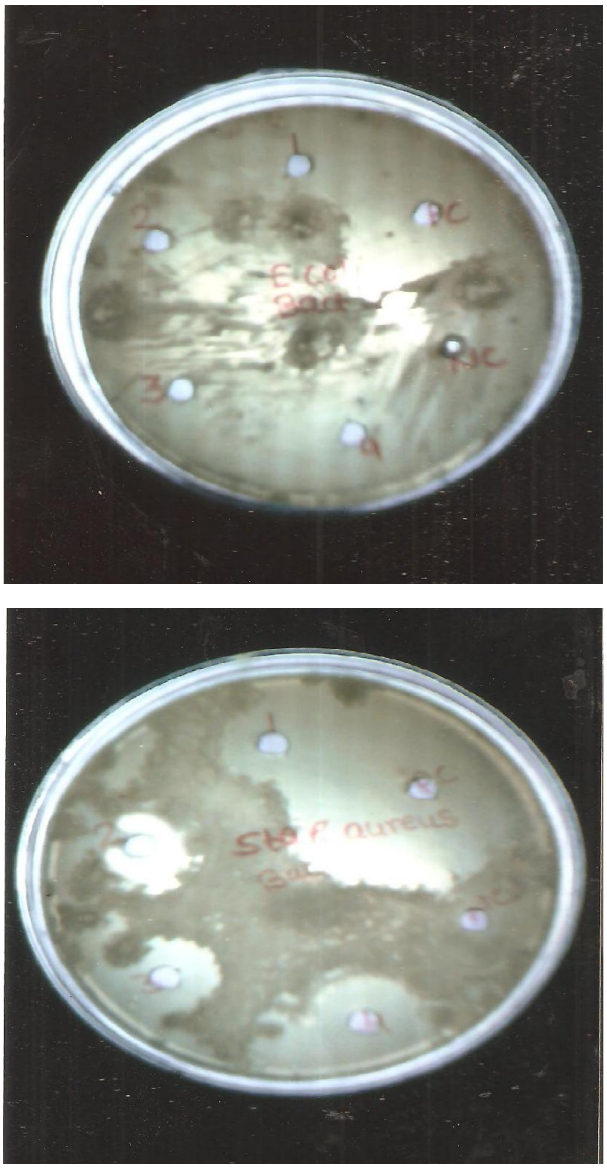


Figure 4. Antibacterial Activity of Essential Fatty acid Semicarbazide (EFASC) *Cucurbita mixta* (Pumpkin) seed oil

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