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# A possible link between mineralogy of loess deposits and high incidence rate of esophageal cancer in Golestan province of Iran

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**Abstract**

Loess and loess-like deposits cover large areas of Golestan province of Iran, a well-known region in the world for its high incidence rate of esophageal cancer (EC). Despite numerous published works on the possible contributing factors for the observed high incidence rate, very little attention has been given so far to a possible link between the mineralogy of loess deposits in the region and EC incidence rate. This paper tries to investigate in a medical geology context a probable link between the mineralogical composition, grain size distribution, and surface morphology of constituent minerals in loess deposits of Golestan province, and the observed high incidence rate of EC. To achieve this end, loess samples from two districts with high incidence rate of EC, i.e., Dashlibroon and Maravehtappeh were collected, analyzed and compared with the low incidence control area (Gorgan). The results clearly indicate higher quartz and zircon minerals content in Dashlibroon and Maravehtappeh compared with Gorgan control area, revealing a probable link between direct and indirect ingestion of these abrading and lesion-forming minerals with EC incidence rate in the area. Gradual decrease of the extent and thickness of loess deposits and resistant heavy minerals content from Maravehtappeh and Dashlibroon towards Gorgan (control area) further confirms the suggested link.

***Keywords****:* Loess deposits; esophageal cancer; Golestan province; Iran

## 1. Introduction

Esophageal cancer (EC) is the 6th most common cause of cancer mortality in the world (Parkin et al. 2005). The incidence of this disease shows a striking geographic variation in the world (Marjani et al. 2008). Golestan province in northeast Iran is located at the western end of the so-called Central Asian Esophageal Cancer Belt and represents one of the highest worldwide rates of EC since the 1970s (Semnani et al. 2010). According to Golestan Population-based Cancer Registry (GPCR) office, during a 5-year period leading to 2008, 9007 new cancer cases were reported to GPCR from 68 healthcare centers. Also, stomach and esophageal cancer were the most common cancers in males, while breast and esophageal cancers were dominant in females (Roshandel et al. 2012). Previous studies in Golestan province suggest opium and tobacco use (Pourshams et al. 2005), hot tea drinking (Islami et al. 2009), local food and nutrients (Fazeltabar Malekshah et al. 2010), drinking water quality (Keshavarzi et al. 2011), Polycyclic aromatic hydrocarbons (Kamangar et al. 2005), high concentration of $SiO_2$ (Jabbari et al. 2008), and zinc deficiency (Nouri et al. 2008; Keshavarzi et al. 2012) as possible environmental risk factors for EC. Raghimi and Ramezani (2007) briefly evaluated the role of loess mineralogy in the etiology of esophageal cancer in Golestan province. Loess is an “Aeolian–glacial sediment” mostly composed of silt or silty loam and normally forms rich soils (Iriondo and Krohling, 2007; Kehl et al. 2009). Thick loess deposits in Golestan Province cover an area of some 388,000 hectares, which is more than 17% of the province surface area (Frechen at el., 2009). Particle size is mostly in the range of silt (50-90%) and accompanied by clay and sometimes sand size grains (Hao et al. 2010). Loess deposits are characterized by lack of stratification and homogeneous sorting in the field. They are generally composed of quartz, feldspar, calcite, dolomite, mica, as well as iron and magnesium minerals with subordinate clay minerals. Due to chemical weathering and oxidation of iron minerals, loess deposits are generally yellow or brown in color (Kuster et al. 2006). Interest in loess deposits is mostly due to their effect on some geological hazards (including subsidence, slope instability, and landslide), and human health. Anomalously high or low concentrations of inorganic elements in loess deposits and loess water resources may have important effects upon human and animal health

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(Dodonov, 2007). Loess deposits are already suggested as a possible risk factor in the regional variation of esophageal cancer mortality (Derbyshire, 2001; Rashid et al. 2009; Wang et al., 2012). As esophageal cancer belt coincides with loess belt of the world, there appears to be a possible relationship between loess deposits and esophageal cancer (Raghimi and Ramezani Mojaveri, 2006).

Exposure to silica dust via loess deposits is very common in many parts of the world, but very little attention has been given to the risk of esophageal cancer among exposed populations. Jabbari et al. (2008) pointed out the increased risk of EC resulting from long-term ingestion of silica particles. Over the past 20 years, various studies have implicated $SiO_2$ as a possible carcinogene, and the International Agency for Research on Cancer (IARC) now considers quartz in group I human carcinogen (Eby, 2004). Saffiotti (1992) have investigated the mechanisms responsible for the carcinogenicity of $SiO_2$. An important factor is that silica dust particles must be small enough to enter the gastrointestinal tract. This size is generally considered to be smaller than 10 µm (<PM10). Loess dust may affect human health either directly or indirectly. Also, the elemental composition of dust may enhance the toxicity of the loess deposits (Selinus et al. 2005). Silica lodged in the esophagus could act as a nidus for nitrosating bacteria, which then produce nitrosamines carcinogenic for the esophagus in-situ. In addition, fibers could act as a nidus for viruses, and infection by viruses has been implicated in esophageal cancer in cattle and man (Craddock, 1993).

Understanding the physicochemical properties of minerals is important in assessing their role in the environment. So, in order to achieve this end, and investigating the probable link between loess deposits and the high incidence rate of esophageal cancer in Golestan province, detailed mineralogical composition, micro-textural relationships, and grain size of minerals were studied.

## 2. Geological setting of the study area

The study area includes Gorgan, Dashlibroon (north of Gonbad city), and Maravehtappeh regions in the Golestan province (36° 05′–36° 24′ N, 53° 51′– 56° 04′ E), located in the northeast of Iran (Fig. 1). Mean annual precipitation and temperature for the study area are summarized in Table 2. The climate of Gorgan city is moderate, damp, and almost Mediterranean. According to Roshandel (2006) the difference between the truncated age standardized incidence rate (TASR) for EC in Kalaleh city (including Maravehtappeh) and Gonbad city (including Dashlibroon) is not considerable and decreases in the following order: Dashlibroon ≈ Maravehtappeh > Gorgan (Table 1).

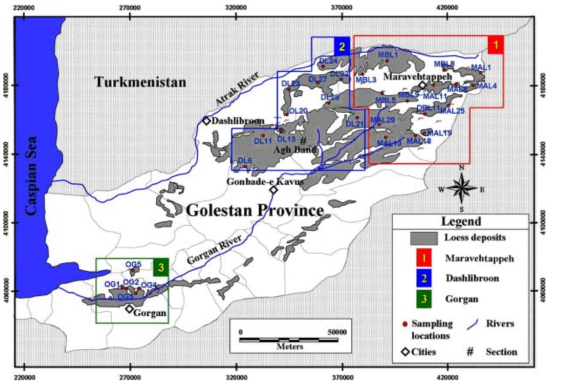


**Fig 1.** Map of the Golestan province showing distribution of loess deposits and location of loess samples Asadi et al. (2012)

Most of the study area falls in the dry and semiarid regions of the province. Loess deposits cover approximately 17 percent of the surface area of mainland Golestan province (Khadjeh et al. 2003). The thickness of the Golestan loess deposits decreases gradually from northeast to southwest. Maximum thickness is reported to be 70 m (Fig. 1) in Agh Band section (Dashlibroon region) and gradually reduces to less than 17m towards the southwest (Gorgan) (Frechen et al. 2009). Large areas of the Gorgan, Dashlibroon, and Maravehtappeh regions are covered by loess deposits which are parts of a loess belt that covers the Middle East and extends northward into Turkmenistan, Qazakistan and Tajikistan. Loess and loessic alluvium are abundant and easily applied to building materials used widely in Golestan province. In recent years, the loess deposits of Mashhad city, in the northeast of Iran (Karimi et al. 2009) and loess and loess-like sediments in other part of Iran have been identified and characterized (Kehl, 2009; Asadi et al. 2012).

## 3. Sampling, sample preparation and analysis

In this study, loess samples were taken at a depth of nearly 1 meter to avoid weathering effects. The samples were collected from sections originally excavated for a regional study of loess sequences. Thus, the three sampled sites cover a wide surface area (Fig. 1) extending from Maravehtappeh and Dashlibroon to Gorgan. A total of 29 loess samples were collected for mineralogical investigations (Table 1). Samples were prepared for detailed particle mineralogy and micro-textural investigations using quantitative X-ray diffractometry (XRD) at Geological Survey of Iran and Scanning Electron Microscopy (SEM) at Shiraz University, respectively. In summary, samples were milled for 12 minutes in ethanol to be nominally b10 μm in size using a McCrone Micronizing Mill and spray-dried to obtain randomly oriented powders. The XRD analysis of the resulting powders was carried out using a Siemens D5000 Diffractometer ($1^o$/min, CuKα radiation, 40 kV, 20 mA, $0.02^o$ step increment, and a scanning range of $2–70^o$). Additionally, <2 μm clay fractions, obtained by timed sedimentation, were prepared as oriented mounts and run in the air-dried state after ethylene glycol solvation and after heating at 300°C for one hour. The SEM analysis was performed on loess samples using Zeiss EVO MAIS instrument at 10 kv. The samples were impregnated with epoxy resin after air-drying, prepared as polished thin sections, and carbon coated.

**Table 1.** Loess samples location and Esophageal cancer incidence (per 100,000) for sampled villages in the study area (TASR= truncated age standardized rate)

| Sample No. | Village name | Town | UTM zone 40 N | | TASR[a] | |
|---|---|---|---|---|---|---|
| | | | X | Y | Male | Female |
| MAL 1 | Past Darreh | Maravehtappeh | 437773 | 4203100 | 63.5 | 85.2 |
| MAL 4 | Ghushehtappeh | Maravehtappeh | 433952 | 4195640 | | |
| MAL 8 | Gundar | Maravehtappeh | 426071 | 4196773 | | |
| MAL 11 | Sheykhlar | Maravehtappeh | 415656 | 4196251 | | |
| MAL 13 | Ghezel Otagh | Maravehtappeh | 392904 | 4165398 | | |
| MAL 18 | Golidagh | Maravehtappeh | 406781 | 4166699 | | |
| MAL 19 | Polyolia | Maravehtappeh | 410997 | 4168221 | | |
| MAL 25 | Yekkeh Chenar | Maravehtappeh | 422815 | 4184197 | | |
| MAL 29 | Arab Gharihaji | Maravehtappeh | 390406 | 4172976 | | |
| MBL 1 | Narli Achisu | Maravehtappeh | 394516 | 4210770 | | |
| MBL 3 | Aghtagheh | Maravehtappeh | 382586 | 4202548 | | |
| MBL 5 | Maravehtappeh | Maravehtappeh | 391834 | 4192183 | | |
| MBL 8 | Bastam Darreh | Maravehtappeh | 420780 | 4205271 | | |
| MBL 9 | Dakalidash | Maravehtappeh | 403444 | 4186368 | | |
| DL 6 | Aghband | Dashlibroon | 326908 | 4149039 | 123.5 | 74.3 |
| DL 11 | Aghband (north) | Dashlibroon | 335853 | 4167571 | | |
| DL 13 | Uchghuei road | Dashlibroon | 344114 | 4170572 | | |
| DL 20 | Uchghuei | Dashlibroon | 347375 | 4179172 | | |
| DL 21 | Narlidagh | Dashlibroon | 380020 | 4176997 | | |
| DL 23 | Huten | Dashlibroon | 348394 | 4194755 | | |
| DL 24 | Kerend | Dashlibroon | 364596 | 4207785 | | |
| DL 27 | Huten-Kerend road | Dashlibroon | 361742 | 4198352 | | |
| DL 28 | Kamar | Dashlibroon | 366275 | 4186207 | | |
| DL 32 | Aitmar | Dashlibroon | 373022 | 4199853 | | |
| OG 1 | Hezarpich | Gorgan | 268154 | 4079632 | 27.2 | 36.9 |
| OG 2 | Gorgan (Mellat Park) | Gorgan | 269634 | 4079411 | | |
| OG 3 | Ghaleh Hasan | Gorgan | 273737 | 4077086 | | |
| OG 4 | Gorgan (east) | Gorgan | 275209 | 4078622 | | |
| OG 5 | Gorgan (north) | Gorgan | 273219 | 4090173 | | |

[a] Truncated age standardized incidence rate in each town (Golestan Cancer Registry Office, 2006)

## 4. Results and discussion

### *4.1. Mineralogy*

Dominant minerals are quartz, feldspar, muscovite, and carbonates (Table 2 and Figs. 2 and 3). Minor minerals include heavy minerals (zircon, tourmaline, apatite, titanite, ilmenite and rutile), phyllosilicates (illite, kaolinite, chlorite, palygorskite, smectite and biotite), gypsum and dolomite. Quartz content varies from 18.8 in Gorgan (control area) to 32.3 in Dashlibroon (high risk area) (Table 2). The increase in quartz content of loess deposits from low to high esophageal cancer areas is significant and requires further investigation. Furthermore, heavy minerals content (especially zircon) in loess deposits is much higher in the areas with high esophageal cancer mortality rate (Dashlibroon and Maravehtappeh areas) than in the control area (Table 2), indicating that oral ingestion or dust inhalation of zircon particles play a role in carcinogenicity. However, a possible link between zircon crystals and esophageal cancer is yet to be reported from other parts of the world. According to O'Neill et al. (1982), zircon crystals may play a part in producing scratches in esophagus (directly or indirectly).

**Table 2.** Mineralogical properties of loess samples at Maravehtappeh (HC), Dashlibroon (HC) and Gorgan (control area)

| Mineralogical and grain size data | Maravehtappeh (n=12) | Dashlibroon (n=11) | Gorgan (n=5) |
|---|---|---|---|
| **Quartz (%)** | 29.9 | 32.3 | 18.8 |
| **Feldspar (%)** | 15.5 | 20.3 | 12.6 |
| **Carbonate (%)** | 27.4 (Cal)-7.2 (Dol) | 21.9 (Cal)-8.9 (Dol) | 42.2 (Cal) |
| **Muscovite (%)** | 11.4 | 13.3 | 16.3 |
| **Gypsum (%)** | 8.9 | 3.4 | n.f. |
| **Clay Minerals (%)** | 6.6 (a) | 8.3 (b) | 10.7 (c) |
| **Heavy Minerals (%)** | 2.1 | 2.5 | 1.5 |
| **Sand (%)** | 3.4 | 3.5 | 2.7 |
| **Silt (%)** | 84.0 | 87.6 | 79.5 |
| **Clay (%)** | 12.4 | 8.8 | 17.7 |
| **$SiO_2$ (wt. %)** | 45.86 | 47.18 | 41.99 |
| **Mean grain size (µm)** | 28.0 | 31.0 | 17.0 |

(n.f.: Not found; n: Number of samples; Cal: Calcite; Dol: Dolomite)

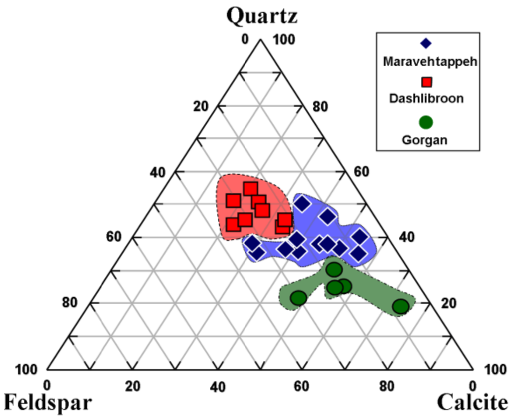


**Fig. 2.** Abundance of quartz, feldspar, and calcite in the Golestan loess deposits

Quartz is the most dominant mineral (40-50 wt. %) in the silt size to fine sand fraction (10 µm-0.05 mm), and is followed by feldspar (about 20-30 wt. %), zircon, muscovite, and biotite (10-20 wt. %), anhydrite and gypsum (<10 wt. %) and tourmaline, apatite, epidote, titanite, hornblende and microfossils (<5 wt. %). In the pelitic fraction, clay minerals (chlorite and illite) predominate and range from 30 to 40 wt. % in all samples.

### *4.2. Particle size distribution and Micro texture of quartz grains*

An important factor in carcinogenicity of minerals is the particle size; morphology and micro texture (Kasper-Zubillaga et al. 2005). The esophagus is potentially exposed to inhaled dust particles because dust deposited in the respiratory tract is ultimately cleared by the mucociliary apparatus and is swallowed (Yu et al. 2005). Particle size distribution curves of loess deposits from the study area are similar and sigmoidal in shape, showing a sharp increase in the silt fraction (approximately 80%) (Fig. 4). Silt-size particles, in turn, are dominated by the coarse silt fraction (35–45%). The sand fraction is less than 10%, mostly consisting of very fine sand (Fig. 4). The median particle size diameter in Gorgan area is 17 µm, while median particle sizes in Maravehtappeh and Dashlibroon areas are 28 and 31 µm, respectively (Table 2).

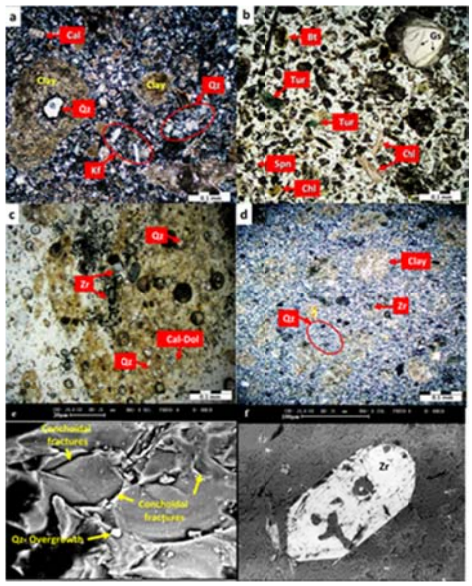

**Fig. 3.** Photomicrographs (a, b, c, d) of loess samples. (a) Loess sample from Gundar village (MAL 8) in Maravehtappeh region: crystals of quartz within clay coating, k feldspar, and carbonates. (b) Wide distribution of tourmaline + biotite + sphene + chlorite + gypsum (DL 20 sample). (c) A typical zircon (from Polyolia village; MAL 19) with tetragonal structure, metamicity rim and pyramidal surfaces at the end of the cross section (d) Assembly of quartz and zircon in the clay coatings in a loess samples from Gorgan area (OG 4). (E) Conchoidal fractures and crystalline nodules with overgrowth texture in quartz grains. (F) A typical crystal of altered zircon with tetragonal structure. Mineral abbreviations: Qz= quartz, Kf= K-feldspar, Zr= zircon, Dol= dolomite, Chl= chlorite, Tur = tourmaline, Gs= gypsum, Bt= biotite, Spn= sphene and Cal= calcite

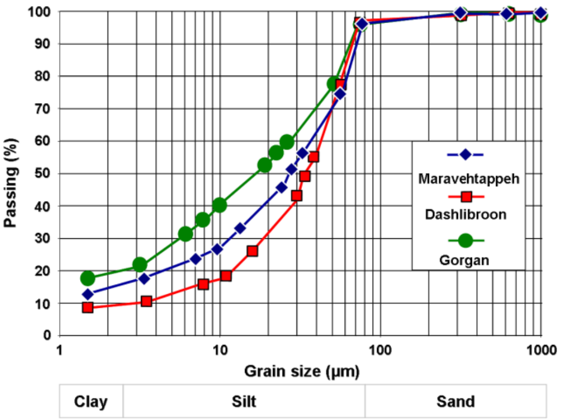


**Fig. 4.** Particle size distribution of Golestan loess deposits. After Asadi et al. (2012)

A gradual decrease is observed in grains size from east to west, and north to south. This means that with increasing distance from the source, particle uniformity and density increases. Soil density also increases, reflecting the direction of paleowinds.

Scanning electron microscopy of very fine grains revealed different shapes and micro textures in the loess deposits. Angular platy quartz grains with sharp edges are most common in the silty deposits; however, some concave faces with conchoidal fractures and crystalline nodes are also present (Fig. 3e). Generally, the surface textures of quartz grains in loess samples of the study area include micro fracture, and crescent, conchoidal, overgrowth, and abrasion textures. Zircon is the most abundant heavy mineral in loess samples. Zircon grains in Golestan loess deposits most commonly display as elongated doubly-terminated prismatic crystals. Indeed, needle-shaped acicular zircon crystals are common (Fig. 3f).

The possible association of $SiO_2$ and esophageal cancer was first described in 1968 among residents of Transkei in South Africa, where contamination of the diet by quartz or silica was thought to be partly responsible for the high incidence rate of esophageal cancer (Yu et al. 2007). Since then several studies have reported that fibrous $SiO_2$ present in certain plants could be linked to the high incidence of esophageal cancer in northeast Iran and northern China via food stuff. O'Neill et al. (1982) reported the high contamination with fibrous silica contaminant (e.g. Phalaris minor grass) in the diet of people living in the north-east of Iran (Turkaman Sahra), where esophageal cancer has a very high incidence rate. Some studies (Yassin et al. 2005; Yu et al. 2007) have revealed the probable link between $SiO_2$ exposure in flour and wheat samples with esophageal cancer. Based on the results of a case control study in Japan (Tsuda et al. 2001) concluded that the gastric and esophageal cancer were related to $SiO_2$ exposure, however, because of the small sample size they did not reach a statistically significant level. The estimated odds ratios (Turkaman Sahra) were higher for esophageal cancer patients (Besharat et al. 2007). Moreover, in Golestan province bread is made from whole wheat contaminated with fine $SiO_2$ particles. It has been hypothesized that damage inflicted by these particles may contribute to the etiology of esophageal cancer in the study area (Mosavi-Jarrahi and Mohagheghi, 2006). In China's high esophageal cancer area, fine mineral particles have been identified in the mucosa of the esophagus and a contribution to cellular growth has been postulated (O'Neill et al. 1982). In this study, the results show Median concentrations of $SiO_2$ in Gorgan, Maravehtappeh, and Dashlibroon regions are 42, 45.86 and 47.18 wt. %, respectively. Median concentration of total $SiO_2$ in loess samples displays an increasing trend from LC to the HC regions and is much higher in Dashlibroon and Maravehtappeh (Fig. 5).

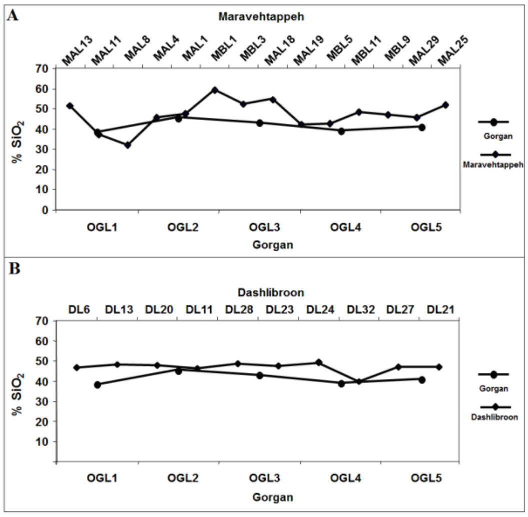


**Fig. 5.** Plot of $SiO_2$ concentration in the loess samples of Dashlibroon (A) and Maravehtappeh (B) in the Gorgan area

## 5. Conclusion

Previous studies indicated that various environmental exposures may be associated with an increased risk of esophageal cancer. The present study was performed to investigate the mineralogical properties of loess deposits and its probable link with high incidence rate of esophageal cancer in high risk Golestan province of Iran. The results from this study show a decreasing trend in Grain size and thickness of loess deposits from northeast to southwest. Determination of surface morphology of minerals with SEM also demonstrated that median concentrations of $SiO_2$

and heavy minerals increase from low cancer area (Gorgan) to high cancer (Maravehtappeh and Dashlibroon) areas. The results of this study are consistent with previous investigation indicating a certain association of quartz and some resistant heavy minerals like zircon with esophageal cancer. Hence, it may be suggested that $SiO_2$ probably plays a major role in the etiology of esophageal cancer in the Golestan province. The suggested mechanism that sharp needle-like quartz grains probably lodge in the esophagus wall and act as a nidus for bacteria and viruses and intensified by local habits such as drinking hot tea needs further investigation.

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