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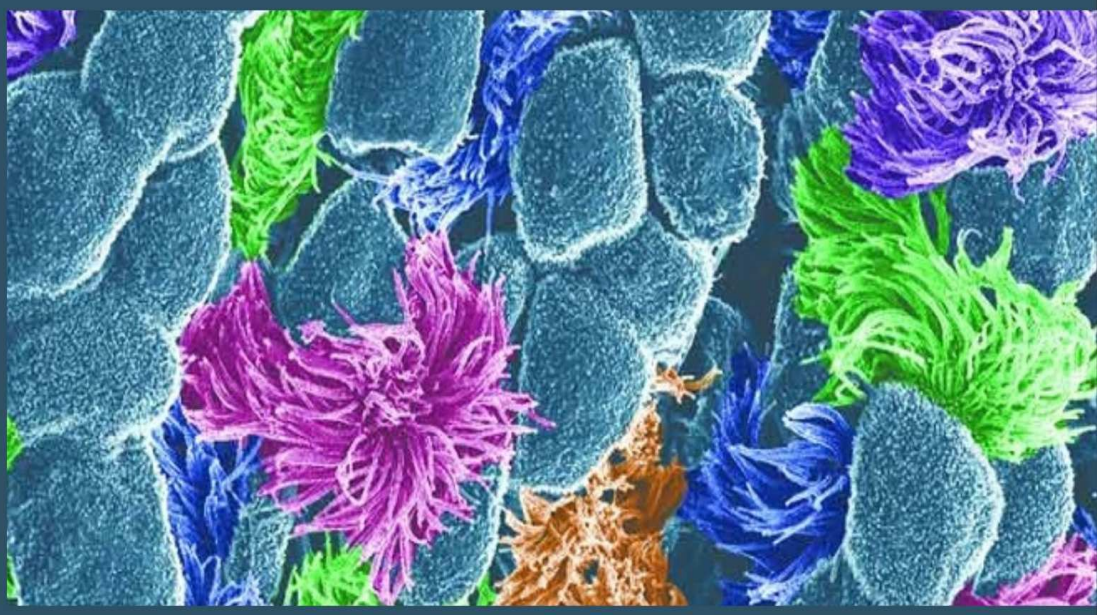

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ADENOCARCINOMA OF STOMACH PRESENTING AS CUTANEOUS BLEED AND MENORRHAGIA IN A YOUNG FEMALE

HARAMOHAN SAHOO*, YASHWANT KASHYAP**, RAVI TANDON***, BR VINAY****, TILAK VIJAY*****, MOHAN KUMAR******, MD FRAYAZ******* AND SAURABH NIGAM********

Declaration

The Declaration of the authors for publication of Research Paper in The Indian Journal of Research Anvikshiki ISSN 0973-9777 Bi-monthly International Journal of all Research: We, *Haramohan Sahoo, Yashwant Kashyap, Ravi Tandon, BR Vinay, Tilak Vijay, Mohan Kumar, Md Frayaz and Saurabh Nigam* the authors of the research paper entitled ADENOCARCINOMA OF STOMACH PRESENTING AS CUTANEOUS BLEED AND MENORRHAGIA IN A YOUNG FEMALE declare that , We take the responsibility of the content and material of our paper as We ourself have written it and also have read the manuscript of our paper carefully. Also, We hereby give our consent to publish our paper in Anvikshiki journal , This research paper is our original work and no part of it or it's similar version is published or has been sent for publication anywhere else.We authorise the Editorial Board of the Journal to modify and edit the manuscript. We also give our consent to the Editor of Anvikshiki Journal to own the copyright of our research paper.

Abstract

Gastric carcinoma mostly affects older people and is uncommon before the age of 40. It has a male preponderance. Bone metastasis in this cancer is rare. Presentation as ecchymosis and menorrhagia in a patient of gastric carcinoma is quite astounding. We report here a case of a 36 year female with gastric carcinoma presenting with multiple ecchymotic patches over the body, menorrhagia and metastasis to bone marrow.

*Key Words:*Young female, Gastric carcinoma, Bone metastasis.

Introduction

Gastric carcinoma is one of the frequently encountered gastrointestinal malignancies. It generally spreads to peritoneal surface, liver, and lymph nodes. Bone metastasis occurs in only 0-17% of cases[1]. But the usual presentation, so far reported in cases with bone metastasis, is mostly the bony pain. We present here an unusual case of carcinoma of stomach metastasising to bones but presenting with ecchymosis and menorrhagia.

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Case Report

A 30 year old lady was admitted with the history of multiple ecchymotic patches over the body for 10 days and increased bleeding per vaginum in her ongoing menstrual cycle for 5 days. There was no history of hematemesis, malena, bony pain, decreased appetite or loss of weight. On clinical examination pallor was present. There were multiple ecchymotic patches all over the body. There was no hepato-splenomegaly. Initial investigations revealed Haemoglobin of 7.0 g/dl, WBC count of 7200/mm^3, Platelet count of 36,000/mm^3. Alkaline phosphatase was markedly elevated (1317U/L). Hepatic and renal functions were normal. Peripheral smears revealed normocytic normochromic anaemia with thrombocytopenia. Patient was transfused with platelet concentrate and packed RBC. After this the bleeding stopped. Bone marrow aspiration was a dry tap.Clot section showed two clusters of metastatic mucin secreting adenocarcinoma cells.A bone marrow biopsy was performed which revealed a cluster of metastatic mucin secreting adenocarcinoma cells. Endoscopy wassubsequently performed for upper and lower GI tract. Upper GI endoscopy revealed a deep irregular ulcer present in the corpus just proximal to antrum and the base of the ulcer was covered with necrotic tissue. Biopsy of the ulcer was done which suggested diffuse adenocarcinoma of stomach on histopathology. CECT abdomen and chest showed metastatic deposits in liver, lungs, and celiac,periportal, hepatogastric and retroperitoneal lymph nodes. Patient was then planned for chemotherapy in the department of medical oncology.

Discussion

Gastric carcinoma is rare before the age of 40 but its incidence steadily climbs thereafter and peaks in the seventh decade of life. Metastasis to bone is an uncommon presentation in gastric carcinoma[2]. In case of bony metastasis the usual presentation is bony pain. But clinical presentation asecchymosis and menorrhagia, as in our case, is extremely rare. Review of literature suggests that gastric carcinomacan spread to bone due to rich supply of blood capillaries in gastric mucosa[3]. And due to bone marrow involvement it can present as depression of hemopoiesis resulting in pancytopenia/bicytopenia/ isolated single lineage cytopenia.But whenever there is bone metastasis in gastric carcinoma, there is always a raised serum alkaline phosphatase as observed in various case reports[4,5,6]. There are a few cases reported in gastric carcinoma patients presenting as cytopenia (Table 1);

STUDY	CLINICAL PRESENTATION	HB (g/dl)	TLC(cells/ cmm)	PLT(cells/cmm)	ALP(U/L)	CYTOPENIA
1.Mladen Mimica et al[5]	a.Backache b.Loss of apetite c.weight loss	8.7	normal	31,000	708	Pancytopenia
2.Ambikavathy Mohan et al[6]	a. loss of apetite b.generalized weakness c. backache	5	4,000	80,000	2,400	Bicytopenia
3.Ahmet SiyarEkinci et al[4]	1. case 1 2. case 2 3.case 3,4,5	↓Hb ↓Hb		↓PLT ↓PLT ↓PLT	781 1523 1783, 628,524	Bicytopenia Single lineage cytopenia Bicytopenia
4.Our case	a.multipleecchymotic patches over body b.menorrhagia	7.0	7200	36,000	1317	Bicytopenia

[TABLE 1; HB- haemoglobin, TLC- total leucocyte count, PLT- platelet count, ALP- Alkaline phosphatase]

Conclusion

Gastric carcinoma presenting as ecchymosis and menorrhagia is difficult to diagnose clinically. However presence of bleeding manifestation with cytopenias in complete blood count with an isolated raised Alkaline Phosphatase should raise a suspicion of an occult metastasis to the bone marrow with a silent primary.

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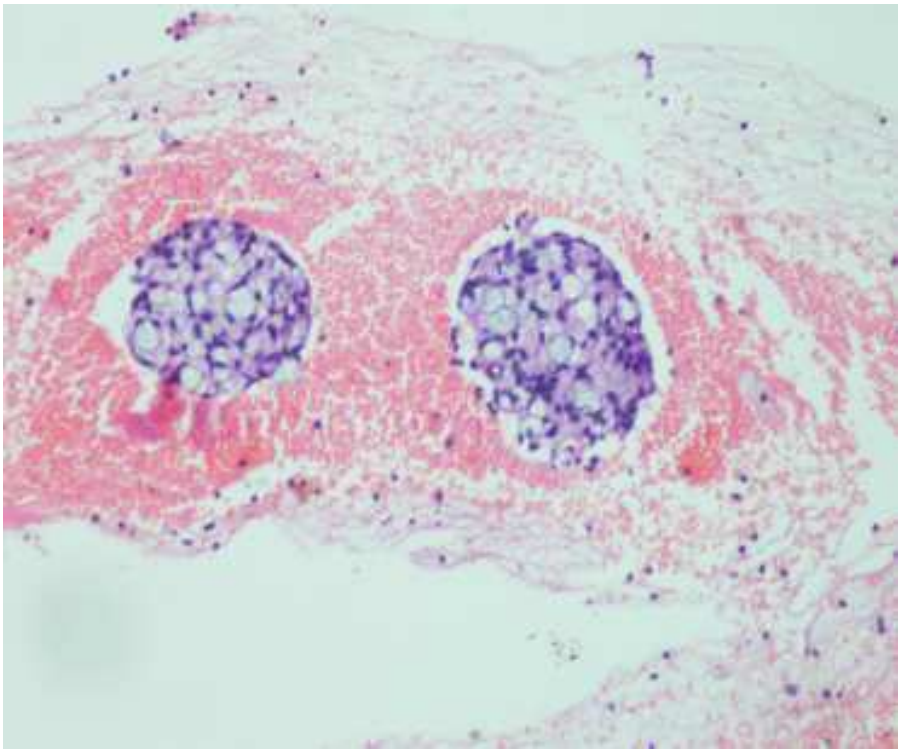
Figures

Figure 1

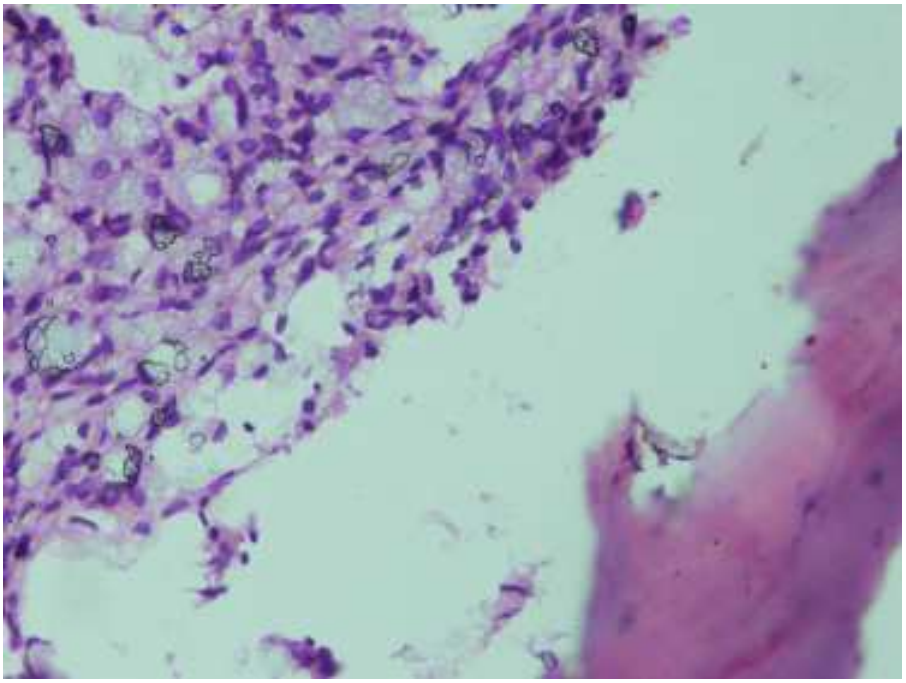
[The patient with ecchymotic patch on right arm]

Figure 2



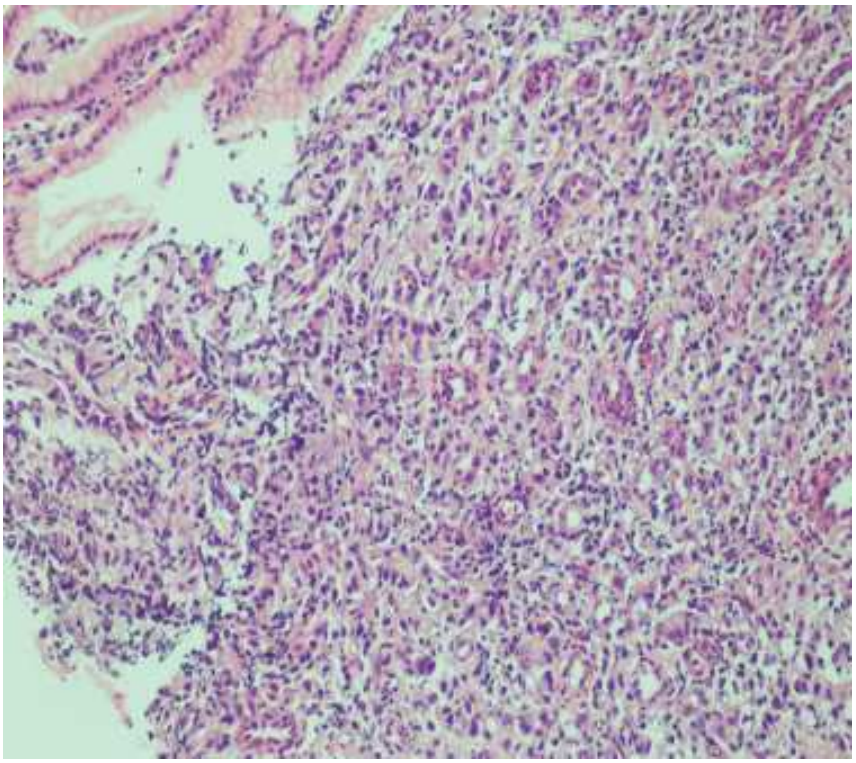
[Clot section shows two clusters of metastatic adenocarcinoma cells H&E200X]

Figure 3



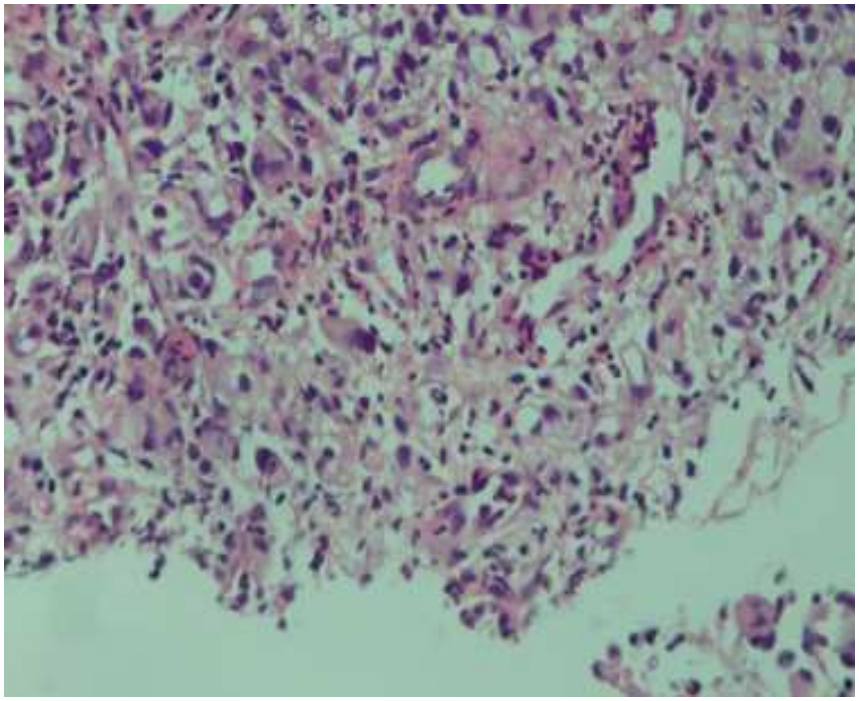
[Trephine biopsy from posterior superior iliac spine showing metastatic mucin secreting adenocarcinoma cells in the intertrabecular space H&E 400X]

Figure 4



[Gastric biopsy; Normal gastric mucosa with diffuse infiltration with signet ring cells H&E 200X]

Figure 5



[Gastric biopsy; diffuse infiltration with signet ring cells H&E 400X]

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LAPAROSCOPY VERSUS OPEN LAPAROTOMY IN ADHESIVE SMALL BOWEL OBSTRUCTION

Dr. DP Singh* AND Dr. Sharadendu Bali**

Declaration

The Declaration of the authors for publication of Research Paper in The Indian Journal of Research Anvikshiki ISSN 0973-9777 Bi-monthly International Journal of all Research: We, *DP Singh and Sharadendu Bali* the authors of the research paper entitled LAPAROSCOPY VERSUS OPEN LAPAROTOMY IN ADHESIVE SMALL BOWEL OBSTRUCTION declare that , We take the responsibility of the content and material of our paper as We ourself have written it and also have read the manuscript of our paper carefully. Also, We hereby give our consent to publish our paper in Anvikshiki journal , This research paper is our original work and no part of it or it's similar version is published or has been sent for publication anywhere else.We authorise the Editorial Board of the Journal to modify and edit the manuscript. We also give our consent to the Editor of Anvikshiki Journal to own the copyright of our research paper.

Introduction

Acute intestinal obstruction is a very common surgical emergency and the small intestine is the most common site for obstruction . The scar tissue formed by the previous surgery is the commonest cause both in the developing and developed countrie[1]. Scar tissue formed by previous surgery manifests as adhesions involving the peritoneal surfaces[2]; adhesions may also develop between any two surfaces during the healing process, adjacent solid organs, the intestine, fallopian tubes, omentum or the abdominal wall. Post operative adhesive obstruction is associated with poor quality of life & very high morbidity which predisposes to repeated hospital admissions to relieve the agony. It is observed that quite a good numbers of patients develop bowel obstruction after abdominal surgery and it seems to be an inevitable complication.[3]

There is no perfectly effective remedy in the literature to prevent these adhesions. Although much effort has been made but there is as yet no sure shot remedy to prevent this catastrophy. After multiple laparotomies the incidence of adhesions increases many folds. So adhesions place a lifelong risk of complications in any individual patient. Lower abdominal and pelvic surgeries like appendicitis, colorectal operations and gynecological interventions lead to more obstructions due to adhesions than upper GI surgeries .It results into acute, sub- acute or chronic small bowel obstruction. There are conservative and operative procedures to relieve the obstruction. Delays in surgical treatment will result in increased mortality and morbidity. But repeated operations will also increase adhesion formation

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with increased severity[6]. The patient may be treated conservatively with nothing orally, repeated nasogastric suctions, IV fluids, electrolyte supplements. Water soluble contrast can also be tried safely as this will act therapeutically as well establish the diagnosis. If the dye appears in the colon within twenty four hours of administration, it denotes resolution of obstruction .The dye can be given orally or with a Ryle's tube which is already placed into the stomach at the time of admission .The oral dye is quite safe .It gives time for release of obstruction and surgery be planned for later . The maximum time for waiting without surgery should not be prolonged for more than seventy two hours. Within this time decision for operation or conservative treatment should be finalized without fail During this period the patient and the surgeon can plan a cool surgery with good recovery, shorter hospital stay, and clean surgery with less contamination of abdominal cavity and so less chances of postoperative adhesion formation.

Many methods have been described in surgical literature to reduce and prevent adhesions formation but nothing succeeded fully. The adhesions formation is the inherent character of tissue repair process produced by inflammatory reaction .Open surgery produces more tissue trauma and so produces more degree of inflammatory tissue repair as compared to laparoscopic operations[7,8]. Certainly there is less tissue handling & damage in laparoscopic surgery[10], hence also called minimally invasive surgery. The laparoscopic surgery is widely used these days due to this very reason to reduce operative time, cause less tissue handling& less tissue trauma. Laparoscopic adhesionolysis can be used in cases of acute and chronic bowel obstruction. Not much prospective studies are there in the literature .We have done a retrospective study in our institution for the laparoscopic adhesionolysis in comparison with open surgery in cases of small bowel obstruction .

Aim of study

The aim of present study was to find most suitable procedure open surgery or laparoscopy to relieve the acute adhesive small bowel obstruction and late adhesion formation

As described in various surgical literature the most preferred conventional method had been open surgical procedure without any choice since this was the only method available at that time .But now as laparoscopy is also available and fully developed, it has also been utilized[13] .Now most of the present day surgeons all over the world are quite expert in this job of laparoscopy including SILS (single incision laparoscopic surgery) and Robotic surgery.

When contemplating to use laparoscopy we planned our mission on some time tested notions. We divided the patients in following categories and the methods to be used.

Criteria for Open surgery[3,4]

1. Age more than 45 years
2. Two or more surgical abdominal interventions
3. Prolonged preoperative period (appearance of pain and hospital admission more than 24 hours later).
4. Deteriorating patient as noticed on BP, Pulse, Respiratory rate, abdominal pain and distension abdomen.

Laparoscopic intervention

1 Young patient less than 45 yrs of age

2 Early presentations within 24-48 hours
3 haemodynamically stable patient
4 Two or one previous surgery

Open surgical technique

The conventional method of surgery adopted was as follows. Incision is made in the abdomen away from the previous scar, abdomen opened and abdominal cavity is inspected. Any abdominal fluid cleaned with suction catheter. Small intestine is examined carefully to find the site of obstruction . Adhesions removed carefully, patency of the gut checked, if any constricting band found it is released. Gangrenous and non viable bowel resected and anastomoses were done. The raw area on gut wall was patched with omentum. Thorough peritoneal lavage was given with normal saline and the abdominal cavity was mop dried as standard surgical procedure .Abdomen closed in single layer with pds loop or prolene .

Laparoscopic method

The operative technique has a major role for the successful outcome of the laparoscopic surgery[5]. Also the experience of surgeon is very crucial .In our institution the operating surgeon and his team was dexterous in laparoscopic surgery with an experience of more than five years. After doing CT scan and USG, the safe site for initial trocar was placed in the left upper quadrant, left iliac region or left flank according to the speculation of abdominal adhesion. These sites seemed appropriate to examine the ileocaecal junction in right iliac fossa and the whole small intestine. These sites, for port placement gave maximum angulations in exploration of small gut.

Materials and Methods

We have taken sixty patients of small bowel obstruction and chronic pain abdomen who presented in our hospital in Accidents and Emergency department with previous abdominal surgery[15] . These patients presented with acute abdominal pain, nausea and vomiting, distension of abdomen and absolute constipation. Detailed history was taken. Complete general physical and systemic examination was done. Examination of abdomen was done meticulously. All the routine investigations including hematological, liver function, renal profile, X-ray abdomen a chest, CT abdomen and USG were carried out.

Initially patients were kept nil orally with nasogastric aspiration at a rate of one hourly. IV fluids Ringer' lactate, normal saline, antibiotics were given. This conservative treatment was given till the patient was stabilized haemodynamically to be fit for emergency operation. During this period close watch on pulse, BP, abdominal distension and severity of pain, nausea vomiting and bowel movement was kept. Oral contrast was not tried due to fear of increase in severity of acute obstruction as stated in the literature. Patient presenting with sign and symptoms of acute obstruction which were thought not be relieved by conservative management were operated surgically or laparoscopically[11] .The criteria for open and laparoscopy surgery was as already discussed in previous paragraphs. Thirty patients were chosen for each category of surgical procedure.

Among sixty patients twenty seven were treated with open laparotomy, twenty three with laparoscopy and ten were treated conservatively. We used the Hasson's open approach to place the first trocar in

left flank thinking it to be the most suitable site for abdominal entry and best possible angulations for instruments.

Analysis of study

There were 42 female and 18 male patients clearly showed more incidence of diseases of in female population.

1. Age;

Age range	No. of Patients
10-20	2
20-30	17
30-40	19
40-50	14
50-60	6
60-70	2

In our study the maximum incidence was in the younger and middle age group .This age is the most productive age in the life of a person.

2. Time elapsed for presentation to hospital due to adhesions formation;

2-4 yrs	6
4-6 yrs	19
6-8 yrs	11
10-12 yrs	13
12-14 yrs	7
14-16 yrs	3
16- 18 yrs	1

Thus the adhesions formed maximally 4-12 yrs after initial surgery .

3. Common diseases producing adhesive obstruction[14]. These were the diseases which produced adhesive obstruction in our series:-1. In young male patients the most common previous surgery was acute appendicitis 2. The other operation was for cholecystectomy 3. The congenital band adhesion was the least.4. In female and young patient it was caesarian section and cholecystectomy 5.In older patients it was hysterectomy, cholecystectomy and caesarian section.

4. Pattern of symptom presentation. All the patients presented with abdominal pain and distension. Forty nine patients presented with vomiting .There were 8-12 episodes of vomiting preceding and during pain. All the patients were nauseated and constipated.

Acute v/s sub acute obstruction. Out of the sixty patients, twenty three patients presented with acute onset without any previous complaint. Twenty eight were suffering from chronic & subacute obstruction which was treated conservatively and nine had features of chronic pain abdomen only. All the patients had nausea and absolute constipation.

Complications and Results

Total fifty patients were treated surgically either open laparotomy or laparoscopically, ten patients were managed conservatively, the following complications were noted in our series.

a) Out of twenty seven laparotomies seven patients had thick fibrous adhesions which were tenacious, and difficult to release .During releasing of tight ,fibrous adhesions there was perforation in bowel in seven cases , primary closure of the perforation was done in two layers.
b) In twenty three patients of laparoscopic adhesionolysis, in four cases adhesions were very thick and difficult to release, so we have proceeded with open surgery and adhesions were released. So the conversion rate was roughly seventeen percent[16].
c) Among fifty patients, in five patents we had to do resection and anastomoses due to stricture and tight adhesion. All these patients fared well after operation.
d) Other major complications like anastomotic leak and dyselectrolemia ,respiratory problems ,prolonged paralytic ileus did not occurr due to meticulous management in surgical intensive care unit of our hospital.
e.) Open surgical patients were allowed orally seventy two hours after surgery ,semi-solid food was started one day after this as usual practice in our hospital. All patients were discharged on seventh to tenth day of admission.
d.) In laparoscopy group bowel movements came earlier within thirty six hours to forty eight hours, liquid sips and water allowed with in forty eight hours , clearly earlier than open surgery[15].
f.) After six months of follow up, forty six patients visited regularly and none developed post-operative adhesions except minor complaints pain abdomen which was relieved with oral medicines . Four patients did not turn up reasons not known.

Inference

1. Previous abdominal operations was the most common cause of acute intestinal obstruction[7].
2 laparoscopic abdominal surgeries were least responsible for post operative adhesions.
3 The adhesions causing obstruction was more in the younger age i.e. between 20-40 yrs., most common symptoms were nausea, vomiting and pain abdomen and distension abdomen.
4. Laparoscopic adhesionolysis took less operative time, minimal post operative problems, early feeding, early discharge from hospital, less expenditure on medicines and disposables.
5. To prevent further post operative complication laparoscopic surgery may come out to be more effective method, rather method of choice in early presenting patients and uncomplicated cases.

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DENTURE RELINING – BOON FOR DENTURE PATIENTS

Dr. Rajul Vivek*

Declaration

The Declaration of the author for publication of Research Paper in The Indian Journal of Research Anvikshiki ISSN 0973-9777 Bi-monthly International Journal of all Research: I, *Rajul Vivek* the author of the research paper entitled DENTURE RELINING – BOON FOR DENTURE PATIENTS declare that , I take the responsibility of the content and material of my paper as I myself have written it and also have read the manuscript of my paper carefully. Also, I hereby give my consent to publish my paper in Anvikshiki journal , This research paper is my original work and no part of it or it's similar version is published or has been sent for publication anywhere else. I authorise the Editorial Board of the Journal to modify and edit the manuscript. I also give my consent to the Editor of Anvikshiki Journal to own the copyright of my research paper.

Abstract

Complete and partial removable dentures can become ill-fitting. This can be due to alveolar ridge resorption, wear and damage to the denture base, among others. Chairside denture relining or repairing broken areas can correct many of these problems. Chairside procedures provide immediate resolution, avoiding the edentulous period of time accompanying laboratory relines.

This paper will discuss the various technique and material for denture relining.

Keywords; Denture Relining, repairing, Denture Liners

Introduction

When residual ridge resorption occurs, dentures tend to become loose. For most patients, denture relining is an economical means of improving a denture's stability and retention, the overall occlusal vertical dimension and, in some cases, facial appearance. Although improvements in retention, stability and occlusion do not always improve chewing efficiency.[1]Materials are used for relines, repairs, border extensions and immediate dentures. These materials should accurately adapt to the denture-bearing surface, be highly polishable, demonstrate low heat generation during intraoral curing and have high mechanical strengths. They should also have easy handling and minimal chemical irritation, odor or taste. This article outlines numerous techniques for improving relining procedures and materials

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Denture Relining Techniques

There are two main methods of relining dentures: the direct (chair side) method and the indirect or processed method (subdivided into the impression and functional impression techniques). In general, the indirect method has been preferred and most frequently taught in dental schools.[2]However, no long-term studies have compared the outcomes of the two methods. There are times and cost savings with the chair side method. There are no long-term studies comparing differences in outcomes between the impression technique and the functional impression technique.

No matter which relining technique is used, it is virtually impossible to place a denture filled with impression material in exactly the correct position.[3]Failure to properly position the denture in three dimensions can result in unwanted changes in the amount of incisal display, the degree of lip support and/or the occlusal contact relationships. The most common errors tend to be having the denture seated too far anteriorly or inferiorly when making the impression [3] which results in an increase in vertical dimension and/or change in denture orientation. These errors can be minimized by using a low-viscosity elastomeric impression material or tissue conditioner.[3]

Considerations for the Selection of Lining Material

Denture reline materials play a key role in modern removable prosthodontics.[4] The criteria for application of a reline material include poor stability and inadequate retention; reduction in vertical dimension; degradation of the denture base; loss of support between the denture and alveolar ridges; improper extension of borders into muccobuccal fold regions; and mucosal irritation.[5] The demand for successful treatment with complete and removable partial dentures (RPDs) has provided the clinician and technician with a plethora of simplified "one-visit" lining materials. Therefore, it is understandable that clinicians have uncertainties about the selection of materials and techniques to achieve optimal results for denture relining procedures.

The clinical consideration for the selection of a denture lining material becomes a function of the properties of the material and the specific clinical situation. The fundamental properties that provide guidelines for acceptability for a clinical situation include hardness, water sorption, and water solubility. A high water sorption and solubility of a lining material can reduce mechanical properties such as hardness, fatigue limit, and transverse strength.[6,7,8] An increase in the values of these mechanical properties can result in dimensional change, separation from the denture base, and discoloration.[9]

An ideal lining material should possess the following characteristics :

- High shear bond strength to denture base materials
- Superior resistance to stain
- Low water sorption
- No soluble components (low solubility)
- Colour stability
- Optimal hardness for specific lining material
- High fatigue limit
- Increased transverse strength
- Minimal dimensional change during polymerization (dimensional stability)
- Ease of finishing
- Abrasion resistance
- Tissue compatibility
- Absence of taste and odour

- Low exothermic temperature release

Soft Denture Liners

Soft denture liner materials have become an asset to the technician and clinician because of their viscoelastic properties.[10,11,12] These materials act as shock absorbers and tissue conditioners that can reduce and distribute occlusal forces to the underlying oral structures during function while enhancing patient comfort.

Hard Denture Liners

Hard denture liners are generally used in prosthetic dentistry to reline immediate dentures, for selected RPDs, and for interim dentures until a final denture is completed.[13] Hard liners can be used when there is an adequate residual ridge, resilient mucosa, and mature and healthy supporting structures. These materials should be selected for the treatment of an unstable and ill-fitting denture.

Conclusion

Knowledge and a desire to create are limited by the products clinicians have available to them for restorative procedures, and knowledge must be integrated with the proper selection of material and technique for each clinical situation. Maintaining the balance between function, comfort, and esthetics with removable and complete dentures requires periodic clinical evaluation and long-term maintenance. However, it is the task of our profession to provide our patients with functional, comfortable and aesthetic removable prostheses. Chair side denture relining is a highly effective, successful treatment that can achieve these goals.

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DENGUE WITH HYPOKALAEMIC MOTOR QUADRIPARESIS

HARAMOHAN SAHOO*, BR VINAY**,YASHWANT KASHYAP***, RAVI TANDON **** AND ASHISH KUNWAR SINGH*****

Declaration

The Declaration of the authors for publication of Research Paper in The Indian Journal of Research Anvikshiki ISSN 0973-9777 Bi-monthly International Journal of all Research: We, *Haramohan Sahoo, BR Vinay, Yashwant Kashyap, Ravi Tandon and Ashish Kunwar Singh* the authors of the research paper entitled DENGUE WITH HYPOKALAEMIC MOTOR QUADRIPARESIS declare that , We take the responsibility of the content and material of our paper as We ourself have written it and also have read the manuscript of our paper carefully. Also, We hereby give our consent to publish our paper in Anvikshiki journal , This research paper is our original work and no part of it or it's similar version is published or has been sent for publication anywhere else.We authorise the Editorial Board of the Journal to modify and edit the manuscript. We also give our consent to the Editor of Anvikshiki Journal to own the copyright of our research paper.

Abstract

Dengue is a mosquito borne arbo viral disease. It is a major public health problem in the tropical and sub-tropical countries, including India. Its presentation varies from an acute self-limiting febrile illness to life threatening hemorrhagic shock syndrome leading to death. Neurological manifestations are uncommon and limited to case reports only, most common being encephalitis, acute disseminated encephalomyelitis, gullainbarre syndrome. Hypokalemicquadriparesis is extremely rare. We present here a case series of two patients of pyrexia due to Dengue virus infection presented with acute onset quadriparesis due to hypokalemia which recovered completely following adequate management without any residual neurological deficit.

Key Words: dengue, hypokalemia, quadriparesis

Introduction

Dengue is one of the most common arboviral , mosquito borne infection prevalent in the tropical and sub-tropical climate in the rainy season. Usually it presents as classical dengue fever, dengue hemorrhagic fever (DHS), dengue shock syndrome (DSS). Neurotropism in dengue infection seems to be rare. However, in past few case reports have described encephalitis, acute disseminated encephalomyelitis,

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transverse myelitis, gullain-barre syndrome. We present here two cases of dengue fever with hypokalemic pure motor quadriparesis which is an extremely uncommon presentation.

Case Report

CASE I; A 28 year male presented to the hospital with high grade fever for 3 days and weakness in both legs and hands for 1 day. Fever, which was associated with severe bodyache, responded to antipyretic medication. Weakness started a day after the onset of fever which initially manifested in both the lower limbs and progressed within a span of 6hours involving whole of the body below neck.

CASE II; A 17 year male presented to the hospital with high grade fever for 2days. Fever was not associated with chills and rigor but was associated with severe myalgia. During the course of the hospital stay one evening patient developed weakness in both the legs simultaneously which involved the upper limbs and the trunk till morning.

In both the cases there was no history suggestive of any sensory and bowel bladder involvement. History of any recent vaccination, diarrhoea, vomiting, recent vigorous exercise or heavy carbohydrate meal was absent. There was no past or family history of such illness.

On examination :

PARAMETERS	CASE I	CASE II
1.vitals	Stable	Stable
2.power in both upper and lower limbs	1/5	2/5
3.reflexes	Diminished	Diminished
4.cranial nerve involvement	Absent	Absent
5.sensory deficit	Absent	Absent

On investigation :

PARAMETERS	CASE I	CASE II
1.Hb	13.3	14
2.TC	4600	2500
3.DC	N48 L44	N47 L45
4.PLT	60,000	25,000
5.Sr k+	1.89	2.1
6.Sr Na+	145	143
7.pH	7.41	7.39
8.Anion Gap	15.6	14.4
9.SGOT	112	128
10.SGPT	84	78
11.ECG Changes	ST-depression, u waves	ST-depression
12.NCV	Normal	Normal
13.ANA	-ve	-ve
14.Dengue check	NS1 Ag+ve, later dengue IgM+ve	NS1 Ag+ve at admission, later dengue IgM+ve

Both the patients were managed conservatively with plenty of fluids and antipyretics with a close watch on haematocrit and platelet count. The motor paralysis improved dramatically after the administration of k+ supplements enterally and parenterally. Within 24 hours serum k+ was found to be within normal limits with complete neuronal recovery. Both the patients got discharged with no residual neurological deficits.

Discussion

Dengue was considered to be a non-neurotropic virus. However, there are few case reports suggestive of neurological manifestations in dengue infection[1,2].Hiraet al[3]. described 12 cases motor weakness in dengue fever out of which 10 had hypokalemic weakness, 1 had GBS, 1 had myositis. Vermaet al.[4] described a case of quadriparesis due to cervical spinal cord compression in a patient of dengue hemorrhagic fever. There are cases of hypokalemia in dengue fever but presentation as a acute pure motor flaccid paralysis owing to hypokalemia in dengue fever is exceedingly rare. The proposed mechanisms of hypokalemia in dengue are due to redistribution of k+ into cells or transient renal tubular abnormalities leading to increased urinary k+ loss[5]. Redistribution of k+ may be due to increased catecholamine levels in response to stress of infection and secondary insulin release[5]. However, these are proposed hypothesis and need evidence based scientific confirmation.

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LOTUS — THE SACRED INDIAN KAMAL : LEGENDS, GERMINATION , PROPAGATION, AESTHETIC AND MEDICINAL USES

Dr. Sharadendu Bali*

Declaration

The Declaration of the author for publication of Research Paper in The Indian Journal of Research Anvikshiki ISSN 0973-9777 Bi-monthly International Journal of all Research: I, *Sharadendu Bali* the author of the research paper entitled LOTUS — THE SACRED INDIAN KAMAL : LEGENDS, GERMINATION , PROPAGATION, AESTHETIC AND MEDICINAL USES declare that , I take the responsibility of the content and material of my paper as I myself have written it and also have read the manuscript of my paper carefully. Also, I hereby give my consent to publish my paper in Anvikshiki journal , This research paper is my original work and no part of it or it's similar version is published or has been sent for publication anywhere else. I authorise the Editorial Board of the Journal to modify and edit the manuscript. I also give my consent to the Editor of Anvikshiki Journal to own the copyright of my research paper.

The Lotus plant and flower, botanically called Nelumbo nucifera, grows in warmth and hence is most commonly seen in the regions of south-east Asia and India. It is the national flower of India[1], and enjoys immense social regard among the societies of China and the south-east Asian countries. Numerous legends are attached with the beautiful flower of lotus, and it is associated with numerous gods and demi-gods of the the Hindu, Jain and Buddhist pantheon.

Legends

The goddesses Lakshmi and Saraswati are often depicted standing or sitting upon a giant pink lotus flower[2]. Brahma the Creator is shown appearing from a lotus flower growing out of the navel of Lord Vishnu[3]. The flower is offered to the great god Shiva as oblation onto his lingam[4]. Thus the lotus is associated with the *tri-murti* of Indian mythology. Another wonderfully beautiful flower is named after the Lord Brahma as *Brahm-kamal*, though this flower which grows on the earth at heights of over 13,000 feet is another plant, Saussurea obvallata[5]. This latter golden hued flower is also reverentially offered to lord Shiva in prayer, and is said to have been instrumental in the transplantation of an elephant head onto Lord Ganesh[6].

The blue water lily, Nymphaea caerulea, is sacred in Egypt, and is sometimes referred to as the blue Egyptian lotus of the Nile[7]. Similarly, the white Egyptian lily , Nymphaea lotus ,is sacred in Egypt and is associated with numerous legends. The lotus/lily is also reverred in other parts of south-east Asia,

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eg.the Nymphaea nouchali or N.stellata (blue colour)is the national flower of Sri Lanka and Bangladesh[8]. This blue lily (*niil kamal*) is also sacred in India to the Godess Durga and is offered to her in prayer. Thus, it may be said that in the general public consciousness, the lotus and lily are considered part of the same family, though not botanically.

Plant Parts

In Indian folk-lore, every part of the lotus plant has a distinct name. The whole plant with flowers is known as *Padmini*, the rhizome is known as *kamalakand*/ *bis*/*kamalkakri*/*bhe*, the tender leaves as *sambartika*, the peduncle as *mrnal* or *visa*, the stamens as *kinjalka*, the torus as *padmakcsa*, the seeds as *karnika*; and the honey formed by bees feeding upon *padma* is known as *makaranda*[9].

The Lotus in Sculpture and Art

The lotus entered into Indian art of all ages and all religions as a conspicuous decorative element. The flower is frequently seen on Buddhist monumemts from the era before Christ. The most striking example is exhibited in the figure of Goddess Lakshmi in the Buddhist sculpture at Udaigiri, Sanchi, where it is frequently repeated on the gateways of the great Stupa[9]. Yogis have used the symbolism of the lotus flower to depict various *tantric* poses and concepts,eg the *padma-asana*.

Most major palaces and buildings of medieval India, eg. in Jaipur and other parts of Rajasthan, have adornments of lotus. Most images of the Goddess Saraswati are seen with the goddess sitting on the lotus flower. For the Sanskrit poets of ancient India, the lotus is the emblem of beauty, to which they constantly compared the beauty of their heroines. In Kumara-sambhava, Kalidasa has compared the arms of Parvati with *mrinal*, *mrnal* being the peduncle of lotus flower[10].

The strongly supportive rib structure of the lotus leaf has proved to be an inspiration for construction of large domes of stadiums, eg. the Olympic stadium in Munich. The lotus flower also provides the basic shape of the Bahai temple in New Delhi and the Opera house of Sydney.

Seed Quality and Embryonic Cellular Repair

Ancient seeds have been found intact in the pyramids, dating back several centuries[11]. Such seeds upon being provided the right environment were able to germinate, testifying to the extreme hardiness and long-lived viability of the seeds. An approximately 1300-year-old lotus fruit, recovered from an originally cultivated but now dry lake-bed in northeastern China, is the oldest germinated and directly ^{14}C-dated fruit known[12]. The soil of the lake-bed from which these lotus fruit were recovered was found to have gamma-radiation of around 2.0mGy/yr(Gray, the unit of absorbed dosage defined as 1 joule/kg; 1Gy=100rad). The total g-irradiation of the old fruits thus works out to 0.1-3 Gy.

Though the chronic exposure of the old fruit to low-dose gamma radiation was probably responsible for the weak growth and mutant phenotypes of the germinated seedlings, it did not affect seed viability. This leads us to the conclusion that the ancient lotus seeds presumably repair cellular damage (due to g-radiation) before germination. Further studies into these repair mechanisms may provide insight into the ageing process applicable to other organisms.

Germination

The seed of the lotus (Nelumbo sp.) is a very hard nut and is almost completely impermeable to water. The seeds are either round and the size of a green pea or oval and the size of a shelled peanut. One end of the seed has a sharp point which is the remains of the floral stigma. On the opposite end is a tiny dimple , a remnant of where the seed was attached to the mother plant. The seed colour can vary from gray to dark brown or black. The shell is very hard and consists of two layers which are tightly bonded together. Inside the shell are two paper thin brown coloured seed coats which enclose the twin cream coloured cotyledons[13].

The extremely thick-walled and hardy seed of the lotus will not germinate easily like grain or legumes. A simple procedure can, however, achieve this easily. This consists of scouring / abrading the seed coat at one or two points– the sharp point or the dimpled end. This can be done simply rubbing the seed onto a sand-paper or on a metallic file. Since rubbing while holding the seed with fingers may be difficult and may injure the finger tips, the seed may be gently held with pliers. Scouring should be done gently on a fine file, and the rubbed area should be repeatedly inspected to check when the appropriate depth is reached. At first a shiny flat surface is produced, uniformly black in colour. As the rubbing proceeds, a thin white circular line will appear ; this indicates the breaking through of the junction between the two fused seed coats. At this point the abrading process should be stopped. Continued rubbing will eventually bring a cream coloured area into view ; As long as this cream coloured area remains just a minute point, it will still be satisfactory. But if the area suddenly brightens into a clear cream colour with a distinct edge, it means that the cotyledons are exposed. Such an abraded seed may not be able to germinate. (See Figure 1).

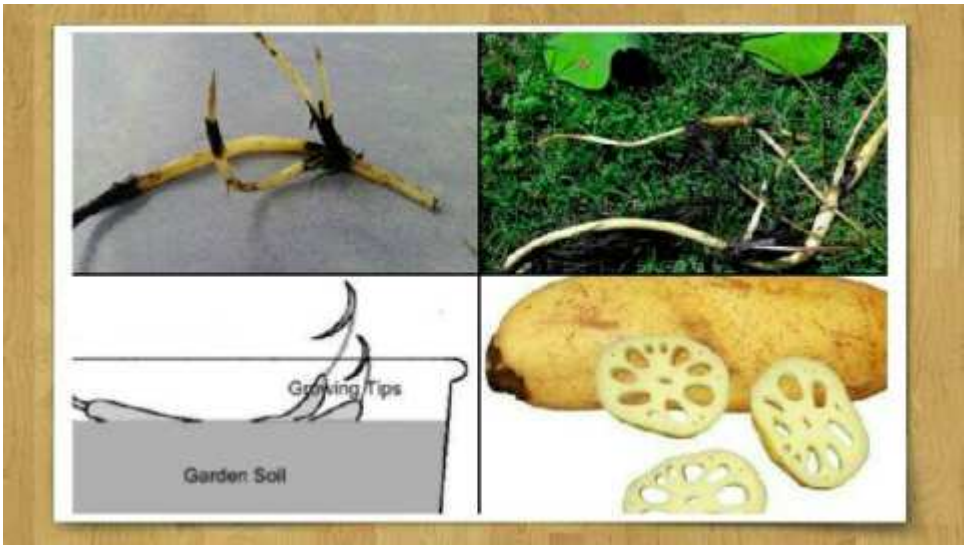
Once the seeds have been properly abraded, they are placed in a bowl or cup of fresh water at room temperature(summers). Ambient temperatures of around 30-35^{0}C are suitable for the germination process. The water should be changed every day ; after a few hours of soaking, the colour of the water becomes dark. Sometimes, the water becomes cloudy, which indicates bacterial / fungal overgrowth, and if this occurs, it may be better to transfer the seeds to a fresh bowl . Upon immersing in water, the seeds rapidly swell up because of imbibing water, and may become double the volume in a day or two.

After this rapid increase in size, there is a dormant period of a few days, usually 2-4. Those seeds that do not germinate within a week of immersion will probably never do so. Germination is heralded by the appearance of the seed splitting and a tiny embryo seen between the separated cotyledons. The

folded over stem soon grows out of the seed ,looking like a fish hook. After this happens, there is rapid growth in the length of the stem, and within 2-3 days, the stem straightens and becomes almost a foot long. So it is better to place the sprouted seeds into a deeper container when germination has occurred. The inrolled first leaf located at the tip of the stem unfurls at around the tenth day after germination, and by this time the second,third and fourth leaves will also have made an appearance. All these leaves emanate from a common node situated next to the seed. Root also start appearing around 10-12 days, and it is a good idea to plant the seedling before this happens to prevent damage to the fine roots. Planting can be simply done by digging a finger into the soil , gently placing the seed vertically into this pit and moving the adjacent soil over the seed. This should require two hands, and is a blind procedure as it is carried out usually underwater. But planting can also be done in wet soil if carried out in pots, subsequently filling the pots with water. Similar process can be adopted if rooting has occurred.

The first few leaves which form will float on the water surface, so the depth of water should be maintained around 6-12 inches. During the first year of growth, only leaves are produced , and flowers are generally not produced until the second year. The plant spreads horizontally under the soil surface by forming rhizomes, with one leaf forming at each internode. Side shoots may also arise from the internodes, allowing for lateral spreading. The leaves progressively increase in diameter, and are eventually lifted clear of the water surface. As winter approaches the plant starts appearing to wilt, and will ultimately seem to be dead; but this is only a phase of hibernation, and new leaves will sprout as soon as temperatures become warm again in spring. During winters, the rhizomes turn into resting thick tubers, and these tubers are much relished in India, Japan and China.

Lotus can also be grown from rhizomes or tubers, by the process known as vegetative reproduction. For this, a section of the underground rhizome is taken, taking care to note that the section has at least 2-3 “eyes”. The section is placed just barely covered by soil, with the growing tapering end almost breaking the soil surface. Water over the soil need only be minimal. Within a few days in warm temperatures, the growing end will sprout, and then a little more water depth can be maintained(1-3 feet). Growing lotus from rhizomes can yield flowers in the first year itself, while plants grown from seeds usually flower in the second growing season. (See Image 2).



Culinary Uses

The nutritious rhizome is a very popular foodstuff in Asian countries. The tuber is sliced into thin flat circles and pickled in North India. The tuber is also consumed as vegetable. Upon roasting, the seeds pop up like pop-corns , and are popularly used in India during fasting — known as *tal makhana*.

Medicinal Benefits

Asian cultures have for ages attached great medicinal importance to the lotus. Almost all parts are used as medicine. Chinese and Indian medical systems have in particular used lotus to ameliorate several disorders. The traditional use of Lotus in the treatment of loose stools, fungal infections, fevers and skin disorders are supported by western scientific investigation. Ancient lotus seeds have been found to contain an enzyme L-isoaspartyl methyltransferase which helps repair proteins and is postulated to play a role in anti-ageing. The latex sap found within the leaves, stems, and flowers has great anti-bacterial activity and has been used to treat sexually transmitted diseases such as gonorrhea and syphilis, as well as other bacterial infections[14].

The astringent qualities of lotus make it efficacious in piles, diarrhea, dysentery and cholera, and it has been used for these conditions in folk medicine for long. The following " folk wisdom " was noted in the Kew online papers :

Roots and rhizomes : In treating smallpox, throat conditions, loss of skin pigmentation, cough, diarrhea and dysentery. The rhizomes when boiled in sesame oil (*til* in Hindi) is cooling for the head and eyes when rubbed on the scalp.

Leaves and stems : Many preparations made from these parts are used to treat haemorrhoids, leprosy, parasitic infestations and vomiting.

Flower : Various parts are used eg. petals,stamens,peduncle. Decoction of dried flowers is made into a syrup to treat coughs. Other conditions treated are diarrhoea, cholera, liver disorders, fevers, bronchitis, skin eruptions, snakebites and scorpion stings.

Fruits and seeds : Utilized to soothe inflamed mucous membranes, lower temperature in fevers, and alleviate halitosis. Seeds taken orally with a rice wash for seven days are beneficial in promoting female fertility.

Lotus finds several mentions in the ancient Ayurvedic texts, like Sushrut and Charak Samhitas, and in the Nighantus(pharmacopoeas). In these texts it has been described as sweet, cooling, astringent, and useful in suppressing increased *kapha* and *pitta*. Lotus is also considered as aphrodisiac and nervine tonic, good for eye diseases and blood impurities, improving the complexion and curative of cutaneous infections.[15]

The medicinal effects of lotus have been assessed in a modern scientific way over the past four decades. Studies carried out at Benares Hindu University using *kamalakanda churna* found beneficial effects in cases of dysfunctional uterine bleeding[16]. Studies carried out in the Pharmacology department of BHU also revealed that the drug possesses a powerful CNS depressant activity.

Recent studies carried out in Thailand, China and india have shown significant effects in conditions like obesity, hyper-lipidemia and diabetes.

Lotus is thus a plant with great economic and health significance, and it is no wonder then, that it is reverred in the Orient and is the national flower of India.

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IN-SILICO PREDICTION OF DRUG TARGETS, MODEL STRUCTURE AND ACTIVE SITE *BACILLUS ANTHRACIS* AMES STRAIN

NEELAM* AND DR. P. KATARA**

Declaration

The Declaration of the authors for publication of Research Paper in The Indian Journal of Research Anvikshiki ISSN 0973-9777 Bi-monthly International Journal of all Research: We, *Neelam and P. Katara* the authors of the research paper entitled *IN-SILICO* PREDICTION OF DRUG TARGETS, MODEL STRUCTURE AND ACTIVE SITE *BACILLUS ANTHRACIS* AMES STRAIN declare that , We take the responsibility of the content and material of our paper as We ourself have written it and also have read the manuscript of our paper carefully. Also, We hereby give our consent to publish our paper in Anvikshiki journal , This research paper is our original work and no part of it or it's similar version is published or has been sent for publication anywhere else.We authorise the Editorial Board of the Journal to modify and edit the manuscript. We also give our consent to the Editor of Anvikshiki Journal to own the copyright of our research paper.

Abstract

Drug target identification is the major thrust of current bioinformatics by mining andwarehousing of host and pathogen genome sequences which is responsible for coding of drug target proteins against which drug can be designed. "B. anthracis", it is also a causative organism for anthrax. Diseases which typically affectherbivoresinfectto any mammal, including humans. Since last few decades; this disease has become a hot topic for scientific community, in which terrorism is becoming more prevalent, as it can be used in biological warfare. Recently, there has also been an increase in the number of cases of injection anthrax, a form of the disease that affects heroin users, in Europe. Currently, vaccine is not available to the general public but few antibiotics have been approved by the FDA for the treatment of inhalation anthrax. The concerns of antibiotic resistance, inadequacies of the current vaccinations and therapies, and recognition of the increasing bioterrorism threat, have encouraged new drug development, for that we need new drug targets. Identification of new targets. Subtractive genome analysis is one of approach used for identification of drug targets. This can be possible by using various available bioinformatics tools, software for sequence analysis purpose, and databases DEG(Database of essential genes) is used find essential proteins for survival of pathogens. Blastp is used for finding non-homologous sequence against human.Blast2GO is used for annotationof drug targetsand proteins such as Ribose-phosphate pyrophosphokinase (RPP), UDP-N-acetylglucomsamine pyrophosphorylase (UDP),Glutamate—tRNA ligase (GTL) and Methionine (MET) is identified as potential drug targets. Homology modeling of these putative targets was done by modeller. Structure is validated by using ProSA; ProCheck out of these four putative passed the filter like Z-score. Active site predicted by using FT site server and 3D Ligand.

Keyword: Drug target, Subtractivegenomics, Metabolicpathway, Homology modelling, Active site

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Introduction

Bacillus anthracis(Spencer, 2003) is the etiologic of anthrax – a common disease of livestock and occasionally of humans – and the obligate pathogen within the genus *Bacillus*. *B. anthracis* is gram – positive endospore - formingrod shaped bacterium width of 1.0 – 1.2 µm and length of 3 – 5 µm. It grows in an ordinary nutrient medium under aerobic or anaerobic condition(Holt et all., 1994). *Bacillus anthracis* is one of few bacteria known to synthesize a protein capsule (poly-D-gamma-glutamic acid). Like *Bordetella pertussis*, it forms a calmodulin-dependent adenylate cyclase exotoxin known as (edema factor), along with lethal factor. They form spores and these spores are dehydrated cell with thick walls and additional layers that form inside the cell membrane. It can remain inactive for many years, but if it comes into a favorable environment, it begins to grow again. It is sometimes called an endospore because it initially develops inside the rod-shaped form. The spores resist heat, drying, and many disinfectants (including 95% ethanol). Because of these attributes, *B. anthracis* spores are extraordinarily well-suited to use (in powdered and aerosol form) as biological weapons. Such weaponization has been accomplished in the past by at least five state bioweapons programs — those of the United Kingdom, Japan, the United States, Russia, and Iraq (Zilinskas, 1999). The Ames ancestor chromosome was sequenced in 2003 and contributes to the identification of genes involved in the virulence of *B. anthracis*.The Ames strain (about 5.23 megabases) is one of the 89 known strains of the anthrax bacterium (*B.anthracis)*. It was isolated from a diseased 14-month-old Beefmasterheifer that died in Sarita, Texas in 1981. The Ames strain came to wide attention in association with the 2001 anthrax attacks. Seven letters mailed to media outlets and US Senators on September 18, 2001 and October 9, 2001 contained anthrax bacteria of this particular strain. This strain is a monomorphic disease, mutating slowly, Because of its virulence. The Ames strain (*Warrick et all., 2002)* is used by the United States as something of a gold standard for development of vaccines and testing their effectiveness, starting in the 1980s, after work on weaponingthe Vollum 1B strain ended and all weaponized stocks were destroyed after the end of the U.S. biological warfare program in 1969 (*Fainaru,2001)*. It has a single chromosome which is a circular, 5,227,293-bp DNA molecule. It also has two circular, extra-chromosomal, double-stranded DNA plasmids, pXO1 and pXO2.

Our study is focused on two main objective first is to find out putative target and second is the active site prediction of that putative target. Subtractive genomic (DebmalyaBarh et al., 2010) strategy is developed by assuming that the novel targets identified in the pathogen.It should be essential for the pathogen, involved in the replication, survival and an important component of various metabolic pathways and mechanisms occurring in the pathogen while at the same time should be absent on the host that is human and should have no homologue in human, so that when a drug or a lead compound is designed considering the potential target it should only be against the mechanism and functionality of the pathogen not in the host.Blast2GO is used for annotation of probable drug targetand gene ontology.EMBOSS(needle) used to find available homologous structure of model organism and Blastp is used to find template for homology modelling. Modeller generate protein model by using python script and visualized in PyMOL. ProSA, ProCheck and PSVS (protein structure validation suits)is used for structures quality assessment and validation. Once validate the structure then necessary to check its active site that bind with ligand, 3-D ligand, FTsite server and active site prediction are various tool that use for active site prediction.

Materials and Methodology

Sequence retrieval; Sequences of *B.anthracis* is downloaded from NCBI FTP site (http://www.ncbi.nlm.nih.gov/ftp/). NCBI provide databases of various formats with different perspectives. Among them FASTA format of protein was chosen for subsequent analysis.

Sequence dataset; Selection of non-duplicate proteins and sequences <100 amino acid residues are discarded by using Perl script.protein sequences <100 is not involve in essential function.

Identification ofessential of proteins; DEG (http://www.tubic.tju.edu.cn/deg/) for detecting the homology of protein sequences. The parameters used in BLASTp are e-value $=10^{-10}$ (i.e. expected value which means that by chance matching probability, its value is less shows good matching of sequences), PAM70 (i.e. Point Accepted Mutation, substitution method of amino acid sequences).

Identification of non-homologous against Human; BLAST in NCBI is now used again to subtract protein sequences(http://www.ncbi.nlm.nih.gov/BLAST/). The parameters used in BLASTp(Altschul et all., 1990) are e-value =, PAM70 andrefseq (73151) database.

Functional Annotation ofProbable Drug Targets; Blast2GO(Conesa et all., 2005) used for getting relevant pathways this software is used to BLAST protein sequences and to get mapping pathways generated by KASS generated by KAAS (KEGG Automated Annotation Server) server at KEGG for the identification potential targets in Blast2GO. It makes use of the BLAST algorithm to identify similar sequence to transfer existing functional annotation from yet characterized sequences to novel one. The functional information is represented by the Gene Ontology.

Similarity with model organism; Those sequences involved in the function of drug targets is needs modeling. For modeling Checked for model organism structure. The model organism of *Bacillus anthracis* is *Bacillus subtilis.* EMBOSS Needle used them to find the optimum alignment of sequence along their entire length. The parameter for similarity and identity is >80%, the structure show 80% similarity and identity with *B. subtilis* , so the homology modelling is a suitable method for 3-D structure modeling of putative target.

Homology modelling

Template search; Basic local alignment protein (Blastp) PDB is used to find available structure in PDB database by using following parameter query coverage 100% and sequence similarity 50%. The chains or template which follows the parameters, their PDB code are used for homology modeling with proteins which are involved in putative drug target.

Modeling of putative drug targets; The templateare used for homology modeling. For the homology modeling prepare python script by using PDB code of template, run these scripts in the modeller, which generate two models on the basis of template. These models need validation for putative drug targets. PyMOL has a powerful and flexible interface, which are used to view the structure in 3-D.it can display more than one object at time which are helpful to aligned the modeled structure with template and These generated model also need validation.

Validation of modeled structure; Structure validation software ProSA, ProCheck and PSVS (Protein Structure Validation Suit) (Bhattacharya et all., 2007) are used to validate the generated model. ProSA are used to check the error in experimental and theoretical model of protein, it also refine the model quality, it calculate overall quality score and energy plot that highlight potential problems spotted in protein structure. The stererochemical quality of a protein structure by residue geometry and overall structure geometry is check by ProCheck, it also used NMR for checking the quality of structure andproducing number of postscript plot analyzing its geometry of amino acid residues of

modeled proteins,the structure quality factor calculated by protein structure validation suite (PSVS), after validation structure is more reliable for further process.

Structural alignment of modeled target and target template; Ideally the target site is a pocket or protuberance having avariety and with molecular adherence surfaces (Anderson, 2003). The ligand-binding site may be an active site as in an enzyme, an assembly site with another macromoleculeoracommunicationsite.This is necessary in the mechanism of the molecule (McCarthy, 1999).Active site prediction is possible after the alignment and validation of the proteinstructure. Theprediction of active site FTsite server, 3D-ligand (Wass et al., 2010) and active site prediction (Singh et all., 2011) are used. Drug target's active site are predicted, every targets have more than one active site but only common site is predicted as active site and it is necessary to have ligand prediction which can bind to that active site. After that Drug Bank (Law et all,. 2014) used to validate our target protein structures RPP, UDP and GTL.

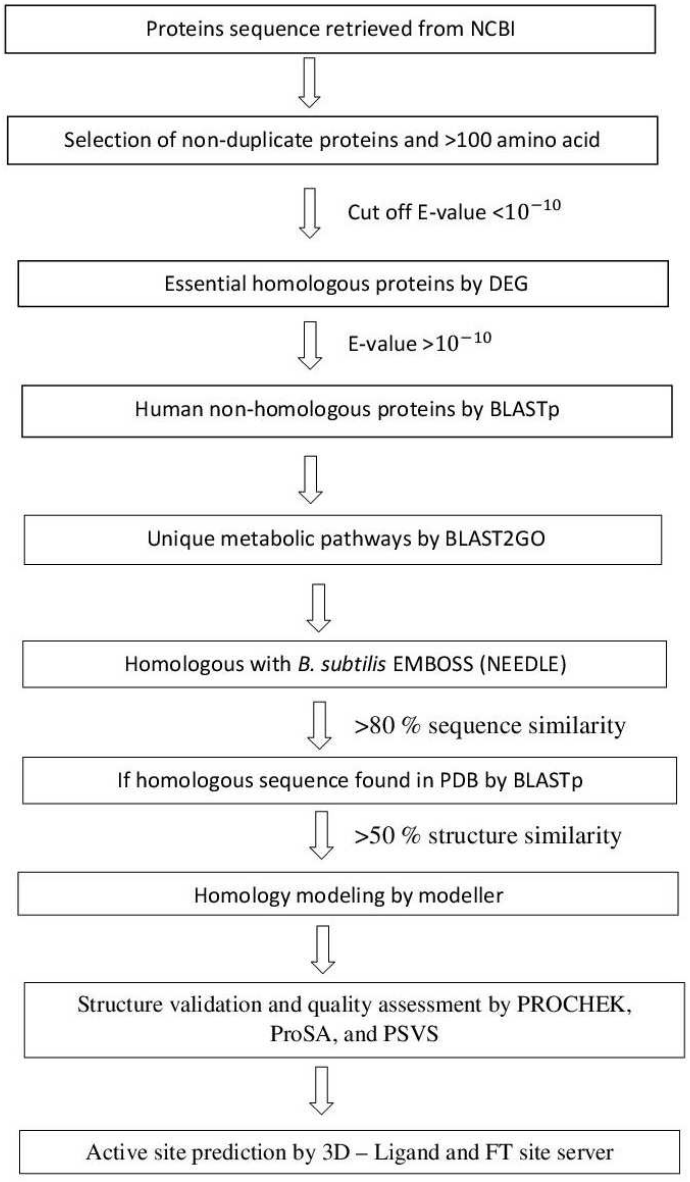


Figure1. Systematic diagram of methodology

Results and Discussions

In this study we investigated the potential target for therapeutic drug through subtractive genome analysis. The basic of *in-silico* subtractive genome analysis is that the essential proteins of a pathogen should be sorted as unique which cannot be found in the host for precise drug usage (M.A. Rahman et al., 2014). The essential genes are the minimum set genes which are required for the survival of an organism under the reasonable condition (Zhang and Lin, 2009).

Putative target finding – In current investigation total 4679 protein sequences was retrieved which were further analyzed through subtractive genome approach. Among these, 3625 protein sequence were sorted out having more than 100 amino acid in length. Because the probability of involvement of proteins having more than 100 amino acid in essential metabolic pathways is greater than the proteins containing less than 100 amino acids(Kumar et al.,2010).

Identification of homologous of protein – now screening through DEG, again the size of protein sequence is reduce to 1570 but only 308 protein sequence is finalized on the basis of DEG homology with ≥ 20 DEG sequences(Fariselli et al., 2007).

Identification of non-homologous against human – lot of protein are playing housekeeping role in wide range of organism, they are almost share by all organism.to avoid accidental targeting of such protein in human, homology search was performed between selected potential protein for drug target and human protein NCBI Blastp using e-value $=10^{-10}$ against human to check the similarity of subtracted 308 protein sequence with human. Unfortunately the Blastp gives zero (0) significant similarity by giving no hits. These sequences have no homology with human so these can be checked for drug targets and does not harm to us.

Annotation of Probable Drug Targets –this step is used for getting relevant pathways. This software used to BLAST the proteins sequences and to get mapping pathways generated by KAAS (KEGG Automatic Annotation Server) server at KEGG (Moriya et al., 2007). In this step the 81 proteins are 430 times automatically annotated to generate 16 uniquemetabolic pathways. These pathways involve different proteins having different sub-cellular localization. Such pathway and involved protein can be used for drug target. We observed that 16 pathways uniquely involved in pathogen's metabolic function and are not common in human, such that these pathways may targeted for drugs.it is known that 16 unique metabolic pathways contains 66 proteins sequences involved and it has 37 enzymes. It is very notable point that from 81 sequences only 66 proteins are involved in forming unique metabolic pathways. The result of subtractive genome analysis (table1) and BLAST2GO also shows the sequences with gi numbers and enzymes with enzyme code numbers in table 2.

T A B L E 1 *Subtractive genome analysis of Ames strain (B. anthracis)*

S.No	Successive analytical steps	Total no. of proteins
1	Proteins sequences from NCBI	4679
2	Protein sequences >100 amino acid residues	3625
3	Homologous proteins found in DEG	1570
4	Human non-homologous sequences	308
5	Essential proteins involved in metabolic pathways	81
6	Unique metabolic pathways(i.e 16)	57
7	Essential unique pathways (i.e 8)	17

T A B L E 2 *Unique metabolic pathways with enzyme code and sequences with gi number*

Pathways	Enzyme Codes	gi Numbers
Purine Metabolism	3.6.1.3- adenylpyrophosphatase	30260361,30260373, 30260331,30260874, 30260291,
	3.6.1.15 – phosphatase	30260361,30260201, 30260373,30260374, 30260291
	2.7.6.1 – phosphokinase	30260241
	2.7.4.3 – kinase	30260322
	2.7.7.6 – RNA polymerase	270000589,30260328, 0260293
	2.7.7.7 – DNA polymerase	30260197,30260221, 30260213
Thiamine	3.6.1.15 – phosphatase	30260361,30260201, 30260373,30260374, 30260291
Pyrimidine metabolism	2.7.4.9 – kinase	30260220
	2.7.7.6 - RNA polymerase	270000589,30260328, 30260293
	2.7.7.7 - DNA polymerase	30260197,30260221, 30260213
Amino acyle t-RNA biosynthesis	6.3.5.7-synthase	30260492
	6.1.1.17-ligase	30260278
	6.1.1.16-ligase	30260280
	6.1.1.10-ligase	30260228
	6.1.1.11-ligase	30260206
	6.1.1.6-ligase	30260268
Biosynthesis of antibiotics	2.6.1.16-transaminase	30260348
	2.3.1.157-N-acetyltransferase	30260240
	2.7.6.1-diphosphokinase	30260241
	2.7.4.3-kinase	30260322
	5.4.2.10-mutase	30260346
	2.7.7.23-diphosphorylase	30260240
Amino sugar and nucleotide sugar	2.6.1.16-transaminase	30260348
	2.3.1.15-N-acetyltransferase	30260240
	2.7.7.10-mutase	30260346
	2.7.7.23-diphosphorylase	30260240
Alanin, Aspartate and glutamate	2.6.1.19-ransaminase(isomerize)	30260348
	2.6.1.19-transaminase	30260495
Porphyrine and chlorophyll	6.1.1.17-ligase	30260278
Propanoate metabolism	2.6.1.19-transaminase	30260495
β – Alanine	2.6.1.19-transaminase	30260495
Lysine biosynthesis	6.1.1.10-ligase	30260422
Peptidoglycan	2.6.1.19-transaminase	30260422
Butanoate	2.6.1.19-transaminase	30260495
Seleno-compound	6.1.1.10-ligase	30260228
Pentose phosphate	2.7.6.1-diphosphokinase	30260241
Drug metabolism	3.1.1.10- ali-esterase	481847676

3-D structure modeling

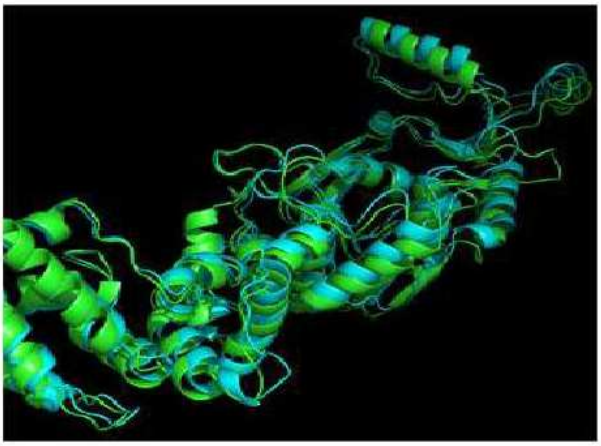
Similarity search – Emboss (needle) is used for global sequence alignment with *B. subtilis*because it belonging to the same family and its structure is also available at PDB but choose only those sequences whose sequence similarity is >80%.only 8 sequence are left from 16 metabolic pathways which are used for template search and homology modeling. Blastp PDB is used to search template for homology modeling, if the target protein has homologous whose structure is already known, the task is relatively, easy and high-resolution models can be built by copying the framework of the solved structure .if structure is homologue does not exist, or exist but cannot be identified, models have to be constructed by using I-TASSER (M.Rashmi et al., 2015)

Homology modeling for putative drug target - If the Protein of both query and template has the same chain then doesnot need to do anything, just create python script and run in the modeller. Modeller generatestwo models of each protein. These generated models are alignedthe template (figure2) and viewed by using PyMOL (Schrodinger, 2010).

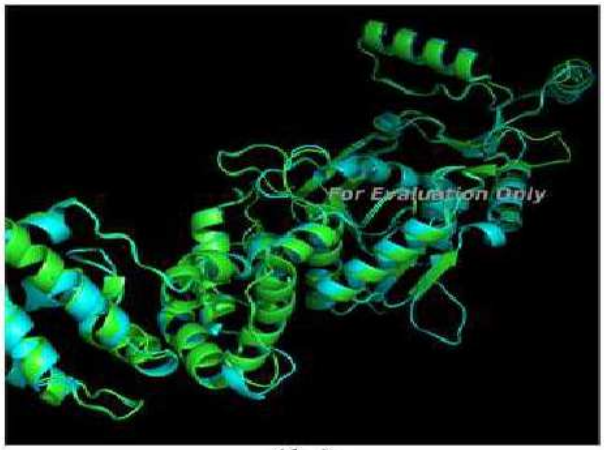
Structure validation and quality assessment - Quality assessment is based negative Z-score of model quality graph (figure3-a) and local model for energy level (figure3-b), negative Z-score of RPP, UDP, GTLare in (table 3).Structure validationresidues in most favoured regions is 93.0%, residues in additional allowed regions is 5.8%, residues in generously allowed regions is 0.2%, residues in disallowed regions is 0.9%,number of non-glycine and non-proline residues is 100.0%, number of end-residues (excl. Gly and Pro) is 1, number of glycine residues (shown as triangles) is 35 and number of proline residue is 18 and total number of residue is 485 (figure 3-c).

T A B L E 3 *protein with Z-score from ProSA*

Proteins	Z-score
RPP	-9.76
UDP	-9.73
GTL	-11.14



(a)



(b)

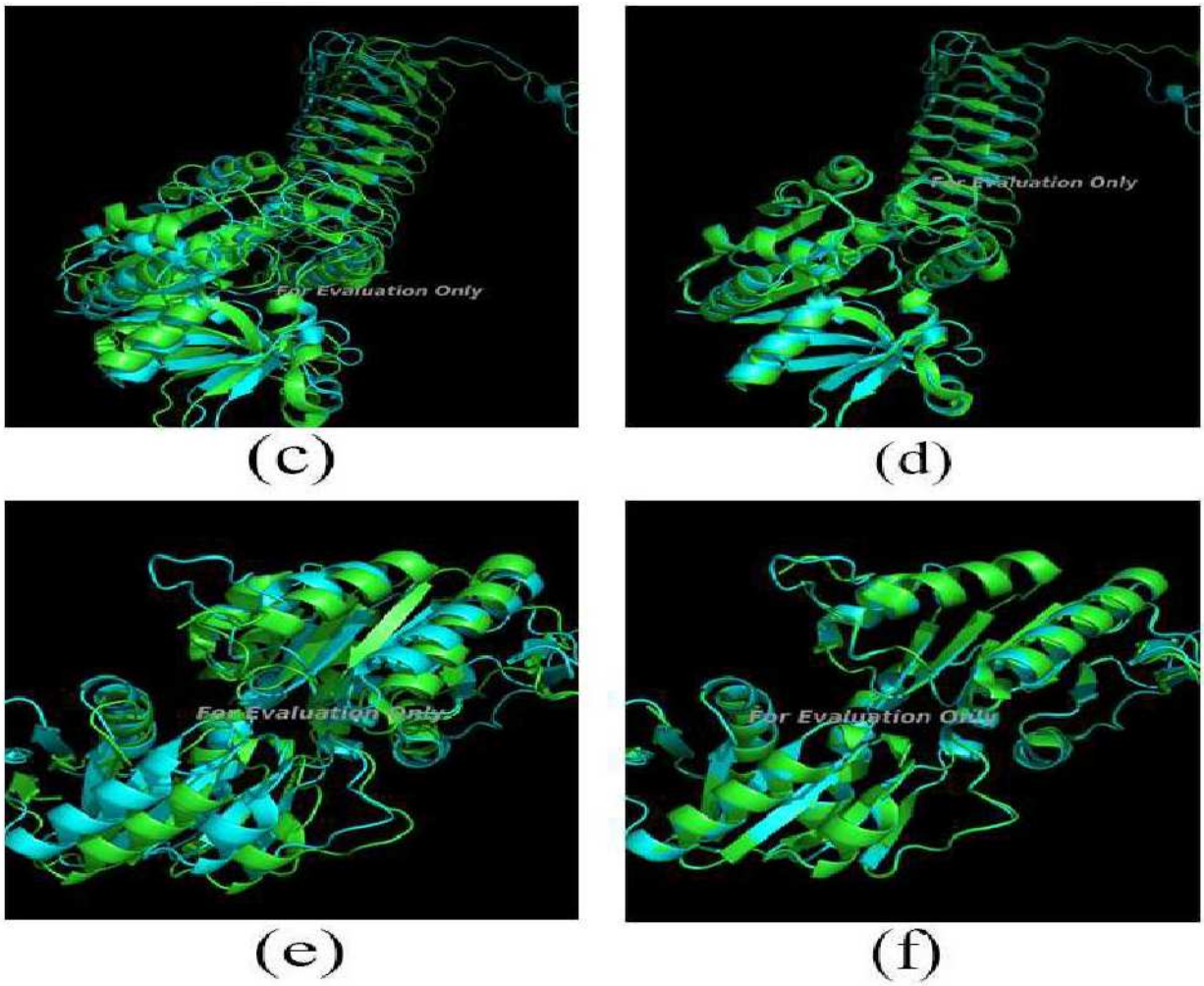
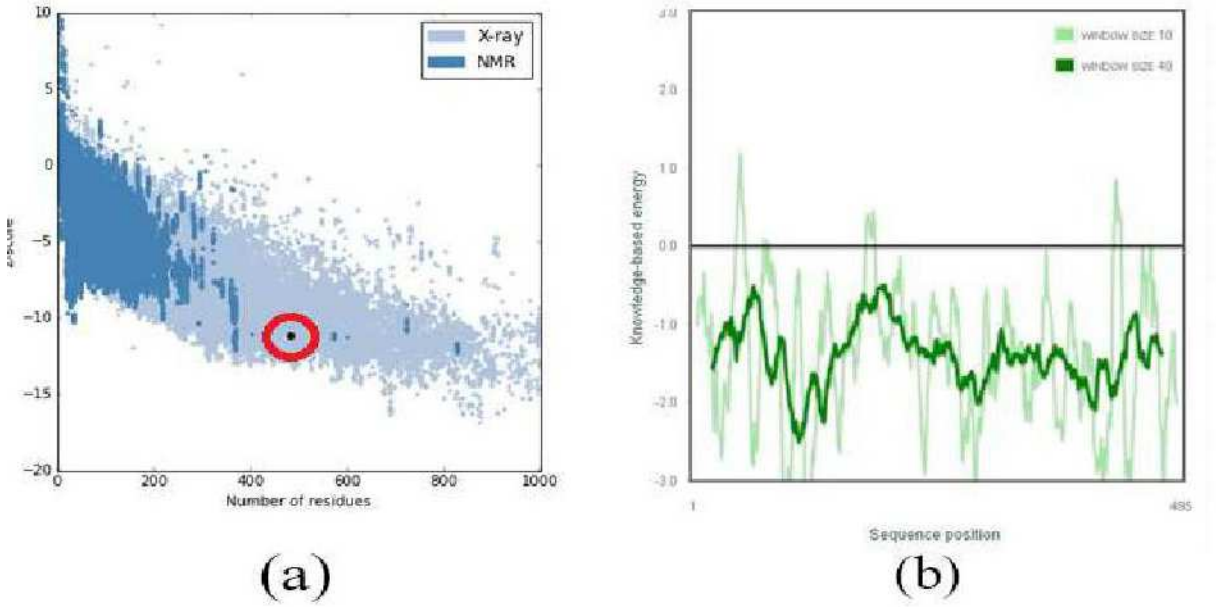


Figure 2. (a)GTL,(c)UDP,(e)RPP are Modeled structure of protein without alignment and (b)GTL,(d)UDP,(f)RPP are aligned with template.



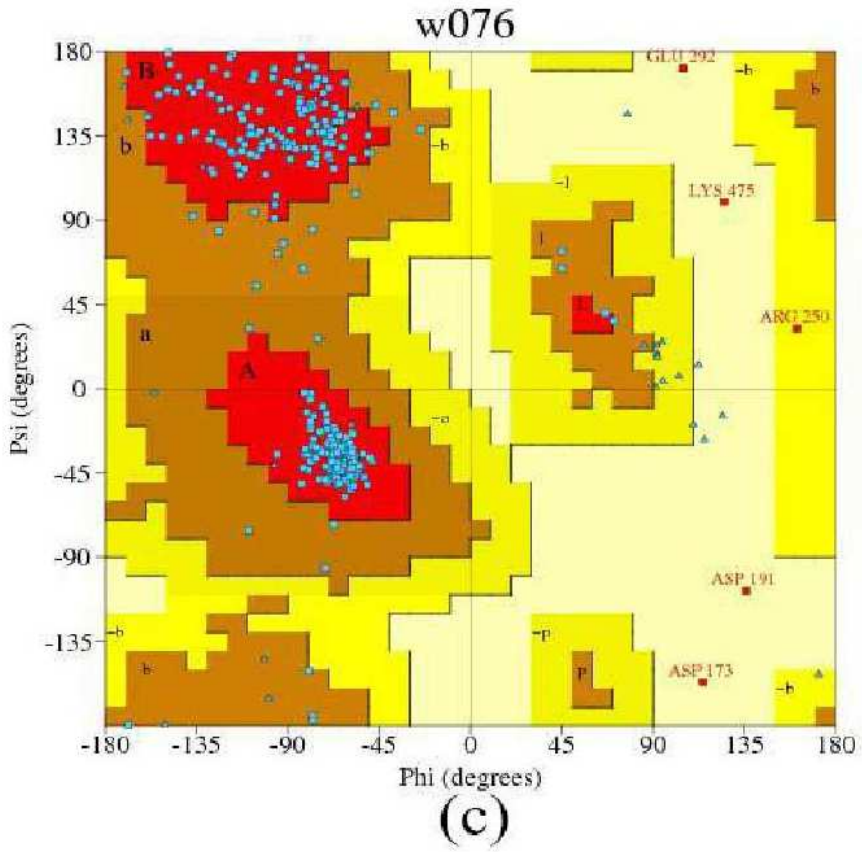


Figure 3. Quality model of GTL (a) with highest negative Z-score, (b) local quality model with negative energy level generated by ProSA and (c) Ramachandran plotBased on an analysis of 118 structures of resolution of at least 2.0 Angstroms and R-factor no greater than 20%, a good quality model would be expected to have over 90% in the most favoured region

Active site prediction

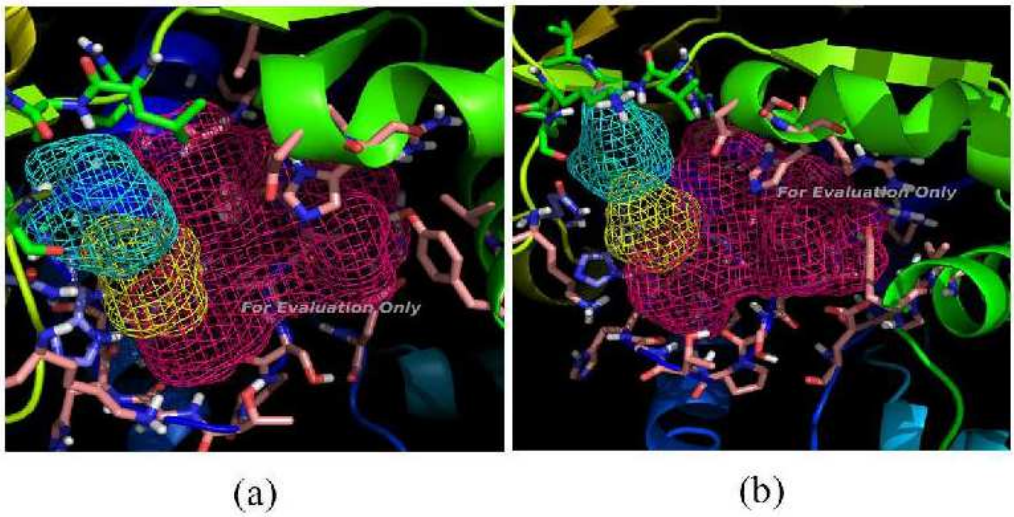


Figure 4. Active site of GTL (a) predicted by 3-D ligand and (b) predicted by FTsite server, in both prediction sites 1 (pink), site2 (cyan) and site 3 is (yellow).

Active sites are predicted by using FTsite server and 3DLigandserver. FTsite and 3-D ligand server predicted putative three common active site in same protein. The common residue in active site 1 is BUT39, PHN26, ACN17, and ADY-17, CHX2, ETH61, and DFO56. Common residue in active site 2 BUT72, PHN67, ADY70, CHX66, ETH77, DFO76, EOL78, DME73.Common residue in active site2 is CHX79 and DME80.when merge these different active site, it look like a single active site

Conclusion

Proteins involved in unique metabolic pathways are considered as potential drug targets, because they have specific functions and metabolism. Protein sequences involved in unique metabolic pathways essential for bacterial survival. We considered three proteins as drug targets and modeled their structures. Active sites found in proteins are also predicted where ligand is going to bind.

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CALCULATION OF GROUND STATE PROPERTIES OF WURTZITE ZINCOXIDE USING LOCAL DENSITY APPROXIMATION AND G-W APPROXIMATION

Dr. Ashok Kumar Singh*

Declaration

The Declaration of the author for publication of Research Paper in The Indian Journal of Research Anvikshiki ISSN 0973-9777 Bi-monthly International Journal of all Research: I, *Ashok Kumar Singh* the author of the research paper entitled CALCULATION OF GROUND STATE PROPERTIES OF WURTZITE ZINCOXIDE USING LOCAL DENSITY APPROXIMATION AND G-W APPROXIMATION declare that , I take the responsibility of the content and material of my paper as I myself have written it and also have read the manuscript of my paper carefully. Also, I hereby give my consent to publish my paper in Anvikshiki journal , This research paper is my original work and no part of it or it's similar version is published or has been sent for publication anywhere else. I authorise the Editorial Board of the Journal to modify and edit the manuscript. I also give my consent to the Editor of Anvikshiki Journal to own the copyright of my research paper.

Abstract

Eigen functions computed in the local density approximation by the full-potential linearized augmented – plane wave or the linearized muffin-tin-orbital method supply the input for generating the Green function G and the screened coulomb interaction w. A mixed basis is used for the expansion to w, consisting of plane waves in the interstitial region and augmented wave function products in the augmentation sphere-regions. The frequency dependence of the dielectric function is computed within the random phase approximation. We have applied the al electron G-w calculation for wurtzite zinc-oxide. The G-w calculation overestimates the screening effect for localized states such as the Zn 3d states, because of the random phase approximation and local density approximation band structure. Self consistent calculations are needed to improve the results. For a four atom system having localized 3d orbitals such as Wurtzite Zincoxide, we can complete the G -w calculation with 32k points in Brillouin zone within 3 days. The G–w band gap of zincoxide is smaller than excrementally obtained value.

Introducation

Density-function theory provides a foundation for modern electronic structure calculations, and the local-density approximation is an efficient way to calculate the ground state properties of the material. The local density approximation Eigen values should not necessarily identified with the quasiparticle energies, although eigen value differences are often used to describe the exited state. Time dependent

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density functions theory can in practice describe the existed state, but a good approximation for the time dependent exchange-correlation kernel is not known. The G -w approximation of Hedus[1] provides a practical method to calculate the quasiparticle energy Hybertsen and Louie[2] presented the first G –w calculation for real material. They employed eigen functions given by the Local density approximation as input, using additionally a pseudopotential approximation. Several methods have been developed within various band structure-calculation schemes[3]. Calculated quasiparticle energies typically agree well with experiment, for many kinds of materials. One is the product basis function developed by Aryasetiawan[4] and Gunnarrson, which is constructed from the products tot he local functions in the muffin-tin-sphere regions. The other is interstitial plane wave that takes zero in the mueein-tin-sphere regions and equals to the usual plane wave in the interstrial region. The mixed basis is by construction essentially a complete basis for the expansion G -w , therefore, for given-eigen functions as input our method can produce resonably well converged quasiparticle energies rather more efficiently than a method that expands w in-plane waves alone.

We have applied this approach to Wurtizite- type Zincoxide, whose valency bands consists extended o 2p and zn 4s orbitals and rather lcoalized zn 3d and o 2s orbitals. Zno is important for optical device technology since the material is optically transparent and can be doped with electrons and holes. Compared with most the II-IV and III-V Compounds such as ZnS, GaN, the position of the cation d levels is rather high and relatively close to the anion p-derived valence band maximum. The effect of the Zn 3d state is not negligible for the various properties. The 3d state couples to the valence-band maximum and pushes it upward, reducing the band gap.

Result and Discussion

In the Green's function approach, the quasiparticle energy and wave function of many-electron system are given as solution of the equation,

$$[E_{kn}\text{-}T\text{-}V_H(r)]\, F_{km}(r)\text{-}\int \Sigma(r,r^1, E_{km})\, f_{km}(r^1)d^3r=0 \quad \ldots\ldots (1)$$

Where T is the kinetic energy operator, V_H is the Hartree potential plus the electrostatic potential from nuclei and Ó is the self energy. In the G –w approximation, the self energy written as

$$Ó(r,r^1,w) = i \int_{-\infty}^{\infty} dw_1/2\pi e^{iw'S}\, G(r,r^1,w+w^1),\, W(r,r^1,w^1) \quad \ldots\ldots (2)$$

A perturbative approach to find ε_{Kn} is

$$[\varepsilon_{Kn}\text{-}T\text{-}V_H(r)\text{-}V_{xc}^{LDA}(r)]\, Økn(r) = 0 \quad \ldots\ldots (3)$$

The first order energy in the Hartree-Fock approximation

$$E_{Kn}^{HFA} = \epsilon_{km} + \langle \Psi_{kn}/\Sigma_x/\Psi_{kn}\rangle - \langle \Psi_{kn}/V_{xc}^{LDA}/\Psi_{kn}\rangle \quad \ldots\ldots (4)$$

The interstitial plane wave is given by

$$\int_G^K (r) = \begin{cases} o & \text{in the muffin-tin sphere region} \\ i(K-G),r & \\ e & \text{in the interstitiol region} \end{cases}$$

The interactions V and W are expressed by the product of two Ks eigen functions in our perturative treatment.

The G –w Calculation is performed with 32k points in the Brillounin zone. The energy cut off of the interstitial plane wave is 10Ry for the Coulomb matrix. All the core and valence electrons are included into calculation of the exchange part of the self energy. We have also examined the Convergence of the quasiparticle energies in k Points, plane waves, unoccupied states and product functions.

Conclusion

We have studied all electron implementation of the G –w approximation and have applied it to the Wurtzite Zincoxide. We have used a procedure for Calculating the self energy in the G –w approximation with the mixed-basis expansion based on the full potential linearized augmented – plane wave and linearized muffin-tin-orbital methods. The mixed basis method works well for this system which has both extended states and localized states the G –w calculation has a good convergence in various parameters and can be performed on a workstation level computer. The G –w band gap of zincoxide smaller than experiment by ~1ev. The self energy correlation is orbital dependent and the localized 02s and Zn 3d states are lowered by ~1ev relative to the local density approximation value, while still higher than experiment.

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BALANCED DIET: A BOON TO CONTROL STRESS

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Declaration

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Abstract

Stress and diet taken by us are related to each other. Stress is body's way of responding to any kind of *demand. It can be caused by both good and bad experiences. When we feel stressed by something going on around us, our bodies react by releasing chemicals into the blood. These chemicals give us more energy and strength, which can be a good thing if their stress is caused by physical danger. But this can also be a bad thing, if our stress is in response to something emotional and there is no outlet for this extra energy and strength. Stress is the feeling of being under too much mental or emotional pressure. Pressure becomes stress when we feel unable to cope. Everyone reacts differently to stress and experiences different stressors, or things that cause stress. Common stressors include work, relationships, and money. Stress can affect how you feel, think, and behave. It can also impact how your body functions. Common signs of stress include anxiety, worrisome thinking, sleeping problems, sweating, loss of appetite, and difficulty concentrating, among others. It is worth taking the time to learn different strategies and techniques for managing your stress before there are serious consequences for your mental and physical well-being. Diet can play an important role in the relief of stress. Eat a balanced diet and avoid foods that may increase tension. Instead of combating with stress, we should control it only by control our diet. In real sence, balanced nutritional diet is a boon to control stress.*

Keywords : Stress, balanced diet, good stress, distress, eustress, mental health, depression, busy lifestyle, muscles tension, eating habits ,edgy personality, physical health, psychological health, fad dieting, energy, cortisol, tension etc.

Stress is a common term used by people when they encounter a problem in their life. Stress is the way human beings react both physically and mentally to changes events and situations in their lives. People experience stress in different ways and for different reasons. The reaction is based on your perception

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of an event or situation. If you view a situation negatively, you will likely feel distressed—overwhelmed, oppressed, or out of control. Distress is the more familiar form of stress. The other form, eustress, results from a "positive" view of an event or situation, which is why it is also called "good stress". Physical and psychological responses to the pressure of daily life are Stress. Stress is a common problem that we all have to deal with in our lives, some more than others. There are many factors that bring stress upon the body, such as the job of the person and certain events that happen in their life. Stress is a fact of life, wherever you are and whatever you are doing. You cannot avoid stress, but you can learn to manage it so it doesn't manage you. When people are suffering from stress when they start to notice changes in body like- Muscle tension, Loss of focus/concentration, anxiety, headaches, increased heart rate, having a short temper, an edgy personality, fatigue, Irritations, trouble falling or staying asleep, problems with memory, loss of appetite. If the stress is not treated, it is possible for further damage to be inflicted on the body, resulting in degeneration. External features such as ulcers and Sores can appear. Stress can also inflict long term illnesses to the body like- Diabetes, Depression, Mental health problems, Heart/Cardiovascular problems, Bowel/Digestive Problems, cancer, lung ailments, accidents, cirrhosis of the liver, and suicide. . One of the main issues with stress is that it can cause unhealthy eating habits. This applies mainly to people who are always on the go and lead a busy lifestyle. People that fall into this category often endure large amounts of stress and have no time to fit a balanced nutrition around their busy schedule. Additionally, stress makes the body crave foods that are high in fats and sugars. This flaw in eating, in time will inflict a greater stress on the body, plus other problems that pose a threat to your physical and mental health. When a person becomes overwhelmed with stress, a common reaction is a sudden urge to eat food. The majority of the time, foods consumed in this situation will be 'convenience foods' that are considered a quick fix to nullify stress. The theory of a quick fix is entirely false however, as these foods/drinks only worsen the problem. Consuming foods that are of a 'junk' nature actually increase the volume of stress on your body. Stress can affect both your body and your mind. People under large amounts of stress can become tired, sick, and unable to concentrate or think clearly.

The following are common examples of how people react with food when they become overwhelmed with stress.

*Fast Food Intake:*It is common in this day and age for people to eat out rather than stay home and cook meals, generally because people don't want to cook after a hard day at work.

Work is normally the biggest cause of this, but there can be countless reasons for

why people do not want to cook, for example family problems. The problem with this convenience is that the foods consumed from a fast food shop/restaurant play a hindrance on your overall health. It is also an expensive habit that can cost you money in the long haul. Money problems also increase stress levels.

*Forgetting/Skipping Meals :*It is important to eat three meals a day and most people know this, but stress can have the effect of making people skip, or forget to eat their meals. People who are overly stressed tend to pick up this habit and find out that later on in the day they will become hungry, and more than likely resort to eating junk food to sort their hunger.

Coffee Intake : Caffeine also has negative side effects on the brain and nervous system if taken in vast quantities. Although it can give you a quick boost when required, the fatigue will catch up once the caffeine has worn off. You should not need caffeine to focus, and if you do, this lack of focus is your body's way of telling you it needs rest. An over excess of caffeine can lead to negative effects such as restlessness, lapses of concentration and a decrease in your ability to be fully effective. Caffeine also has a massive impact on the hormones in your body. The following hormones are increased under the influence of caffeine.

1. Adenosine; Alerts you but causes sleep problems in the future.

2. Adrenaline; Gives you an extra boost but will make you feel fatigued once the adrenaline has worn off.

3. Cortisol; The Stress hormone. Makes you crave fatty foods.

4. Dopamine; Initially makes the person feel good but once worn off, generates a low and possible dependence/addiction

Eating the Wrong Food Types -The problem people have when under stress is that they crave foods that are high in the nutrients which should be limited. This is down to the hormone called cortisol (An adrenal-cortex hormone that is active in carbohydrate and protein metabolism) that is produced when under stress. A person that is stressed will generally go for foods that have high contents of fats and sugars.

*Fat Dieting :*When people become stressed, they tend to put on weight. This is due to the amount of cortisol produced which in turn, leads to a high amount of fatty foods consumed. Due to this problem, people try to lose weight quick by either going on fad diets, or cutting out food entirely. This can be a very dangerous choice to make as you are not getting all the vital nutrients you need for your body to function properly. The results may look good for you in the short run, but in the long term your body will suffer because of this.

*Constantly Picking at Foods :*When people become stressed, they notice that they begin to eat much more than they normally would. When a person is not stressed, they only tend to eat food when they are hungry (ideally this should only be three times a day). The situation is very different under stress; in fact it is quite the opposite. Under stress, a person will eat

When they are not even hungry and constantly pick at fatty snacks.

*Thomas A Edison:*The doctor of the future will give no medication, but will interest his patients in the care of the human frame, diet and in the cause and prevention of disease.

Diet can play an important role in the relief of stress. Eat a balanced diet and avoid foods that may increase tension e.g. coffee, tea, and foods high in sugar. When you're feeling tense, there are many ways to manage and, in fact, reduce stress levels. Your diet and nutrition choices can make your stress levels go up or down. Certain foods provide comfort and actually increase levels of hormones in the body that naturally fight stress. Other types of foods and beverages can reduce stress by lowering the levels of hormones that trigger it.

*Beverages and drink:*Sometimes, it's the effect of a food or drink that can help reduce stress, not necessarily its nutrients. A warm cup of tea, milk can actually calm many people. There's the soothing effect of sipping a warm drink, regardless of the flavour - but certain herbs, like lavender and chamomile, have been shown to have a relaxing effect on their own. A centuries-old home remedy for getting a better night's sleep, warm milk helps because it has a relaxing effect on the body. Calcium-rich foods are an essential part of a healthy diet for bone health, but they also help with stress reduction. Milk and other dairy foods with calcium and added vitamin D can help muscles relax and stabilize mood.

Gratify with Dark Chocolate: Dark chocolate in the diet can reduce stress in two ways its chemical impact and its emotional impact. Chocolate feels like such an indulgence that it can be a real treat to simply taste a piece of it, and that feeling alone can help to reduce stress, Dark chocolate, which is also rich in antioxidants, can also help to reduce stress by lowering levels of stress hormones in the body.

Select Carbohydrates: Carbohydrates have been found to increase levels of serotonin, a chemical in the body that can boost mood and reduce stress. Once serotonin levels are increased, people under stress experience improved cognitive function, meaning they can concentrate and work better. Carbohydrates in the diet that can reduce stress — savouring a bowl of pasta or macaroni and cheese feels soothing and can help you to relax. Just make sure to choose healthy carbohydrates like sweet potatoes and whole-grains for better nutrition, and limit fat-laden, calorie-dense toppings.

Enjoy Avocados: Avocados (tropical American tree bearing large pulpy green fruits) Is not only delicious mashed into guacamole or sliced onto a salad — they're also packed with omega-3 fatty acids. These healthy essential acids are known to reduce stress and anxiety, boost concentration, and improve mood.

Get essential fats: Fatty fish are also a good source of omega-3 fatty acids and an excellent way to use diet and nutrition to reduce stress because they also offer a major benefit to cardiovascular health. Omega-3 fatty acids and fatty fish have also been found to ease depression, because the chemicals improve communication between nerve cells. Fatty fish include tuna, halibut, salmon, herring, mackerel, sardines, mackerel and lake trout.

Nuts for energy: Nuts are full of vitamins, including B vitamins, and healthy fatty acids as well .B vitamin are an important part of a healthy diet and can help to reduce stress. Almonds, pistachios, and walnuts can even help lower blood pressure levels. According to one study, pistachios in particular were found to have a role in reducing stress levels. Just remember to limit servings to just a handful a day to avoid excess calories.

Take More Vitamin C-Some studies have found that high levels of vitamin C help ease stress levels. One double-blind study reported on the value of taking 3,000 milligrams of vitamin C in a slow-release formula to reduce stress and levels of the stress-related hormone cortisol. Another study looked at the stress reduction effects of taking a supplement containing 1,000 mg of C, plus B vitamins, calcium, and magnesium. Eating citrus fruits, including oranges, grapefruits, and strawberries is a good start, but you would need a supplement to reach such high levels of these nutrients.

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